麻醉与监护论坛

Forum of Anesthesia and Monitoring

中华医学会麻醉学分会 Chinese Society of Anesthesiology

ISSN 1682-9018 04>

2011 Jul/Aug Vol 18 Issue 4

ISSN 1682-9018
CN(HK) NR 2650/910/02

第18卷 第4期

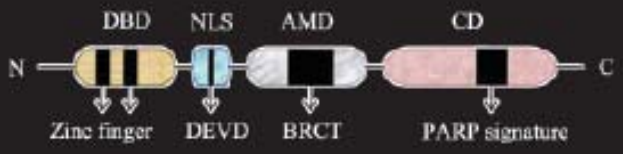
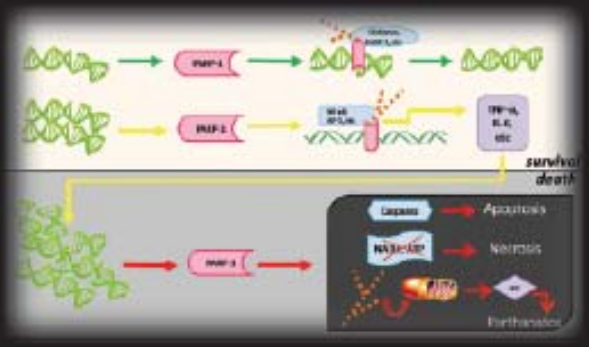


Figure 1. PARP-1 composed of four main domains of interest: ① the N-terminal DNA-binding domain (DBD) containing two zinc finger motifs essential for the recognition of DNA breaks, ②the nuclear localization signal domain (NLS) with DEVD (Asp-Glu-Val-Asp) motif which can be recognized and clove by caspases, ③ the automodification domain (AMD) comprising BRCA (breast cancer susceptibility gene) C-terminus-like (BRCT) motif that mediates protein-protein interaction and PARP-1 autoribosylation, and ④the C-terminal catalytic domain (CD) with a "PARP signature" motif necessary for its catalysis.

Figure 2. Poly (ADP-ribosyl)ation is a type of post-translational modifications mainly catalyzed by PARP-1. Basic features of poly (ADP-ribosyl)ation include: ①PARP-1 initiates the reaction by converting nicotinamide adenine dinucleotide (NAD+) into ADP-ribose, with the liberation of nicotinamide. ②PARP-1 catalyzes ADP-ribose to bind to amino acid residue on acceptor proteins. ③PARP-1 frequently cleaves NAD+ into nicotinamide and ADP-ribose, elongates the latter to form a poly (ADP-ribose) polymer, and accomplishes the poly (ADP-ribosyl)ation of target proteins. ④PARG eliminates poly (ADP-ribosyl)ation of acceptor proteins, producing free ADP-ribose. These processes consume NAD+ irreversibly.



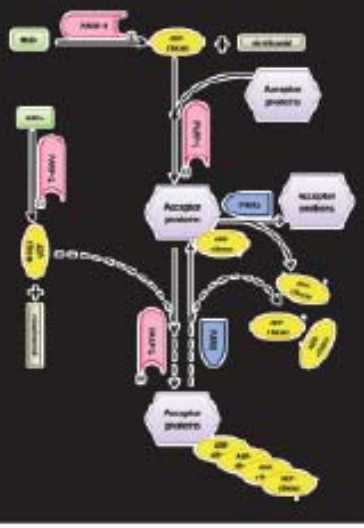


Figure 3.Based on the evidence given in this review, we have tried to propose a brief and simplified model in which PARP-1 functions as a physiological or pathological protagonist. ①The physiological function of PARP-1 is to modify histones, PARP itself and other nuclear proteins to repair DNA damage and maintain genomic integrity (green arrow under pink background). ②Following severe DNA damage, overactivation of PARP-1promotes the transcriptional regulation, most notably the NF-κB and AP-1driven expression of a large number of proinflammatory factors (e.g. TNF-α, IL-6) (yellow arrow under pink background). These inflammatory mediators are critical to aggravate tissue injury, and then stimulate PARP-1, resulting a vicious cycle (yellow arrow under grey background). ③ Lethal insult can induce massive PARP-1 activation, and ultimately cell death (red arrow under grey background). In apoptosis, early PARP-1 activation may assist the caspases which clove PARP-1 to inactive fragments and allows cells with irreparable damage to be eliminated in a safe way. However, drastic activation of PARP-1 depletes substrate NAD+ and consequently ATP, inducing necrosis. Moreover, the rapid activation of PARP-1 and accumulation of PAR polymer can mediate the translocation of AIF from the mitochondria to nucleus, and then cause a distinctive PARP-1-dependent parthanatos.

In this respect, PARP-1 would be a potential target for therapeutic intervention in clinical medicine in the future, and promising pharmacological inhibitors of PARP-1 could exert a protective role towards various pulmonary inflammatory disorders.

Figure related to "Poly (ADP-ribose) polymerase-1 and inflammatory lung injury" by Bu-wei Yu, pp.252.

宝莱特
BIOLIGHT
Developing with us 我们一起成长

宝莱特A系列高端插件式监护仪全线精彩上市！

A系列产品注册号:国食药监械（准）字2011第3210153号

AnyView A6　AnyView A5　AnyView A3　AnyView A2

120转运宝

国内首创、国际领先

AnyView A系列插件式监护仪

- 可升级高端监护参数：灌注指数、灌注变异指数、高铁血红蛋白、碳氧血红蛋白、总血红蛋白、总血氧含量。

原装进口，来自英国的经典之作，
集安全、稳定、信息监测一体的全能麻醉工作平台

PRIMA SP系列(101/102)

全球销量第一的麻醉剂蒸发罐

宝莱特公司签约鞭龙麻醉机、蒸发罐
中国大陆地区总代理

欢迎访问：www.blt.com.cn
客户呼叫热线：400 881 8233

GOLDWAY

粤医械广审（文）第2011040061号

深圳市金科威实业有限公司

卓越的重症麻醉临床监护解决方案

- 良好抗干扰的能力
- 专业的麻醉监测参数
- 高性能的有创监测参数
- 保证围手术期不间断监护

G60
病人监护仪

UT6000C
病人监护仪

G40
病人监护仪

UT4000Fpro
病人监护仪

UT4800
中央监护仪

Goldway is a Philips company

PHILIPS

FORUM OF ANESTHESIA
《麻醉与监护论坛》
AND MONITORING

出版者：香港醫療信息有限公司
主　辦：中華醫學會麻醉學分會、香港醫療信息有限公司
编　輯：《麻醉與監護論壇》編委會、編輯部

编委会办公及投稿地址：
上海交通大学医学院附属瑞金医院麻醉科
地址：上海市茂名南路205号瑞金大厦1411室　邮编：200025
电话：021-64737666　传真：021-64737002
邮箱：lyelectron@yahoo.com.cn 或 famttyy@sina.com

定价：港币五十元
本刊已向中华人民共和国香港特别行政区政府新闻处根据香港法例第268章(本地报刊注册条例)登记注册。
2011 Jul/Aug Vol.18 Issue 4 第18卷 第4期 创刊于1993年

PALL Medical

颇尔湿热交换呼吸通路过滤器

全系列高端机械式疏水过滤器

安全如此重要，请选用最好的滤器

同时滤除

气体

液体

途径传播的细菌和病毒

保护病人和医护工作者

滤器经过验证可滤除结核杆菌，

葡萄球菌，HCV，HIV等。

北京办事处
北京市经济技术开发区宏大南路12号
电话：010-67802288
传真：010-67802238
邮编：100176
网址：http://www.pall.com

广州办事处
广州滨江中路308号 广州海运大厦16K室
电话：020-84108668
传真：020-84102031
邮编：510220

上海办事处
上海市张江高科技园区哈雷路917弄
福缘科苑3号楼
电话：021-61695656
传真：021-61695606
邮编：201203

Pall 公司 - 全球过滤技术领导者

颇尔过滤器（北京）有限公司

FORUM OF ANESTHESIA AND MONITORING

Publisher: Medical Information Limited
Sponsors: Chinese Society of Anesthesiology, Medical Information Limited
Editing: Editorial Board and Editorial Office of Forum of Anesthesia and Monitoring

Editorial Board in 2011

Editorial Board Office Address:

Department of Anesthesiology,Ruijin Hospital, Shanghai Jiao Tong University School of Medicine

Address: Room 1411，Shanghai Ruijin Building，No.205 Maoming South Road，200025
Tel: 021-64737666 Fax: 021-64737002
E-mail: lyelectron@yahoo.com.cn, famttyy@sina.com

Headquarter: Hong Kong
Rm,2104,21/F,Admiralty Center Tower 1,
NO.18 Harcourt Rd., Hong kong
Tel: (852)35693099 Fax: (852)28654177
E-mail: fam_advertising@medicalinfo.cc

Singarpore(Representative Office)
Singarpore 9 Temasek Boulevard,
Suntec Tower 2 #33-02, Singapore 038989
Tel: (65)68269931 Fax: (65)68269897
E-mail: fam_Singapore@medicalinfo.cc

Shanghai(Lian Luo Chu)
3F,No.1 Building, Xinzhuang Industrial Zone,
No.3266 Jindu Rd.,Shanghai, 201108
Tel: 021-54830451 54830497
Fax: 021-54429643
E-mail: fam@medicalinfo.cc

Xiamen(Lian Luo Chu)
Rm.102, No.143 Tiyu Rd., Xiamen 361000
Tel: (0597)2102095 Fax: (0597)2102095
E-mail: fam_cu@medicalinfo.cc

Forum of Anesthesia and Monitoring (FAM), bimonthly, is a technical publication published by Medical Information Limited, which is distributed to domestic readers,all copies are free of charge except Hongkong,Macau,Taiwan and overseas. FAM is not responsible for views expressed, nor does it guarantee, directly or indirectly, the quality or efficacy of products or services described in advertisements or the product information section of magazine.

Printer: Network Telecom Information Limited, Printing Division, Hong kong
Address: Rm,2104,21/F,Admiralty Center Tower 1, NO.18 Harcourt Rd., Hong kong

Pricing:HK$50
International Standard Serial Number: ISSN 1682-9018
Periodical(Hong kong)Number Registered: CN(HK)-NR 2650/910/02
Forum of Anesthesia and Monitoring magazine had been registered to Hong Kong Special Admin-istrative Region Government,People's Republic of China,in accordance with the Registration of Local Newspapers(Periodical) Ordinance, Cap.268 and its subsidiary legislation.
2011 Jul/Aug Vol.18 Issue 4 Commenced publication in 1993.


耐乐品®
(盐酸罗哌卡因注射液)
盐酸罗哌卡因注射液
原创
品
牌
品
质超群
• 第一个纯左旋长效酰胺类局麻药[1]
• 无菌聚丙烯安瓿，效期长达三年[1]
• 原创品牌，瑞典原装进口，品质值得信赖[1]
耐乐品®简明处方资料[Naropin_V(2)]
AstraZeneca
阿斯利康
为生命护航

麻醉与监护论坛

Forum of Anesthesia and Monitoring

中华医学会麻醉学分会

ISSN 1682-9018

2011 Jul/Aug Vol.18 Issue 4

ISSN 1682-9018
CN(HK)-NR 2650/910/02

第18卷 第4期

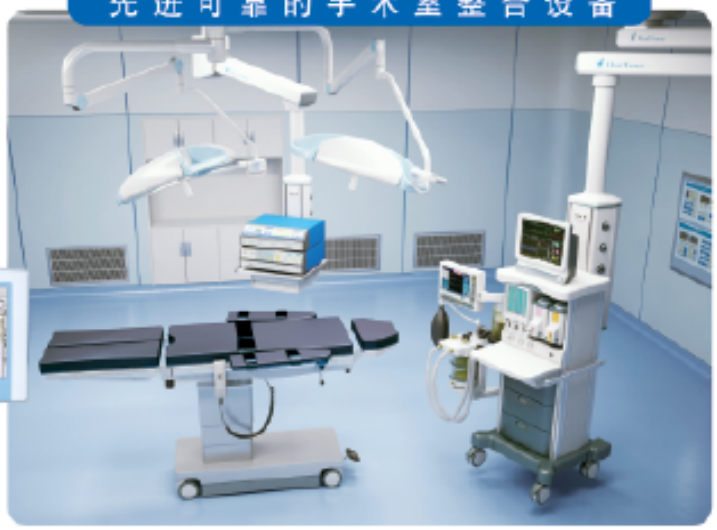
目 次

力 康
Heal Force

Heal Force Anaesthesia Series 力康麻醉系列

精确监控 驭驾从容

先进可靠的手术室整合设备



Anaeston麻醉工作站

- 紧凑型设计，精确控制潮气量，动态潮气量补偿
- 多种呼吸模式，经典欧美达呼吸回路模块
- HF高精度蒸发罐，兼容欧美达Tec5、7罐
- 配合多参数监护及CSI监测模块成为强大工作站
- 可配合麻醉全程信息管理系统

ANAESTON5000 麻醉机

麻醉机

钠石灰

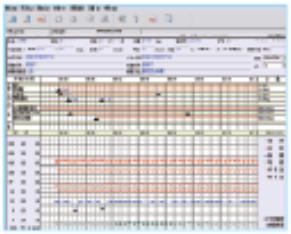
蒸发罐

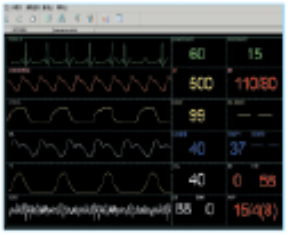
CSI意识(麻醉)深度监护仪

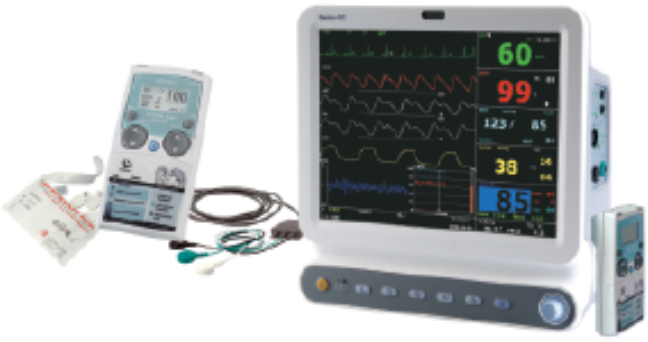
- 首创手持移动监测意识（麻醉）深度设备
- 麻醉中意识水平，肌松状态直观显示
- 麻醉药物经济化使用控制
- 提升麻醉机和蒸发罐的效能
- 可同步无线传输至力康麻醉机，监护仪

TrackAO 手术麻醉管理软件系统

- 提供完整的麻醉科电子病历系统
- 手术全流程管理，自动生成麻醉记录单
- 能直接采集多厂家、多型号的手术监护等医疗设备数据
- 能自由选择监测数据种类同屏显示
- 强大的科研查询及病例分析功能







力 康 —— 让生命更健康

Heal Force leads you to healthier life

向全球提供更优性价比的整体医疗及实验室设备

Provide the world with cost effective integrated medical and laboratory equipment

力康集团|力新仪器(上海)有限公司
Nison Instrument (Shanghai) Limited
全国客户服务中心电话：800-820-6044
了解产品详情,敬请登陆：www.healforce.com

P/N:AD-NISON-MZIT-20110124

FORUM OF ANESTHESIA AND MONITORING

Publisher: Medical Information Limited
Sponsors: Chinese Society of Anesthesiology, Medical Information Limited
Editing: Editorial Board and Editorial Office of Forum of Anesthesia and Monitoring

2011 Jul/Aug Vol.18 Issue 4

ISSN 1682-9018
04>

Contents


喜保福宁 SEVOFLURANE
七氟烷·SEVOFLURANE
全身吸入麻醉剂
一吸呵成 化繁为简
昨天，今天，明天，雅培麻醉一路陪伴
[注意事项]：详见说明书
Abbott
Anesthesia
雅培麻醉

Instructions for Authors

Types of Papers

Eight types of articles are published.

1.Clinical Investigations

2.Laboratory Investigations

3.Review Articles

4.Case Reports/Case Discussion

5.Technical Communications

6.Clinical Experience

7.Letters to the editors

8.Others (including continuing education, subject construction, comprehensive information, etc.)

Maximum Word Allowance

1.Clinical Investigations: 3000 words (excluding Abstract)

2.Laboratory Investigations: 3000 words (excluding Abstract)

3.Review Articles: 4000 words

4.Case Reports/Case Discussion: 800 words

5.Technical Communications: 1500 words

6.Special Articles: 2000 words

7.Letters to the editors: 200 words

Arrangement of Articles

Arrange all articles in the following order.

1.Title page

2.Abstract and Key Words (not required for all article types)

3.Body Text (Introduction, Materials and Methods, Results, Discussion)

4.References

5.Tables (each table should be a separate file)

6.Figures (each figure should be a separate file) and Figure Legends

Detailed Information

Title Page (Page 1). It includes:

1.Title

2.First name and surname of each author with his or her highest academic degree (M.D., Ph.D., etc.) and academic rank (Professor, Associate Professor, etc.)

3.Mailing address, phone, fax numbers, e-mail address, the department, institution, city, state and country of the corresponding author

4.Individuals or organizations to be acknowledged. Provide complete name, degrees, academic rank, department, institution, city, state and country

5.Abstract and Key Words (new page). Abstract contains for paragraphs of Background, Methods, Results and Conclusions, with the words less than 250 (except for Review Articles and Case Reports)

Text. The body of the manuscript should typically be divided into four parts (except for Case Reports):

1.Introduction (new page). This should rarely exceed one paragraph in length

2.Materials and Methods (new page). A subsection entitled “Statistical Analysis” should appear at the end of the section when appropriate

3.Results (new page)

4.Discussion (new page)

References (new page). Number references in sequence in they appear in the text. Original articles should rarely have more than 25 items. For a review article, up to 35 items are acceptable. Case Reports rarely need more than 10 items. Using the following reference formats:

1.Journal: Carli F, Mayo N, Klubien K, Schricker T, Trudel J, Belliveau P: Epidural analgesia enhances functional exercise capacity and health-related quality of life after colonic surgery: Results of a randomized trial. ANESTHESIOLOGY 2002; 97: 540-9

2.Book: Barash PG, Cullen BF, Stoelting RK: Clinical Anesthesia, 3rd edition. Philadelphia, Lippincott-Raven, 1997, pp23-4

3.Chapter: Blitt C: Monitoring the anesthetized patient, Clinical Anesthesia, 3rd edition. Edited by Barash PG. Cullen BF, Stoelting RK. Philadelphia, Lippincot t-Raven, 1997, pp563-85

Tables. Number tables consecutively in order of appearance (Table 1, etc.). Each Table should be submitted as a separate file. Each Table must have a title and a caption.

Figures and Figure Legends.

1.Each figure should be submitted as a separate file

2.Figures must be clearly labeled and cited in the consecutive numeric order

3.Scan precision≥300dpi, size≥6×8cm

4.Written permission must be obtained from the author and publisher if any figure or table from a previously published document is used

5.Supply a legend for each figure

Additional Information

Units of Measurement.

1.If two items are present, please use mol/l, mg/ml, mg/kg, etc.

2.If more than two items are present, negative exponents should be used (i.e., ml • kg^{-1} • min^{-1} instead of ml/kg/min)

3.The units for pressers are mmHg or cmH_2O

Abbreviations. Define all abbreviations except those approved by the International System of Units. Don’t create new abbreviations for drugs, procedures, experimental groups, etc.

Drug Names and Equipment. Use generic names. If a brand name is used, insert it in parentheses after the generic name. Provide manufacturer’s name, city, state, and country.

Statistics. Detailed statistical methodology must be reported. Describe randomization procedures. Describe the specific tests used to examine each part of the results: do not simply list a series of tests. Variability should be expressed either as median ± range (or percentiles) for nonparametric data or mean ± standard deviation for normally distributed data.

Note

All manuscripts are submitted in electric format via computer disc and mailed to the Editorial Office along with the typed format: Room 1411,Shanghai Ruijin Building,No.205 Maoming South Road,200025 E-mail:lyelectron@yahoo.com.cn, famttyy@sina.com

1.An abstract in chinese is necessary

2.Document files should be prepared in “ custom paper ” size (“A-4”)

3.Manuscripts should be double or triple spaced to allow room for editing

4.Receipt of submitted manuscripts will be acknowledged as soon as possible

5.Authors should keep copies. No submitted materials will be returned to the authors

SMIC

上海医疗器械股份有限公司

麻醉机系列产品

“益生”牌手术室设备系列

（上海医疗设备厂）

营销总部地址：上海市和田路300号 邮编：200070

电话：021-51035006 传真：021-56321021 网址：www.smicc.com E-mail:sc@smicc.com

Poly (ADP-ribose) Polymerase-1 and Inflammatory Lung Injury

*Li-Jie Jia, M.S.† ; Han Lu, Ph.D. ‖ ; Fu-Jun Zhang, M.D., Ph.D.‡ ; Bu-Wei Yu, M.D., Ph.D.**

† Graduate Student
‖ Resident
‡ Associate Professor
Deputy Director
Department of Anesthesiology, Ruijin Hospital, Shanghai JiaoTong University School of Medicine, 197 RuiJin Er Road, Shanghai 200025, P.R. China

Abstract

Poly (ADP-ribose) polymerase-1 (PARP-1) is an enzyme catalyzing synthesis of poly (ADP-ribose) (PAR) polymer and poly (ADP-ribosyl)ation of the target protein. Poly (ADP-ribosyl)ation, a type of protein post-translational modifications, plays a significant role in physiological and pathological conditions including inflammatory pulmonary injury. PARP-1 could be stimulated by DNA breaks, and contributes to DNA repair and maintenance of genomic integrity. However, in pulmonary inflammatory disorders, overactivation of PARP-1 facilitates the transcription of proinflammatory genes and promotes inflammatory responses, resulting in a vicious cycle. Furthermore, excessive activation of PARP-1induced by lethal damage causes cell death, such as necrosis and a distinctive PARP-1-dependent parthanatos, aggravating inflammatory responses and leading to systemic dysfunctions. The remarkable beneficial effects of inhibition of PARP-1 have been detected under inflammatory situations, in vitro and in vivo. In this respect, PARP-1 would be a potential target for therapeutic intervention in clinical medicine in the future, and promising pharmacological inhibitors of PARP-1 could exert a protective role towards various pulmonary inflammatory disorders.

Key words:poly (ADP-ribose) polymerase-1, poly (ADP-ribosyl)ation, inflammation, lung injury, inhibitor, post-translation modification

Corresponding Author: Bu-wei Yu, E-mail:yubuwei@yahoo.com.cn

Introduction

Protein post-translational modifications including phosphorylation , acetylation, methylation , ubiquitination, sumoylation and poly (ADP-ribosyl)ation are vital cellular processes required for signaling transduction and cell survival [1-5]. Poly (ADP-ribosyl)ation is the post-translational modification mainly for nuclear proteins, and involves the production of PAR polymer and its binding to acceptor proteins [5]. This post-translational regulation is mostly catalyzed by poly (ADP-ribose) polymerase (PARP) enzymes. PARP-1 is the canonical representative of PARP superfamily as accounting for approximate 85% of the total cellular PARP activity [6]. Initially identified as an enzyme that performs central roles in repair of damaged DNA, PARP-1 can be activated by DNA strand nicks and breaks and participates in maintenance of genomic integrity [7,8]. Additional functions of PARP-1 have now been demonstrated in biochemical and molecular studies [9,10]. Apart from its role in repairing DNA damage, PARP-1 is also implicated in multiple cellular processes [11,12], and regulates protein expression at transcriptional level [13], cell death via necrosis, apoptosis or other forms [14,15], cellular replication and differentiation [16]. Therefore, PARP-1 is well considered to participate in various physiological and pathophysiological conditions, such as regulation of astrocyte and microglial function [17], aging [18], vasoconstriction [19], cardiac remodeling [20], septic shock , as well as inflammation [21,22].

Inflammation is a part of the complex biological response to harmful stimulation, and is a protective attempt to remove the stimuli and initiate the healing process. However, inflammatory response is a sword with two blades. Massive inflammatory responses exacerbate tissue injury and cause local or systemic disease, especially in disordered situations. Recently, it has been recognized by authorities that the inflammatory lung injury is common all around the world, and is a major cause of death among the young, the old, and the chronically ill [23,24]. People who are hospitalized for any reason are also at high risk for lung infection. In more serious conditions, despite marked therapeutic treatment progresses, the mortality rate of acute lung injury (ALI) or, acute respiratory distress syndrome (ARDS) associated with severe trauma remains high [25]. To find out the mechanisms of inflammatory lung injury is an

important challenge, and this review will focus on the role performed by PARP-1.

PARP-1 and poly (ADP-ribosyl)ation

PARP-1, also known as poly (ADP-ribose) synthase-1 or NAD+

ADP-ribosyltransferase-1, is an abundant nuclear enzyme present in eukaryotes with about 0.5~2×106 copies in the cell [26]. This monomeric enzyme is a 113 kDa protein composed of four main domains of interest [5,27]: the N-terminal DNA-binding domain (DBD) containing two zinc finger motifs essential for the recognition of DNA breaks, the nuclear localization signal domain (NLS) with DEVD (Asp-Glu-Val-Asp) motif which can be recognized and cleaved by Caspases, the automodification domain (AMD) comprising BRCA (breast cancer susceptibility gene) C-terminus-like (BRCT) motif that mediates protein-protein interaction and PARP-1 autoribosylation, and the C-terminal catalytic domain (CD) with a "PARP signature" motif necessary for its catalysis (Figure 1).

Poly (ADP-ribosyl)ation is a type of post-translational modification mainly catalyzed by PARP-1. PARP-1 initiates this reaction by converting donor nicotinamide adenine dinucleotide (NAD+) molecules into ADP-ribose, with the liberation of nicotinamide. Then, PARP-1 catalyzes ADP-ribose to bind to glutamate, and less commonly to aspartate or lysine residues on a number of nuclear proteins. Subsequently, PARP-1 frequently cleaves NAD+ into nicotinamide and ADP-ribose, elongates the latter to form a PAR polymer linked by non-covalent bonds and accomplishes the poly (ADP-ribosyl)ation of target proteins [5]. The PAR chains can be linear up to approximate 200 units or branched every 20-50 units [28]. In addition, poly (ADP-ribosyl)ation is a fast dynamic process indicated by short in half life of the polymer, and the enzyme poly (ADP-ribose) glycohydrolase (PARG) plays a major role in its turnover to free ADP-ribose [29]. Although poly (ADP-ribosyl)ation could be eliminated by PARG, it consumes NAD+ irreversibly (Figure 2).

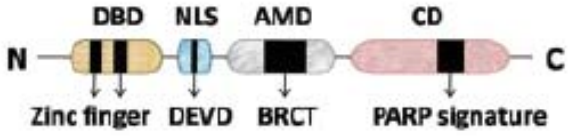


Figure 1: PARP-1 composed of four main domains of interest: ①the N-terminal DNA-binding domain (DBD) containing two zinc finger motifs essential for the recognition of DNA breaks, ②the nuclear localization signal domain (NLS) with DEVD (Asp-Glu-Val-Asp) motif which can be recognized and clove by caspases, ③the automodification domain (AMD) comprising BRCA (breast cancer susceptibility gene) C-terminus-like (BRCT) motif that mediates protein-protein interaction and PARP-1 autoribosylation, and ④the C-terminal catalytic domain (CD) with a "PARP signature" motif necessary for its catalysis.

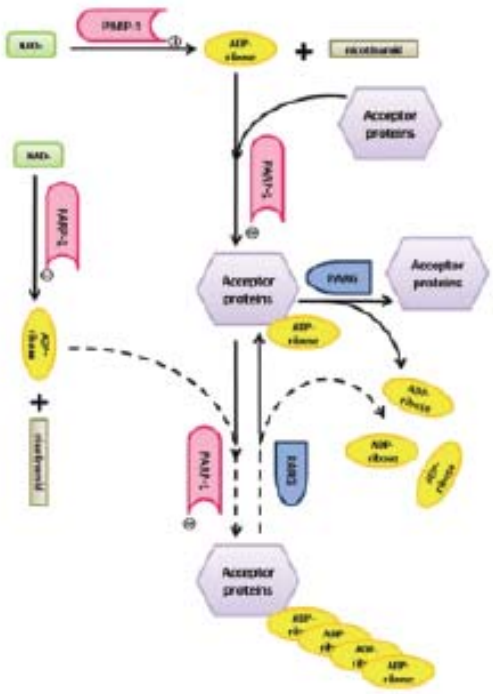


Figure 2: Poly (ADP-ribosyl)ation is a type of post-translational modifications mainly catalyzed by PARP-1. Basic features of poly (ADP-ribosyl)ation include: ①PARP-1 initiates the reaction by converting nicotinamide adenine dinucleotide (NAD+) into ADP-ribose, with the liberation of nicotinamide. ②PARP-1 catalyzes ADP-ribose to bind to amino acid residue on acceptor proteins. ③PARP-1 frequently cleaves NAD+ into nicotinamide and ADP-ribose, elongates the latter to form a poly (ADP-ribose) polymer, and accomplishes the poly (ADP-ribosyl)ation of target proteins. ④PARG eliminates poly (ADP-ribosyl)ation of acceptor proteins, producing free ADP-ribose. These processes consume NAD+ irreversibly.

Functions of PARP-1

Role in repairing DNA nicks and breaks after stress

PARP-1 acts as a survival factor in DNA damage. The hypothesis that PARP-1 may relate to repair of DNA was evolved with the identification of its character of binding DNA directly. The appearance of single or double strands breaks in DNA molecules contribute to the activation of PARP-1. And PARP-1 also involves in base excision repair pathway [30-33]. Upon binding to injury DNA through the second zinc finger domain, PARP-1 functions as dimers and catalyzes the poly (ADP-ribosyl)ation of the neighboring PARP-1 molecule (automodificaton) and some nuclear proteins like DNA polymerase, topoisomerase, DNA ligase-2, endonucleases and histones [7,12,34-39]. The high negative charge of PAR polymer dramatically affects the function of target proteins, and causes the histones to be electrostatically repelled from binding to DNA, disrupting the tightly condensed nucleosomal structure [40]. This process is not only necessary for DNA repair but also chromatin remodeling and transcriptional regulation. Moreover, histones have high-affinity PAR polymer binding sites that draw them out of nearby chromatin to bind to the polymer cloud around automodified PARP-1 molecules attached to strand breaks, loosening up chromatin [41]. In addition, during the repair process, an anionic PAR polymer around the nicks is also thought to repel other free ends of DNA, preventing dangerous translation events [42].

Despite the positive role in sensing and repairing DNA damage, PARP-1 participates in promoting cell death in the presence of extensive DNA injury [43]. Necrosis is determined by the severe DNA-damaging stimuli. Intensive DNA injury induces overactivation of PARP-1, depleting cellular NAD+ pools [44,45]. NAD+ is an essential cofactor in energy metabolism and the synthesis of ATP. And the balance of redox potential directly depends on NAD+ levels in cells. Thereby a decrease in the cellular stores of NAD+ reduces production of ATP through oxidative phosphorylation [44,45]. Thus, aberrant overactivation of PARP-1 will cause necrotic cell death under extreme conditions, as more energy would be invested in repairing damage than is feasible [46,47]. Necrosis is triggered by severe stimuli whereas apoptosis is initiated by a mild one. It is well established that an outstanding feature of apoptosis is the dependence on ATP for ordered degradation of cellular structures in the last phase, during which Caspases-3, 6, and 7 digest substrate proteins and dismantle the cell through the formation of apoptotic bodies. For the correct apoptotic machinery going on, it is need to prevent a massive NAD+ depletion by inactivating PARP-1. Interestingly, PARP-1 is one of the substrates of Caspases, and Caspase-3 and Caspase-7 recognize the DEVD motif in the NLS domain of PARP-1and cleave it, generating two inactive fragments, ~89KDa and ~24KDa [48-52]. This performance saves cellular NAD+, preserves energy required to carry on apoptotic process, and finally allows cell with irreparable DNA breakage to be eliminated in a safe way [53,54].

Generally, in physiological conditions, PARP-1 activated by genotoxic stimuli facilitates DNA repair by catalyzing modification of DNA-dependent proteins, leading to cellular resistance to stresses. Under pathological conditions, more severe DNA damage induces aberrant overactivation of PARP-1. As the competence of Caspases, the main executor enzymes of the apoptotic process, PARP-1 is substantially cleaved to inactivate fragments, leading to apoptosis. The third route is induced by massive stress. The lethal activation of PARP-1 depletes cellular stores of NAD+ and consequently ATP, and induces necrosis in the end. Therefore, the changeable PARP-1 activity could play double roles, as represented in the Yin-Yang paradigm [55].

Role in regulating pro-inflammatory protein expression at transcriptional level

Substrates of PARP-1 enzymatic activity includes PARP-1 itself and a variety of transcriptional factors that interact with PARP-1in nucleus, and accordingly, poly (ADP-ribosyl)ation participates in regulation of gene expression. Normally, PARP-1 itself acts as a down-regulator in transcription of its own gene by binding to the DNA secondary structure (hairpins) in the promoter region [56,57]. Soldatenkov et al demonstrated that auto-modification of PARP-1 disturbed its binding to hairpin motifs due to the formation of highly anionic long-branched PAR polymer [56]. Therefore, auto-modification of PARP-1 increases its own expression by releasing the negative effect on the promoter, and this regenerative feedback boosts efficiency of PARP-1when activated.

Furthermore, several lines of evidences suggest that PARP-1 functions as a specific promoter cofactor

for nuclear factor-kappa B (NF-ΚB) , which is one of the main pro-inflammatory transcription factors [58-64]. Once modified by PARP-1, NF-ΚB is assisted to interact with other nuclear proteins, bind DNA and activate the transcription of several genes implicated in different processes, uppermost inflammatory response. There are lots of inflammatory cytokines driven by NF-ΚB, and their expressions can be greatly up regulated by the formation of a PARP-1/ PAR/NF-ΚB complex, most notably tumor necrosis factor-α (TNF-α), interleukin-6(IL-6), intercellular adhesion molecules (ICAM) , IL-1, macrophage inflammatory protein-1(MIP-1), MIP-2, P-selectin [61,65-73], as well as other pro-inflammatory products like inducible nitric oxide synthase (iNOS) that has been linked with the development of inflammatory cell injury [64,74-76]. However presently there is no consensus on the literature regarding the modulation of NF-ΚB mediated transcription whether depends on the physical interaction between PARP-1, PAR polymer and subunits of NF-ΚB, or alternatively on the automodification of PARP-1 itself [77,78]. Moreover, the poly (ADP-ribosyl)ation of histones leads to looseness of chromatin and also enhances the accessibility of genes for the transcription machinery and thus promotes their transcriptions [5].

PARP-1 increases inflammation-related gene expressions at transcriptional level also by modifying other pro-inflammatory transcription factors, including activator protein-1 (AP-1), AP-2, signal transducer and activator of transcription-1 (STAT-1) , hypoxia-inducible factors –α (HIF-α) and peroxisome proliferator activated receptor γ (PPARγ) [4,79-81]. Stress generates DNA strand breaks, then potentiates PARP-1, and sequently promotes transactivation of kinds of transcription factors by poly (ADP-ribosyl)ation modification, resulting in greater expressions of the downstream products, which attract and activate immune cells, and lead to significant amplification of the inflammatory response. This vicious cycle contributes to the systemic inflammatory response syndrome (SIRS) and circulatory shock, if without control.

Role in a new form of cell death: Parthanatos

Recently, a solid body of literature have supported a proposal that excessive activation of PARP-1 induces a distinct cell-death program [14]. Yu etc designated this PARP-1-dependant cell death Parthanatos after Thanatos, which is the personification of death instinct in Greek Mythology, to distinguish from other forms of cell demise [82]. The first studies reported parthanatos was caused by energy failure in cells, but more recently it has been found that PAR polymer mediated apoptosis-inducing factor (AIF) release is the commitment point for parthanatos [15,82-86]. Evidences reveal that when PARP-1 overactivation occurs, PAR polymer is synthesized hand over fist in the nucleus and released into the cytoplasm, and appears to be a pro-death signaling molecule that functions in the cross talk between mitochondria and nuclear, to stimulate mitochondrial AIF release and translocation to nucleus [82-84,87]. AIF, a mitochondrial oxidoreductase, exists through the mitochondrial membrane. When it enters the cytosol, and finally ends up in the cell nucleus, this factor will trigger chromatin condensation and DNA degradation in order to prepare for cell death [88]. The PAR polymer level is increased up to 500-fold when DNA strand breaks, then lauches parthanatic process [5]. PARG, an enzyme to degrade PAR polymer, inhibits PARP-1-dependent AIF release and is capable of preventing parthanatos [89]. Although Caspases could be activated in the late period of parthanatos, the process is not affected by broad-spectrum Caspases inhibitors [89]. However, the specific mechanism by which PAR polymer leads to AIF release is still unknown [84]. PAR polymer could bind to some proteins in mitochondria, and then the poly (ADP-ribosyl)ation of these acceptors triggers AIF release from mitochondria. Alternatively, due to its highly charged nature, PAR could conceivably depolarize mitochondria, leading to permeability transition and subsequent AIF release [82].

From what aforementioned, the distinctive biochemical characteristics of parthanatos include the rapid activation of PARP-1, accumulation of PAR in the early stage, and migration of AIF from mitochondria to nuclear. Although parthanatos shares some morphological features in common with apoptosis and necrosis, there are entitative differences between them. Comparing with apoptosis, necrosis, and autophagy, parthanatos does not cause apoptotic bodies, induce cell degradation, and form bubble structure, respectively [14]. Thus, parthanatic cell death is considered to be a novel manner, and it can be speculated that elucidating mechanisms and interfering with parthanatos might offer innovative therapeutic approaches

for the treatment of cellular injury.

PARP-1 and inflammatory lung injury

PARP-1 in the inflammatory conditions of lung

Inflammation occurs as a defensive response that contributes to profound physiological adaption for removing the pathogenic stimuli. However, it is well established that this two-blade sword does much harm to the body as well (e.g. cell injury and death). There are studies supporting protection of PARP-1in stress. Pagano. A, etc reported an essential role of PARP-1 in the control of cell repair and tissue remodeling after hyperoxia-induced lung injury [90], and Piskunova,T.S. etc found deficiency in PARP-1increases lung adenocarcinomas [91].

Nevertheless, an amount of evidences have verified that hyperactivation of PARP-1 plays a deleterious role in the development of pulmonary inflammatory process for its specific function. Compressing a large body of literature into a short space, PARP-1 is confirmed to be aberrantly activated in inflammatory conditions, and then intensifies the vicious cycle in inflammatory responses through regulation of potent signaling cascades, enhancement of expression of inflammatory mediators and the paradigm "PARP activation-cell death" or even necrosis. These research models include asthma challenged by ovalbumin [67,92-94], pneumonia and other airway injuries induced by carrageenan [95-99], zymosan [72], bleomycin [100], Pseudomonas aeruginosa [101,102] and lipopolysaccharide (LPS) [71,103]. ALI/ARDS is the most severe condition in pulmonary injury characterized by dyspnea, progressive refractory hypoxia and high mortality. PARP-1 is recognized to be concerned with ALI resulting from septic shock in a murine cecal ligation and puncture model [104], organ damage after thermal injury [105], acute pancreatitis [64,68] as well as lung injury after hypothermic cardiac arrest and extracorporal circulation[106]. In addition, Je Hyeong Kim etc reported for the first time that overactivation of PARP-1 plays an important role in the ventilator-induced lung injury caused by two-hour mechanical ventilation in normal mice lung [61]. Besides, it is also necessary to be mentioned that increased activity of PARP-1 has been observed in peripheral blood mononuclear cells in patients with chronic obstructive pulmonary disease (COPD) [65]. It indicates that a local disorder such as COPD is sufficient to lead to activation of PARP-1 in circulating leukocytes, and then, PARP-1 activation in circulation might mediate certain systemic effects of local disease and remote organ injury.

Given the underlying mechanisms by which PARP-1promotes pulmonary inflammatory response, it is be speculated that intervention of PARP-1 could represent a novel therapeutic strategy to attenuate cellular injury and to limit the inflammatory processes that characterize many pulmonary disorders [107].

Effect of inhibition of PARP-1

Over recent decades, a multitude of direct and

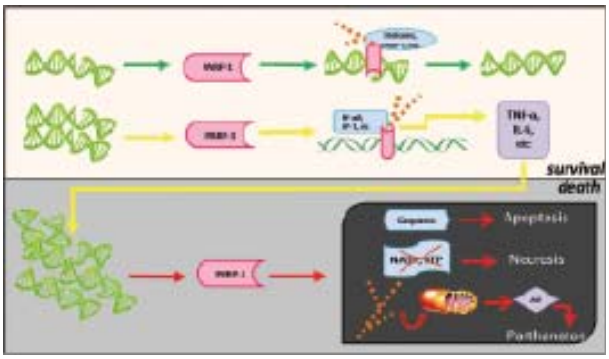


Figure 3: Based on the evidence given in this review, we have tried to propose a brief and simplified model in which PARP-1 functions as a physiological or pathological protagonist. ①The physiological function of PARP-1 is to modify histones, PARP itself and other nuclear proteins to repair DNA damage and maintain genomic integrity (green arrow under pink background). ②Following severe DNA damage, overactivation of PARP-1promotes the transcriptional regulation, most notably the NF-κB and AP-1driven expression of a large number of proinflammatory factors (e.g. TNF-α, IL-6) (yellow arrow under pink background). These inflammatory mediators are critical to aggravate tissue injury, and then stimulate PARP-1, resulting a vicious cycle (yellow arrow under grey background). ③Lethal insult can induce massive PARP-1 activation, and ultimately cell death (red arrow under grey background). In apoptosis, early PARP-1 activation may assist the caspases which clove PARP-1 to inactive fragments and allows cells with irreparable damage to be eliminated in a safe way. However, drastic activation of PARP-1 depletes substrate NAD+ and consequently ATP, inducing necrosis. Moreover, the rapid activation of PARP-1 and accumulation of PAR polymer can mediate the translocation of AIF from the mitochondria to nucleus, and then cause a distinctive PARP-1-dependent parthanatos.

circumstantial studies have suggested that pharmacological inhibition or genetic ablation of PARP-1provides remarkable protection in lung injury characterized predominantly by inflammation, such as asthma, airway inflammatory injury, ALI in septic shock and multiple organ dysfunction syndrome. Nicotinamide and 3-AB (3-aminobenzamide) were the first compounds used to inhibit poly (ADP-ribosyl) ation [55]. Despite their different modes, they were found to produce dramatic results in alleviation of pulmonary inflammatory response [46,75,108]. Other PARP-1 inhibitors, such as PJ34 (N-(6-oxo-5,6-dihydro-phenanthridin-2-yl)-N,N-dimethyacetamide HCl) [68,69,109,110], TIQ-A (5-aminois oquinolinone,thieno[2,3-c]isoquinolin-5-one) [67,93], 5-AIQ(5-aminoisoquinolinone) [72,92,100] and INO-1001 [101,106] were soon investigated for their ability to interrupt the destructive signaling cycles mediated by PARP-1. Furthermore, PARP-1 knockout mice are resistant to ovalbumin or LPS induced airway inflammation [63,67,111]. In addition, In various animal models, the protective effect of some anti-inflammatories are related to suppression of PARP-1, including 1,7-dimethylxanthine, a caffeine metabolite [65], tempol, a membrane-permeable radical scavenger [104], flavonoids [66], methylguanidine [112], anthocyanins from blackberry [70], pyrrolidine dithiocarbamate [58], and Celecoxib, a selective COX-2 inhibitor [73].

It seems odd that PARP-1 is conserved across animal species and expressed constitutively at high level, given that animals can be treated beneficially with potent inhibitors, and mice are viable when it is deleted. Besides, there are no currently known examples of natural mutation of PARP-1family, implying that PARP-1is so helpful that complete loss is not competitive in the long term. Nevertheless, inhibition of PARP-1 in some challenging conditions, especially in intensive care units, must have positive significance when the duration of treatment would be brief, and the risks would be likely minimal. However, there is a long way to go for its clinical applications.

Conclusions

PARP-1 is a multi-talented molecule, and the poly (ADP-ribosyl)ation mainly catalyzed by it contributes to a wide variety of cellular responses. Based on the evidence given in this review, we have tried to propose a brief and simplified model (Figure 3) in which PARP-1 functions as a physiological or pathological protagonist. The physiological functions of PARP-1is to repair DNA damage and maintain genomic stability. However, in the company of severe DNA damage, overactivation of PARP-1up-regulates proinflammatory genes at transcriptional level, and aggravates damage, resulting a vicious cycle. Furthermore, lethal stimulation is capable of inducing excessive PARP-1 activation, and ultimately cell death, such as apoptosis, necrosis, and PARP-1-dependent parthanatos.

PARP-1 could be aberrant stimulated in pulmonary pathological conditions, promotes inflammatory response, exacerbates tissue injury, and contributes to systemic dysfunctions. The remarkable beneficial effects of inhibition of PARP-1 have been discovered in vitro and in animal models under inflammatory conditions. In this respect, we suppose that PARP-1 will be a potential target for therapeutic intervention in clinical medicine in the future, and promising pharmacological inhibitors of PARP-1 enzyme could exert a protective role towards various pulmonary disorders.

Acknowledgements

This work was partly supported by research grants No. 81072703 (to Dr. Yu) from the National Natural Science Foundation, Beijing, P.R. China, a research grant No. 10411951700 (to Dr. Zhang) from Science and Technology Commission of Shanghai Municipality, Shanghai, P.R. China.The authors confirm that there are no conflicts of interests.

REFERENCES

[1] Liu B, Shuai K. Summon SUMO to wrestle with inflammation. Mol Cell. 2009; 35: 731−2.
[2] Choudhary C, Kumar C, Gnad F, Nielsen ML, Rehman M, Walther TC, Olsen JV, Mann M. Lysine Acetylation Targets Protein Complexes and Co−Regulates Major Cellular Functions. Science. 2009; 325: 834−40.
[3] Shukla A, Chaurasia P, Bhaumik SR. Histone methylation and ubiquitination with their cross−talk and roles in gene expression and stability. Cell Mol Life Sci. 2008.
[4] Liu B, Yang Y, Chernishof V, Loo RR, Jang H, Tahk S, Yang R, Mink S, Shultz D, Bellone CJ, Loo JA, Shuai K. Proinflammatory stimuli induce IKKalpha−mediated phosphorylation of PIAS1 to restrict inflammation and immunity. Cell. 2007; 129: 903−14.
[5] D'Amours D, Desnoyers S, D'Silva I, Poirier GG. Poly(ADP−ribosyl)ation reactions in the regulation of nuclear functions. Biochem J. 1999; 342: 249−68.
[6] Shieh WM, Ame JC, Wilson MV, Wang ZQ, Koh DW, Jacobson MK, Jacobson EL. Poly(ADP−ribose) polymerase null mouse cells synthesize ADP−ribose polymers. J Biol Chem. 1998; 273: 30069−72.
[7] Shall S, de Murcia G. Poly(ADP−ribose) polymerase−1: what have we learned from the deficient mouse model? Mutat Res−DNA Repair. 2000; 460: 1−15.
[8] Woodhouse BC, Dianov GL. Poly ADP−ribose polymerase−1: an international molecule of mystery. DNA Repair (Amst). 2008; 7: 1077−86.
[9] Burkle A. Poly(ADP−ribose) − The most elaborate metabolite of NAD. Febs J. 2005; 272: 4576−89.
[10] Schreiber V, Dantzer F, Ame JC, de Murcia G. Poly(ADP−ribose): novel functions for an old molecule. Nat Rev Mol Cell Biol. 2006; 7: 517−28.
[11] Sodhi RK, Singh N, Jaggi AS. Poly(ADP−ribose) polymerase−1 (PARP−1) and its therapeutic implications. Vascul Pharmacol. 2010; 53: 77−87.
[12] Virag L. Structure and function of poly(ADP−ribose) polymerase−1: role in oxidative stress−related pathologies. Curr Vasc Pharmacol. 2005; 3: 209−14.
[13] Kraus WL, Lis JT. PARP goes transcription. Cell. 2003; 113: 677−83.
[14] Wang LB, Zhang LY, Shan CH. [A new form of cell death: Parthanatos]. Yi Chuan. 2010; 32: 881−5.
[15] Yu SW, Wang H, Poitras MF, Coombs C, Bowers WJ, Federoff HJ, Poirier GG, Dawson TM, Dawson VL. Mediation of poly(ADP−ribose) polymerase−1−dependent cell death by apoptosis−inducing factor. Science. 2002; 297: 259−63.
[16] Saxena A, Saffery R, Wong LH, Kalitsis P, Choo KH. Centromere proteins Cenpa, Cenpb, and Bub3 interact with poly(ADP−ribose) polymerase−1 protein and are poly(ADP−ribosyl)ated. J Biol Chem. 2002; 277: 26921−6.
[17] Chiarugi A, Moskowitz MA. Poly(ADP−ribose) polymerase−1 activity promotes NF−kappaB−driven transcription and microglial activation: implication for neurodegenerative disorders. J Neurochem. 2003; 85: 306−17.
[18] Burkle A, Brabeck C, Diefenbach J, Beneke S. The emerging role of poly(ADP−ribose) polymerase−1 in longevity. Int J Biochem Cell Biol. 2005; 37: 1043−53.
[19] Albadawi H, Crawford RS, Atkins MD, Watkins MT. Role of poly(ADP−ribose) polymerase during vascular reconstruction. Vascular. 2006; 14: 362−5.
[20] Szabo C. Cardioprotective effects of poly(ADP−ribose) polymerase inhibition. Pharmacol Res. 2005; 52: 34−43.
[21] Esposito E, Cuzzocrea S. Superoxide, NO, peroxynitrite and PARP in circulatory shock and inflammation.

Front Biosci. 2009; 14: 263–96.
[22] Cuzzocrea S. Shock, inflammation and PARP. Pharmacol Res. 2005; 52: 72–82.
[23] Scalera NM, File TM. How long should we treat community–acquired pneumonia? Curr Opin Infect Dis. 2007; 20: 177–81.
[24] [Anon]. Guidelines for the management, of adults with hospital–acquired, ventilator–associated, and healthcare–associated pneumonia. Am J Resp Crit Care. 2005; 171: 388–416.
[25] Stapleton RD, Wang BM, Hudson LD, Rubenfeld GD, Caldwell ES, Steinberg KP. Causes and timing of death in patients with ARDS. Chest. 2005; 128: 525–32.
[26] Yamanaka H, Penning CA, Willis EH, Wasson DB, Carson DA. Characterization of human poly(ADP–ribose) polymerase with autoantibodies. J Biol Chem. 1988; 263: 3879–83.
[27] Hottiger MO, Hassa PO, Luscher B, Schuler H, Koch–Nolte F. Toward a unified nomenclature for mammalian ADP–ribosyltransferases. Trends Biochem Sci. 2010; 35: 208–19.
[28] Hayashi K, Tanaka M, Shimada T, Miwa M, Sugimura T. Size and shape of poly(ADP–ribose): examination by gel filtration, gel electrophoresis and electron microscopy. Biochem Biophys Res Commun. 1983; 112: 102–7.
[29] Lin W, Ame JC, Aboul–Ela N, Jacobson EL, Jacobson MK. Isolation and characterization of the cDNA encoding bovine poly(ADP–ribose) glycohydrolase. J Biol Chem. 1997; 272: 11895–901.
[30] Durkacz BW, Omidiji O, Gray DA, Shall S. (ADP–ribose)n participates in DNA excision repair. Nature. 1980; 283: 593–6.
[31] Dantzer F, Schreiber V, Niedergang C, Trucco C, Flatter E, De La Rubia G, Oliver J, Rolli V, Menissier–de Murcia J, de Murcia G. Involvement of poly(ADP–ribose) polymerase in base excision repair. Biochimie. 1999; 81: 69–75.
[32] Benjamin RC, Gill DM. Poly(ADP–ribose) synthesis in vitro programmed by damaged DNA. A comparison of DNA molecules containing different types of strand breaks. J Biol Chem. 1980; 255: 10502–8.
[33] Audebert M, Salles B, Calsou P. Involvement of poly(ADP–ribose) polymerase–1 and XRCC1/DNA ligase III in an alternative route for DNA double–strand breaks rejoining. J Biol Chem. 2004; 279: 55117–26.
[34] Smulson ME, Simbulan–Rosenthal CM, Boulares AH, Yakovlev A, Stoica B, Iyer S, Luo R, Haddad B, Wang ZQ, Pang T, Jung M, Dritschilo A, Rosenthal DS. Roles of poly(ADP–ribosyl)ation and PARP in apoptosis, DNA repair, genomic stability and functions of p53 and E2F–1. Adv Enzyme Regul. 2000; 40: 183–215.
[35] Yung TM, Sato S, Satoh MS. Poly(ADP–ribosyl)ation as a DNA damage–induced post–translational modification regulating poly(ADP–ribose) polymerase–1–topoisomerase I interaction. J Biol Chem. 2004; 279: 39686–96.
[36] Smith S. The world according to PARP. Trends Biochem Sci. 2001; 26: 174–9.
[37] Lindahl T, Satoh MS, Poirier GG, Klungland A. Post–translational modification of poly(ADP–ribose) polymerase induced by DNA strand breaks. Trends Biochem Sci. 1995; 20: 405–11.
[38] de Murcia G, Menissier de Murcia J. Poly(ADP–ribose) polymerase: a molecular nick–sensor. Trends Biochem Sci. 1994; 19: 172–6.
[39] Yelamos J, Schreiber V, Dantzer F. Toward specific functions of poly(ADP–ribose) polymerase–2. Trends Mol Med. 2008; 14: 169–78.
[40] Rouleau M, Aubin RA, Poirier GG. Poly(ADP–ribosyl)ated chromatin domains: access granted. J Cell Sci. 2004; 117: 815–25.
[41] Althaus FR, Hofferer L, Kleczkowska HE, Malanga M, Naegeli H, Panzeter P, Realini C. Histone shuttle driven by the automodification cycle of poly(ADP–ribose)polymerase. Environ Mol Mutagen. 1993; 22: 278–82.
[42] Kirkland JB. Poly ADP–ribose polymerase–1 and health. Exp Biol Med (Maywood). 2010; 235: 561–8.
[43] Hassa PO. The molecular "Jekyll and Hyde" duality of PARP1 in cell death and cell survival. Front Biosci. 2009; 14: 72–111.
[44] Ying WH, Alano CC, Garnier P, Swanson RA. NAD(+) as a metabolic link between DNA damage and cell death. J Neurosci Res. 2005; 79: 216–23.
[45] Zong WX, Ditsworth D, Bauer DE, Wang ZQ, Thompson CB. Alkylating DNA damage stimulates a regulated form of necrotic cell death. Genes Dev. 2004; 18: 1272–82.
[46] Pulido EJ, Shames BD, Selzman CH, Barton HA, Banerjee A, Bensard DD, McIntyre RC, Jr. Inhibition of PARS attenuates endotoxin–induced dysfunction of pulmonary vasorelaxation. Am J Physiol. 1999; 277: L769–76.
[47] Nanavaty UB, Pawliczak R, Doniger J, Gladwin MT, Cowan MJ, Logun C, Shelhamer JH. Oxidant–induced cell death in respiratory epithelial cells is due to DNA damage and loss of ATP. Exp Lung Res. 2002; 28: 591–607.
[48] Germain M, Affar EB, D'Amours D, Dixit VM, Salvesen GS, Poirier GG. Cleavage of automodified poly(ADP–ribose) polymerase during apoptosis. Evidence for involvement of caspase–7. J Biol Chem. 1999; 274: 28379–84.
[49] Tewari M, Quan LT, O'Rourke K, Desnoyers S, Zeng Z, Beidler DR, Poirier GG, Salvesen GS, Dixit VM. Yama/CPP32 beta, a mammalian homolog of CED–3, is a CrmA–inhibitable protease that cleaves the death substrate poly(ADP–ribose) polymerase. Cell. 1995; 81: 801–9.
[50] Nicholson DW, Ali A, Thornberry NA, Vaillancourt JP, Ding CK, Gallant M, Gareau Y, Griffin PR, Labelle M, Lazebnik YA, et al. Identification and inhibition of the ICE/CED–3 protease necessary for mammalian apoptosis. Nature. 1995; 376: 37–43.
[51] Chaitanya GV, Steven AJ, Babu PP. PARP–1 cleavage fragments: signatures of cell–death proteases in neurodegeneration. Cell Commun Signal. 2010; 8: 31.
[52] Gobeil S, Boucher CC, Nadeau D, Poirier GG. Characterization of the necrotic cleavage of poly(ADP–ribose) polymerase (PARP–1): implication of lysosomal proteases. Cell Death Differ. 2001; 8: 588–94.
[53] Boulares AH, Yakovlev AG, Ivanova V, Stoica BA, Wang G, Iyer S, Smulson M. Role of poly(ADP–ribose) polymerase (PARP) cleavage in apoptosis. Caspase 3–resistant PARP mutant increases rates of apoptosis in transfected cells. J Biol Chem. 1999; 274: 22932–40.
[54] Simbulan–Rosenthal CM, Rosenthal DS, Iyer S, Boulares AH, Smulson ME. Transient poly(ADP–ribosyl)ation of nuclear proteins and role of poly(ADP–ribose) polymerase in the early stages of apoptosis. J Biol Chem. 1998; 273: 13703–12.
[55] Giansanti V, Dona F, Tillhon M, Scovassi AI. PARP inhibitors: new tools to protect from inflammation. Biochem Pharmacol. 2010; 80: 1869–77.
[56] Soldatenkov VA, Chasovskikh S, Potaman VN, Trofimova I, Smulson ME, Dritschilo A. Transcriptional repression by binding of poly(ADP–ribose) polymerase to promoter sequences. J Biol Chem. 2002; 277: 665–70.
[57] Oei SL, Herzog H, Hirsch–Kauffmann M, Schneider R, Auer B, Schweiger M. Transcriptional regulation and autoregulation of the human gene for ADP–ribosyltransferase. Mol Cell Biochem. 1994; 138: 99–104.
[58] Cuzzocrea S, Rossi A, Pisano B, Di Paola R, Genovese T, Patel NS, Cuzzocrea E, Ianaro A, Sautebin L, Fulia F, Chatterjee PK, Caputi AP, Thiemermann C. Pyrrolidine dithiocarbamate attenuates the development of organ failure induced by zymosan in mice. Intensive Care Med. 2003; 29: 2016–25.
[59] Sheehan M, Wong HR, Hake PW, Zingarelli B. Parthenolide improves systemic hemodynamics and decreases tissue leukosequestration in rats with polymicrobial sepsis. Crit Care Med. 2003; 31: 2263–70.
[60] Hassa PO, Hottiger MO. The functional role of poly(ADP–ribose)polymerase 1 as novel coactivator of NF–kappaB in inflammatory disorders. Cell Mol Life Sci. 2002; 59: 1534–53.
[61] Kim JH, Suk MH, Yoon DW, Kim HY, Jung KH, Kang EH, Lee SY, Suh IB, Shin C, Shim JJ, In KH, Yoo SH, Kang KH. Inflammatory and transcriptional roles of poly (ADP–ribose) polymerase in ventilator–induced lung injury. Crit Care. 2008; 12: R108.
[62] Espinoza LA, Tenzin F, Cecchi AO, Chen Z, Witten ML, Smulson ME. Expression of JP–8–induced inflammatory genes in AEII cells is mediated by NF–kappaB and PARP–1. Am J Respir Cell Mol Biol. 2006; 35: 479–87.
[63] Boulares AH, Zoltoski AJ, Sherif ZA, Jolly P, Massaro D, Smulson ME. Gene knockout or pharmacological inhibition of poly(ADP–ribose) polymerase–1 prevents lung inflammation in a murine model of asthma. Am J Respir Cell Mol Biol. 2003; 28: 322–9.
[64] Virlos I, Mazzon E, Serraino I, Genovese T, Di Paola R, Thiemerman C, Siriwardena A, Cuzzocrea S. Calpain I inhibitor ameliorates the indices of disease severity in a murine model of cerulein–induced acute pancreatitis. Intensive Care Med. 2004; 30: 1645–51.
[65] Geraets L, Haegens A, Weseler AR, Brauers K, Vernooy JH, Wouters EF, Bast A, Hageman GJ. Inhibition of acute pulmonary and systemic inflammation by 1,7–dimethylxanthine. Eur J Pharmacol. 2010; 629: 132–9.
[66] Geraets L, Haegens A, Brauers K, Haydock JA, Vernooy JH, Wouters EF, Bast A, Hageman GJ. Inhibition of LPS–induced pulmonary inflammation by specific flavonoids. Biochem Biophys Res Commun. 2009; 382: 598–603.
[67] Oumouna M, Datta R., Oumouna–Benachour K, Suzuki Y, Hans C, Matthews K, Fallon K, Boulares H. Poly(ADP–ribose) polymerase–1 inhibition prevents eosinophil recruitment by modulating Th2 cytokines in a murine model of allergic airway inflammation: a potential specific effect on IL–5. J Immunol. 2006; 177: 6489–96.
[68] Mota RA, Sanchez–Bueno F, Saenz L, Hernandez–Espinosa D, Jimeno J, Tornel PL, Martinez–Torrano A, Ramirez P, Parrilla P, Yelamos J. Inhibition of poly(ADP–ribose) polymerase attenuates the severity of acute pancreatitis and associated lung injury. Lab Invest. 2005; 85: 1250–62.
[69] Virag L, Bai P, Bak I, Pacher P, Mabley JG, Liaudet L, Bakondi E, Gergely P, Kollai M, Szabo C. Effects of poly(ADP–ribose) polymerase inhibition on inflammatory cell migration in a murine model of asthma. Med Sci Monit. 2004; 10: BR77–83.
[70] Rossi A, Serraino I, Dugo P, Di Paola R, Mondello L, Genovese T, Morabito D, Dugo G, Sautebin L, Caputi AP, Cuzzocrea S. Protective effects of anthocyanins from blackberry in a rat model of acute lung inflammation. Free Radic Res. 2003; 37: 891–900.
[71] Liaudet L, Pacher P, Mabley JG, Virag L, Soriano FG, Hasko G, Szabo C. Activation of poly(ADP–Ribose) polymerase–1 is a central mechanism of lipopolysaccharide–induced acute lung inflammation. Am J Respir Crit Care Med. 2002; 165: 372–7.
[72] Cuzzocrea S, McDonald MC, Mazzon E, Dugo L, Serraino I, Threadgill M, Caputi AP, Thiemermann C. Effects of 5–aminoisoquinolinone, a water–soluble, potent inhibitor of the activity of poly (ADP–ribose) polymerase, in a rodent model of lung injury. Biochem Pharmacol. 2002; 63: 293–304.
[73] Cuzzocrea S, Mazzon E, Sautebin L, Dugo L, Serraino I, De Sarro A, Caputi AP. Protective effects of Celecoxib on lung injury and red blood cells modification induced by carrageenan in the rat. Biochem Pharmacol. 2002; 63: 785–95.
[74] Kiefmann R, Heckel K, Doerger M, Schenkat S, Kupatt C, Stoeckelhuber M, Wesierska–Gadek J, Goetz AE. Role of PARP on iNOS pathway during endotoxin–induced acute lung injury. Intensive Care Med. 2004; 30: 1421–31.
[75] Kao SJ, Liu DD, Su CF, Chen HI. Niacinamide abrogates the organ dysfunction and acute lung injury caused by endotoxin. J Cardiovasc Pharmacol. 2007; 50: 333–42.
[76] Dugo L, Marzocco S, Mazzon E, Di Paola R, Genovese T, Caputi AP, Cuzzocrea S. Effects of GW274150, a novel and selective inhibitor of iNOS activity, in acute lung inflammation. Br J Pharmacol. 2004; 141: 979–87.
[77] Nakajima H, Nagaso H, Kakui N, Ishikawa M, Hiranuma T, Hoshiko S. Critical role of the automodification of poly(ADP–ribose) polymerase–1 in nuclear factor–kappaB–dependent gene expression in primary cultured mouse glial cells. J Biol Chem. 2004; 279: 42774–86.
[78] Chang WJ, Alvarez–Gonzalez R. The sequence–specific DNA binding of NF–kappa B is reversibly regulated by the automodification reaction of poly (ADP–ribose) polymerase 1. J Biol Chem. 2001; 276: 47664–70.
[79] Veres B, Radnai B, Gallyas F, Jr., Varbiro G, Berente Z, Osz E, Sumegi B. Regulation of kinase cascades and transcription factors by a poly(ADP–ribose) polymerase–1 inhibitor, 4–hydroxyquinazoline, in lipopolysaccharide–induced inflammation in mice. J Pharmacol Exp Ther. 2004; 310: 247–55.
[80] Huang D, Yang C, Wang Y, Liao Y, Huang K. PARP–1 suppresses adiponectin expression through poly(ADP–ribosyl)ation of PPAR gamma in cardiac fibroblasts. Cardiovasc Res. 2009; 81: 98–107.
[81] Aguilar–Quesada R, Munoz–Gamez JA, Martin–Oliva D, Peralta–Leal A, Quiles–Perez R, Rodriguez–Vargas JM, Ruiz de Almodovar M, Conde C, Ruiz–Extremera A, Oliver FJ. Modulation of transcription by PARP–1: consequences in carcinogenesis and inflammation. Curr Med Chem. 2007; 14: 1179–87.
[82] Yu SW, Andrabi SA, Wang H, Kim NS, Poirier GG, Dawson TM, Dawson VL. Apoptosis–inducing factor mediates poly(ADP–ribose) (PAR) polymer–induced cell death. Proc Natl Acad Sci U S A. 2006; 103: 18314–9.
[83] Andrabi SA, Dawson TM, Dawson VL. Mitochondrial and nuclear cross talk in cell death: parthanatos. Ann N Y Acad Sci. 2008; 1147: 233–41.
[84] Wang Y, Dawson VL, Dawson TM. Poly(ADP–ribose) signals to mitochondrial AIF: a key event in parthanatos. Exp Neurol. 2009; 218: 193–202.
[85] Hong SJ, Dawson TM, Dawson VL. Nuclear and mitochondrial conversations in cell death: PARP–1 and AIF signaling. Trends Pharmacol Sci. 2004; 25: 259–64.
[86] Dawson VL, Dawson TM. Deadly conversations: nuclear–mitochondrial cross–talk. J Bioenerg Biomembr. 2004; 36: 287–94.
[87] Koh DW, Lawler AM, Poitras MF, Sasaki M, Wattler S, Nehls MC, Stoger T, Poirier GG, Dawson VL, Dawson TM. Failure to degrade poly(ADP–ribose) causes increased sensitivity to cytotoxicity and early embryonic lethality. P Natl Acad Sci USA. 2004; 101: 17699–704.
[88] Susin SA, Lorenzo HK, Zamzami N, Marzo I, Snow BE, Brothers GM, Mangion J, Jacotot E, Costantini P, Loeffler M, Larochette N, Goodlett DR, Aebersold R, Siderovski DP, Penninger JM, Kroemer G. Molecular characterization of mitochondrial apoptosis–inducing factor. Nature. 1999; 397: 441–6.
[89] Andrabi SA, Kim NS, Yu SW, Wang H, Koh DW, Sasaki M, Klaus JA, Otsuka T, Zhang Z, Koehler RC, Hurn PD, Poirier GG, Dawson VL, Dawson TM. Poly(ADP–ribose) (PAR) polymer is a death signal. Proc Natl Acad Sci U S A. 2006; 103: 18308–13.
[90] Pagano A, Metrailler–Ruchonnet I, Aurrand–Lions M, Lucattelli M, Donati Y, Argiroffo CB. Poly(ADP–ribose) polymerase–1 (PARP–1) controls lung cell proliferation and repair after hyperoxia–induced lung damage. Am J Physiol Lung Cell Mol Physiol. 2007; 293: L619–29.
[91] Piskunova TS, Yurova MN, Ovsyannikov AI, Semenchenko AV, Zabezhinski MA, Popovich IG, Wang ZQ, Anisimov VN. Deficiency in Poly(ADP–ribose) Polymerase–1 (PARP–1) Accelerates Aging and Spontaneous Carcinogenesis in Mice. Curr Gerontol Geriatr Res. 2008: 754190.
[92] Suzuki Y, Masini E, Mazzocca C, Cuzzocrea S, Ciampa A, Suzuki H, Bani D. Inhibition of poly(ADP–ribose) polymerase prevents allergen–induced asthma–like reaction in sensitized Guinea pigs. J Pharmacol Exp Ther. 2004; 311: 1241–8.
[93] Naura AS, Hans CP, Zerfaoui M, You D, Cormier SA, Oumouna M, Boulares AH. Post–allergen challenge inhibition of poly(ADP–ribose) polymerase harbors therapeutic potential for treatment of allergic airway inflammation. Clin Exp Allergy. 2008; 38: 839–46.
[94] Havranek T, Aujla PK, Nickola TJ, Rose MC, Scavo LM. Increased poly(ADP–ribose) polymerase (PARP)–1 expression and activity are associated with inflammation but not goblet cell metaplasia in murine models of allergen–induced airway inflammation. Exp Lung Res. 2010; 36: 381–9.
[95] Cuzzocrea S, Mazzon E, Dugo L, Serraino I, Ciccolo A, Centorrino T, De Sarro A, Caputi AP. Protective effects of n–acetylcysteine on lung injury and red blood cell modification induced by carrageenan in the rat. FASEB J. 2001; 15: 1187–200.
[96] Cuzzocrea S, Santagati S, Sautebin L, Mazzon E, Calabro G, Serraino I, Caputi AP, Maggi A. 17beta–estradiol antiinflammatory activity in carrageenan–induced pleurisy. Endocrinology. 2000; 141: 1455–63.
[97] Cuzzocrea S, McDonald MC, Filipe HM, Costantino G, Mazzon E, Santagati S, Caputi AP, Thiemermann C. Effects of tempol, a membrane–permeable radical scavenger, in a rodent model of carrageenan–induced pleurisy. Eur J Pharmacol. 2000; 390: 209–22.
[98] Cuzzocrea S, Mazzon E, Calabro G, Dugo L, De Sarro A, van De LF, Caputi AP. Inducible nitric oxide synthase–knockout mice exhibit resistance to pleurisy and lung injury caused by carrageenan. Am J Respir Crit Care Med. 2000; 162: 1859–66.
[99] Cuzzocrea S, Sautebin L, De Sarro G, Costantino G, Rombola L, Mazzon E, Ialenti A, De Sarro A, Ciliberto G, Di Rosa M, Caputi AP, Thiemermann C. Role of IL–6 in the pleurisy and lung injury caused by carrageenan. J Immunol. 1999; 163: 5094–104.
[100] Genovese T, Mazzon E, Di Paola R, Muia C, Threadgill MD, Caputi AP, Thiemermann C, Cuzzocrea S. Inhibitors of poly(ADP–ribose) polymerase modulate signal transduction pathways and the development of bleomycin–induced lung injury. J Pharmacol Exp Ther. 2005; 313: 529–38.
[101] Murakami K, Enkhbaatar P, Shimoda K, Cox RA, Burke AS, Hawkins HK, Traber LD, Schmalstieg FC, Salzman AL, Mabley JG, Komjati K, Pacher P, Zsengeller Z, Szabo C, Traber DL. Inhibition of poly (ADP–ribose) polymerase attenuates acute lung injury in an ovine model of sepsis. Shock. 2004; 21: 126–33.
[102] Lange M, Connelly R., Traber DL, Hamahata A, Nakano Y, Esechie A, Jonkam C, von Borzyskowski S, Traber LD, Schmalstieg FC, Herndon DN, Enkhbaatar P. Time course of nitric oxide synthases, nitrosative stress, and poly(ADP ribosylation) in an ovine sepsis model. Crit Care. 2010; 14: R.129.
[103] Albertini M, Clement MG, Lafortuna CL, Caniatti M, Magder S, Abdulmalek K, Hussain SN. Role of poly–(ADP–ribose) synthetase in lipopolysaccharide–induced vascular failure and acute lung injury in pigs. J Crit Care. 2000; 15: 73–83.
[104] Yuksel BC, Serdar SE, Tuncel A, Uzum N, Ataoglu O, Atan A, Hengirmen S, Iskit AB, Guc MO. Effect of tempol, a membrane–permeable radical scavenger, on mesenteric blood flow and organ injury in a murine cecal ligation and puncture model of septic shock. Eur Surg Res. 2009; 43: 219–27.
[105] Avlan D, Unlu A, Ayaz L, Camdeviren H, Nayci A, Aksoyek S. Poly (adp–ribose) synthetase inhibition reduces oxidative and nitrosative organ damage after thermal injury. Pediatr Surg Int. 2005; 21: 449–55.
[106] Szabo G, Soos P, Mandera S, Heger U, Flechtenmacher C, Bahrle S, Seres L, Cziraki A, Gries A, Zsengeller Z, Vahl CF, Hagl S, Szabo C. INO–1001 a novel poly(ADP–ribose) polymerase (PARP) inhibitor improves cardiac and pulmonary function after crystalloid cardioplegia and extracorporal circulation. Shock. 2004; 21: 426–32.
[107] Gero D, Szabo C. Poly(ADP–ribose) polymerase: a new therapeutic target? Curr Opin Anaesthesiol. 2008; 21: 111–21.
[108] Cuzzocrea S, Zingarelli B, Gilad E, Hake P, Salzman AL, Szabo C. Protective effects of 3–aminobenzamide, an inhibitor of poly (ADP–ribose) synthase in a carrageenan–induced model of local inflammation. Eur J Pharmacol. 1998; 342: 67–76.
[109] Lobo SM, Orrico SR., Queiroz MM, Cunrath GS, Chibeni GS, Contrin LM, Cury PM, Burdmann EA, de Oliveira Machado AM, Togni P, De Backer D, Preiser JC, Szabo C, Vincent JL. Pneumonia–induced sepsis and gut injury: effects of a poly–(ADP–ribose) polymerase inhibitor. J Surg Res. 2005; 129: 292–7.
[110] Vaschetto R, Kuiper JW, Musters RJ, Eringa EC, Della Corte F, Murthy K, Groeneveld AB, Plotz FB. Renal hypoperfusion and impaired endothelium–dependent vasodilation in an animal model of VILI: the role of the peroxynitrite–PARP pathway. Crit Care. 2010; 14: R.45.
[111] Zerfaoui M, Naura AS, Errami Y, Hans CP, Rezk BM, Park J, Elsegeiny W, Kim H, Lord K, Kim JG, Boulares AH. Effects of PARP–1 deficiency on airway inflammatory cell recruitment in response to LPS or TNF: differential effects on CXCR2 ligands and Duffy Antigen Receptor for Chemokines. J Leukoc Biol. 2009; 86: 1385–92.
[112] Marzocco S, Di Paola R, Genovese T, Sorrentino R, Britti D, Scollo G, Pinto A, Cuzzocrea S, Autore G. Methylguanidine reduces the development of non septic shock induced by zymosan in mice. Life Sci. 2004; 75: 1417–33.

安建雄 范 婷 钱晓焱
马银娜 林艳君 方七五
清华大学玉泉医院麻醉与疼痛医学科 北京 100049

全脊髓麻醉治疗慢性疼痛

Total Spinal Anesthesia on Treatment of Chronic Pain

Jian-xiong An, Ting Fan, Xiao-yan Qian, Yin-na Ma, Yan-jun Lin, Qi-wu Fang
Department of Anesthesia and Pain Medicine, Yu Quan Hospital affiliated to Tsinghua University, Beijing 100049

一、概述

全脊髓麻醉(total spinal anesthesia,TSA)一般指椎管内麻醉时的一种严重并发症,系蛛网膜下腔麻醉或硬膜外麻醉时因阻滞平面过高使整个脊髓甚至脑干也被阻滞的临床综合症。随人们认识的深入,TSA也被人类用于治疗手段。Koster最早用TSA用于头、颈及胸部手术麻醉[14]。Evans曾以TSA做为全麻方法完成腹部外科手术[12]。Tsumura等[1,2]最早在上世纪70年代初报道将TSA用于治疗挥鞭样损伤后慢性疼痛综合症,随后不断有关于TSA治疗其它慢性疼痛的报道[4,6,8,9]。

关于TSA的名称,Yokoyama等为更准确地表达用于治疗目时的TSA的含义，称之为“故意全脊髓麻醉（intentional total spinal anesthesia）”,也有冠以“人为全脊髓阻滞(induuced total spinal block)”,我们认为,中文可能译为“治疗性全脊髓麻醉或阻滞”更贴切。而Kotani等[7]在新英格兰医学杂志发表的高水平研究实际上是“脊髓节段性阻滞或注射”。

二、全脊麻对顽固性疼痛的疗效

TSA用于治疗顽固性疼痛主要集中在日本国,上世纪70年代初,Tsumura等[1,2]先后报告TSA 可治疗挥鞭样损伤后综合症。TSA后被日本卫生与福利省批准用于顽固性疼痛的治疗[10]。在很长时间内，有关TSA治疗痛症只是零星的个案报告。Yokoyama等[8]用交叉试验研究(crossover study)对12例顽固性疼痛,包括疱疹后神经痛、挥鞭样损伤后综合症、手术失败腰背痛以及复杂性局部疼痛综合症等,采用交叉试验法分别静脉(IV)和椎管内(TSA)注射利多卡因,结果显示,虽然两种给药途径后血药浓度和血流动力学相似,但TSA后24小时内疼痛显著减轻,其中有5例疼痛消失,镇痛作用可维持7天,但30天后镇痛作用消失。本研究提示一定浓度局麻药的镇痛作用部位在脊髓,而且单次TSA镇痛作用在头两天最明显,并可以持续一周,但无长期作用。这一结论和椎管内注射激素治疗不同。

Takahashi等对6例顽固性疼痛病人进行TSA,结果5/6病人在接受TSA后次日疼痛缓解达50%以上,长期随访有两例长期疗效[13],然而作者没有解释随访具体时间。

我国严相默教授应用TSA治疗顽固性疼痛起因于一次意外事件:当作者实施硬膜外阻滞治疗外伤后颈部疼痛时,意外发生全脊髓麻醉,有趣的是当病人经抢救清醒后,原有疼痛消失却没有留下任何神经系统并发症,受此事件启发,严教授等不仅用TSA治疗外伤性头颈部疼痛,还对2例“斜颈”和两例“大脑书写中枢性震颤”进行治疗并获得满意疗效[9]。本研究的特点是不将TSA适应症扩大到中枢性震颤,但对疼痛疗效的评估,特别是远期疗效的随访没有描述， 因为慢性疼痛的疗效关键是远期疼痛缓解的评价。

疱疹后神经痛（PHN）是世界范围内公认的疼痛顽症之一。以往从无行之有效的治疗方法，然而，有关脑脊液注射激素治疗本病的报道却令人为之一振。Yamashiro等[4]报告72岁患胸部带状疱疹后神经痛,每周5次硬膜外阻滞仍然不能缓解疼痛,睡眠和日常生活严重受扰,患病105天后,作者将20毫克醋酸甲基强的松龙与1%利多卡因混合液注入硬膜外腔,疼痛显著减轻,睡眠不再受影响。然而每周一次,共四次注射后,疼痛不再继续减轻.在病程154天后,作者将同样混合液经L2间隙注入蛛网膜下腔,疼痛消失,长期随访无复发。蛛网膜下腔阻滞时,脑干听觉反应进行监测,发现对听觉反映抑制在注射利多卡因后40分钟才能恢复。

Kikuchi等等[6]将25名病史1年以上的带状疱疹后神经痛患者随即分为两组,将醋酸甲基强的松龙60毫克分别注入硬膜外注射(n=12)和蛛网膜下腔,每周一次,共四次,随访24周结果显示,蛛网膜下腔组病人持续性针刺样疼痛显著减轻。症状改善显著优于硬膜外注射组。脑脊液白介素8检测结果提示疼痛改善与激素抑制炎症反应有关。Kotani[7]等将277例病史一年以上的带状疱疹后神经痛病人随机分为常规服药、鞘内单纯利多卡因和鞘内利多卡因(3% 3ml)加醋酸甲基强的松龙(60mg)三组， 连续治疗四周,后两组每周经L2-3鞘内注射一次,然后对所有病历随访2年。结果第一组疼痛无改变,而鞘内单纯利多卡因组疼痛只有轻微(20%)而短暂缓解;鞘内利多卡因加强的松龙组90%镇痛效果满意,疼痛程度平均缓解70%,而口服镇痛药也减少70%,这种效果一直保持到治疗后两年。这三组病人疼痛的共同性质为灼痛、刺痛和痛觉过敏(神经病理性疼痛)。有7例效果不满意者病程均在5年以上。脑脊液检

测结果提示，激素对PHN患者白介素8有抑制作用。随访未发现类固醇激素类副作用，治疗后2年MRI检查未发现激素应用可致脊柱异常改变。然而，该研究设计上有缺陷,应再设一组单独鞘内醋酸甲基强的松龙组,以便更能明确起效药物种类。也有作者批评鞘内给药的危险性的担心和伦理学问题,这些担心与他们从事专业有关。非麻醉专业医生对这种治疗持有异议乃情理之中。

三、全脊麻治疗疼痛的机制研究

全脊髓麻醉治疗疼痛的确切机理尚不清楚，有关研究报告可谓寥寥无几。Takahashi等[13]用脑电频谱指数分析法（Power spectral analysis of EEG）对6例用TSA治疗的疼痛病人研究发现,TSA对皮层脑电活动抑制轻,在意识丧失的阶段脑电活动接近异丙酚或异氟醚麻醉觉醒时的水平。无惊厥时异常放电现象发生,认为与电惊厥（electroconvulsion）镇痛机制不同,完全阻断脑干传导,而皮层处于“安静”状态。此研究和以往用脑电或脑内局麻药浓度测定研究得出的假想(Ide.et al.1977;Kaplan,et al,1999;Yanagida,et al.1978)相一致,即与脑刺激和电休克等中枢动力性治疗不同,TSA其镇痛机制可能催眠疗法有相似处,在脑干水平完全阻断上传信息,而大脑皮层也被孤立地处于轻度抑制状态,这与以往报告的任何介入性治疗机制都不同,很可能是TSA调节大脑及痛觉感知的途径。Goda等[3]用同样的方法通过监测心率和周围血流改变,认为TSA同时抑制迷走和交感神经,结果两种作用相互抵消，从而没有表现为迷走或交感神经单独的过度抑制。

Kimura等[5]用红外线温度计和激光多普勒流量计分别监测全脊髓麻醉后皮肤温度和血流变化.但类似研究对揭示TSA的镇痛机制意义不大。

我们用BIS监测仪对TSA意识水平的观察发现，与全身麻醉比，TSA时BIS值的变化与意识水平改变与全身麻醉时表现类似,提示局部麻醉药作用于脑时,对意识的抑制与其他全麻醉药有共同处。伴随意识的消失,BIS值逐渐降低,最低时可达29。然后逐渐恢复,然而Takahashi[13]报告用脑电频谱指数监测时病人表现为一直接近麻醉觉醒前浅镇静水平，这种差别可能与两种研究所采用设备的工作原理不同所致。

全脊髓麻醉后时局麻药中加入激素镇痛效果显著而持久，这自然让人联想到这类药物缓解疼痛可能与其抗炎作用有关。Kikuchi等[6]将60毫克醋酸甲基强的松龙分别注入PHN患者硬膜外和蛛网膜下腔,每周一次,共四次，疗程结束后一周时脑脊液检测发现蛛网膜下腔脑脊液中白介素8(IL-8)显著低于硬膜外注射组，而蛛网膜下腔给药组疼痛缓解也显著优于对照组，作者据此认为,此类病人疼痛改善与类固醇激素减轻脑脊液中炎症反应有关。Kotani[7]等对一个较大样本的研究中，对无痛志愿者和采用不同方法治疗PHN患者的脑脊液检测发现，PHN患者CSF中白介素8显著高于无痛志愿者组;而经治疗的PHN患者中,鞘内联合应用局麻药利多卡因和强的松龙患者的CSF白介素8浓度减少50%,但常规口服药物和鞘内单纯注射利多卡因组则无改变。作者据此推测鞘内类固醇激素治疗PHN疼痛是通过抑制CSF炎症反应实现的。

TSA镇痛机制也可以用哲学原理解释，神经系统可塑性理论和疼痛生理膜板学说（罗非，1995）认为，在没有明显病理损伤的情况下，神经递质运转失调可以导致疼痛发生,类似计算机硬件完好但软件运行出现障碍。TSA镇痛作用类似计算机“格式化”。换言之，TSA可能使的紊乱的神经运转恢复正常。

四、、故意全脊麻的实施

术前禁食6h，入室后常规心电,脉搏氧饱和度无创血压监测,开放静脉通道后预先预充500-100ml液体，必要时中心静脉置管并监测CVP。注射东莨菪碱0.3mg或阿托品0.2-0.3mg。取侧卧位，选择颈7胸1或胸3～4椎间隙，用23G腰穿针进行正中法蛛网膜下腔穿刺，也有作者经C1-2在X线引导下穿刺。[13]。脑脊液外流后注入1～1.5%利多卡因20ml或0.3-0.4ml/kg，30～60s内注完后拔针，取平卧位后面罩过度换气，为避免病人不适,也可在病人意识丧失前给予异丙酚(0.8-1.4mg/kg)和利多卡因。意识丧失后插入喉罩或气管导管,机械通气直到有效自主呼吸恢复。病人一般在椎管内给药后10～20min瞳孔散大、对光反射消失、全身肌肉松弛，密切观察BP、RR、SpO_2、CVP、$P_{Et}CO2$及ECG，调节输液速度以控制血压平稳。约维持60min后，自主呼吸、颈部肌张力及膈肌呼吸逐渐恢复，随后神志恢复，待对答反应恢复，自主呼吸及循环稳定后拔管送回病房[5, 9, 11, 13]。

五治疗性全脊髓麻醉的安全性

以往全脊髓麻醉被列为严重致命性麻醉并发症,然而,由于人们对全脊髓麻醉的认识深入,麻醉技术和知识的进步,全脊髓麻醉已经鲜有不良后果发生。主动或治疗性全脊髓麻醉由于适应症选择恰当,监测手段,机械通气、药物、静脉通道建立等充分准备， 严重低血压等很少发生。实际上少有关于TSA治疗疼痛时严重并发症的报道。Takahashi等[13]报告6例病人中有4例在眼睛接近睁开时发生心动过缓(小于50次/分)，注射阿托品后恢复。Takahashi等的研究还表明，病人没有治疗其间不适感和记忆[13]，实际上，即使是意外全脊髓麻醉后气管插管和机械通气时,很少需要镇静药,病人通常无记忆[12, 15]。

有趣的是，即使鞘内反复注射类固醇激素，也没有发现明显的副作用，Kotani等[7]等对鞘内注射激素病人于疗程结束后以及治疗后两年后随访，未见类固醇激素副作用，MRI检查也未发现有脊柱异常改变。

我们在临床实践时发现，在充分准备和采取预防性措施后，病人在TSA时血压不但无明显降低，反而稍有升高。而术后调查也未发现病人有术中苏醒或不良记忆。BIS监测虽然增加成本，但对预防精神心理伤害可能有重要价值。

六、故意全脊麻的适应症

不应列为常规疼痛治疗办法,只有在常规方法难以奏效时,方可考虑使用本法,采用办法前要对病人条件进行全面评

估,避免用于高年龄和有严重心血管功能障碍的病人,脊髓阶段性给药而无需全脊髓麻醉的病人,适应症可适当放宽。适合本法治疗的主要疼痛疾病有:挥鞭样损伤后颈部疼痛综合征、外伤后头痛,带状疱疹后神经痛、局部复杂疼痛综合症,手术失败后腰背或颌面部疼痛等。

禁忌:病人不愿意接受TSA;有椎管穿刺禁忌症如局部感染,凝血功能障碍者;高龄及有严重心血管等重要脏器功能障碍者,有精神心理障碍不能合作者。

七、小结

总之,局麻醉药TSA对顽固性慢性疼痛有短暂疼痛缓解,多数研究认为其长期疗效不肯定;然而局麻药中加入类固醇激素甲基强的松龙时,其近远期疗效都获得肯定,为治疗顽症PHN提供了一线曙光。然而,在这一领域的研究远嫌不够,多数工作集中在日本,而且缺乏大样本,多中心的随机对照研究。TSA治疗慢性疼痛的机理尚不清楚,

参考文献

[1] Tsumura Y, Hoshiga T, Yukimachi T, Clinical studies on total spinal block. I. Clinical observation and the therapeutic effects in chronic whiplash injury.Masui. 1972, 21(4):352-60.
[2] Tsumura Y, Hoshiga T Subarachnoidal injection therapy in chronic cases of the so-called whiplash syndrome. Acta Anaesthesiol Scand. 1971;15(1):61-4.
[3] Goda Y, Kimura T, Goto Y, et al. Power spectral analysis of heart rate and peripheral blood flow variations during total spinal anesthesia.Masui. 1989;38(10):1275-81.
[4] Yamashiro H, Ogata R, Kawahara K. A complete relief of intractable postherpetic neuralgia with intrathecal methylprednisolone acetate Masui. 1990 ;39(1):106-10.
[5] Kimura T, Goda Y, Kemmotsu O et al.Regional differences in skin blood flow and temperature during total spinal anaesthesia. Can J Anaesth. 1992 ;39(2):123-7.
[6] Kikuchi A, Kotani N, Sato T. et al. Comparative therapeutic evaluation of intrathecal versus epidural methylprednisolone for long-term analgesia in patients with intractable postherpetic neuralgia. Reg Anesth Pain Med. 1999.24:287-93.
[7] Kotani N, Kushikata T, Hashimoto H, et al. Intrathecal methylprednisolone for intractable postherpetic neuralgia. N Engl J Med 2000;343:1514-9.
[8] Yokoyama M, Itano Y, Kusume Y. et al Total spinal anesthesia provides transient relief of intractable pain. Can J Anesth. 2002;49:810-3.
[9] 严相默 李昌熙 金英兰.全脊髓麻醉疗法在疼痛临床中的应用. 中国麻醉与镇痛 1999; 1:51.
[10] Kimura T, Komatsu T, Hirabayashi A. et al. Automomic imbalance of the heart during total spinal anesthesia evaluated by spectral analysis of heart rate variability. Anesthesiology 1994;80:694-8.
[11] 严相默.临床疼痛学, 延吉, 延边人民出版社1996, 162-3.
[12] Evans TI, Total spinal aneasthesia. Anaesth Intensive Care 1974;2:158-63.
[13] Takahashi M, Murakami M, Nakaho T,et al. Power spectral analysis of the electroencephalogram during induced total spinal block. J Anesth;2001;15:83-7.
[14] Koster H. Spinal anesthesia with special reference to its use in surgery of the head, neck and thorax. Am J serg.1928;5:554-70.
[15] Brown DI, Spinal, epidural and caudal anesthesia. In: Miller RD, Miller's Anesthesia. 6th ed , Philadephia, Churchill Livingstone, 2005, pp 1676.

刘洋 王月兰 宋秀梅

山东省千佛山医院麻醉科，250014

摘要

机械通气致肺损伤的机制研究众多，生物学损伤是致伤关键。机械通气致肺损伤的致死因素之一就是肺水肿的发生发展或以全身炎症反应综合症及多器官功能衰竭而终结，因此研究并探讨肺水肿的发生机制并干预其发生至关重要，本文就就生物学损伤及机械性损伤致VILI肺水肿的发生机制的最新研究做一综述，以期预防肺水肿的发生，为临床麻醉及重症监护过程中VILI致肺水肿的发生奠定理论基础。

关键词：机械通气，肺水肿，肺损伤

机械通气致肺水肿损伤机制的研究进展

Mechanism of Lung injury induced by mechanical ventilation

Yang Liu, Yue-lan Wang, Xiu-mei Song

Department of Anesthesiology, Qianfoshan Hospital, Shandong Province 250014

Abstract

Mechanism of Lung injury induced by mechanical ventilation proves multitude. biological damage is a key cause in VILI. One of the lethal factor in the development of lung injury induced by mechanical ventilation is the vulnerant pulmonary edema usually ends on systemic inflammatory response syndrome and multiple organ failure, therefore to explore the mechanism of pulmonary edema, and do the intervention in the course of occurrence is critical. this article will review the latest research done on biological damage and mechanical damage caused by VILI in order to prevent the occurrence of pulmonary edema, in order to establish theoretical basis for Clinical Anesthesia and Intensive Care Units during the VILI induced pulmonary edema.

Key Words: Mechanical ventilation；Pulmonary edema；Lung injury

引言

机械通气做为一种治疗手段，在临床麻醉与重症监护中应用广泛。动物试验和临床试验均表明，机械通气本身可使既存的肺损伤或正常肺损伤加重，并产生机械通气相关性肺损伤（Ventilator induced lung injury，VILI）。研究表明，当高压通气被限定在30cm水柱或潮气量由每公斤12毫升减少至每公斤至6毫升时，861例急性呼吸窘迫综合征患者的死亡率从40%降低到31%，这些结果表明，VILI至少影响9%的死亡率。有关VILI的发生机制研究众多，VILI不仅包括由机械通气产生的压力直接作用导致的漏气，高跨肺压也被证实会导致更加微妙的伤害，超微结构的异常如血管内皮细胞脱离，血管内泡，破坏或损坏的肺泡上皮细胞和与肺泡基底膜裸露区，都是机械损伤继发于肺泡过度膨胀的证据[1,2]，继发的肺组织内的炎症反应及炎症介质的级联扩大致全身炎症反应综合症，这些病理生理学变化统称为生物学损伤[3,4,5]，生物伤反应迅速波及广泛，多以脏器功能衰竭（MOF）终结并死亡。

肺水肿是VILI肺损伤的主要表现。VILI时肺组织内液体生成过多及清除减少，机械力破坏了肺微循环血气屏障，使肺血管通透性增加，内皮细胞及上皮细胞的破坏或凋亡、细胞间连接断裂，是VILI致肺水肿的发生关键。渗出或漏出的液体聚集在肺组织内不能排除，进一步加重了肺细胞水肿、肺泡腔内透明膜形成，进一步发展成ARDS，研究表明，干预肺水肿的发生可以明显降低VILI死亡率。近年来有关机械通气致肺水肿的发生机制，国内外研究认为生物学损伤固然重要，但机械性损伤是机械通气致肺损伤与其他原因致肺损伤水肿发生的重要标志，更是肺损伤发生的闸门，本文就生物学损伤及机械性损伤两方面综述对机械通气致肺损伤肺水肿的发生机制做一总结。

1. 机制

生物伤或是机械伤，在VILI肺水肿的发生中相辅相成，作用密不可分。机械力刺激所致肺损伤发生时，剪切力所致的直接作用发生较早，并有机械力感受器传导的生物学通路损伤机制的参与；而生物学损伤效应已被人们所熟知，即炎症反应、炎症介质级联散播效应，作用到效应细胞内各种信号转导途径，参与基因的调控，诱导细胞凋亡、损伤、迁移或各种表型的改变，继发于机械力破坏肺组织结构之后，与机械性损伤形成恶性循环，在VILI致肺水肿及肺损伤的发生中发挥了重要的作用。

（1）生物学损伤

①炎症反应

中性粒细胞参与了早期肺损伤炎症反应的发生，损伤肺组织中肺泡灌洗液（BALF）中中性粒细胞的计数与损伤程度成正比，且报道动物实验中中性粒细胞缺失小鼠的肺损伤程度减轻[6-9]。不同于其他组织，肺组织微循环中粒细胞的渗出需要更长的时间，且肺组织内炎症刺激作用于粒细胞表面G蛋白受体，降低了其变形能力，导致其在炎症早期聚集在肺组织间质内[10-14]，却不能进入肺泡腔内，因此机械通气致肺损伤的发生过程中炎症反应虽然发生较早，水肿仅局限于肺泡间质，水肿的进一步发展及肺泡性肺水肿的发生却有赖于肺泡屏障的破坏。

中性粒细胞的进一步趋化、聚集及粘附需要有选择素、整联蛋白及趋化因子的帮助。其中抗炎因子IL-22，通过胞内STAT磷酸化路径传递，减轻细胞损伤，增强细胞的抗牵拉能

力，体内吸入IL-22可以增加VILI模型小鼠的成活时间，并减轻肺水肿的发生[15]。肺泡巨噬细胞可能是调整机械通气致肺损伤（VILI）的主要致敏细胞。在ALI/ARDS早期病人，机械性牵张可导致中性粒细胞基质金属蛋白-9（MMP-9）明显升高，说明肺巨噬细胞在肺重塑过程中的重要作用

肺泡上皮细胞也是炎症介质释放的主要载体之一。肺组织Ⅰ型上皮细胞占90%，覆盖于肺泡表面，主要是扁平鳞状上皮，少量的Ⅱ型肺泡上皮细胞主要分泌表面活性物质，在Ⅰ型上皮细胞损伤时还具有增值转化为Ⅰ型上皮细胞的修复功能。体外实验表明，机械力牵张肺泡Ⅱ型上皮细胞可以诱导产生IL-8，TNF-α，IL-2，IL-6等，趋化激活各种炎症细胞到损伤部位发挥作用。肺泡上皮细胞分泌的大量炎症介质在VILI中也起着重要作用。Bethmann AN等在离体通气的肺组织中，检测出IL-6，TNF-α等mRNA的表达，推测在机械通气过程中，肺组织等能释放炎症因子导致VILI，及释放炎性因子入血。大潮气量机械通气可引起肺泡上皮细胞TNF-α表达增加，有报道称人类肺泡Ⅱ型上皮细胞A549能够产生IL-8，且体外actinomycinD能够阻断环形牵张作用于肺上皮细胞引起的IL-8 mRNA的表达。

肺组织内还有单核-巨噬细胞系统、肺血管内皮细胞及其他细胞等不仅参与肺泡结构的构成，组成肺水肿保护屏障，且在肺损伤发生过程中还具有肺泡上皮细胞及中性粒细胞等炎症介质释放的类似作用，参与肺内炎症反应的发生。

②酶与自由基

一氧化氮（NO）、活性氧族（ROS）在VILI肺水肿的发生机制中占有不可或缺的位置。机械牵张力刺激肺组织细胞产生NO[16,17]，NO可直接增加肺组织血管水通透性，机制与NO合成过程中氧自由基的产生有关[18-21]。除直接作用外，NO及ROS通过损伤细胞内cAMP通路降低肺泡上皮细胞的水清除能力（alveolar fluid clearance，AFC）[19]，磷酸肌醇3（PI-3）存在于中性粒细胞及肺组织内皮细胞，Faneli等研究证实PI-3参与了VILI肺水肿的发生，其机制与细胞内NO生成增多、cAMP通路损伤有关[24-26]；位于肺泡细胞胞膜上的小窝蛋白caveolin不仅参与胞内信号转导，且与一氧化氮合成酶NOS结合，调整其活化状态，也参与肺水肿的发生，且有报道称CO可以通过上调小窝蛋白的表达延缓肺损伤水肿的发生[21]。

③受体及信号通路

cAMP通路激活可以增加肺泡上皮细胞的水清除能力[22,23]。腺苷受体A2B、A2A通过cAMP通路增加AFC[27,28]，NF-κb抗体可以减轻VILI肺水肿的程度[29]，Rho-ROCK通路可以增加内皮细胞内骨架蛋白的生成，调节内皮细胞收缩，从而增加细胞间隙，增加肺血管水通透性[30]。活化蛋白C（activated protein C，APC）通过与内皮细胞膜上蛋白C受体（endothelial protein C receptor，EPCR）降低ROCK蛋白表达，减少肺内液体的漏出，从而保护肺组织水肿的发生[31]。

细胞核转录因子NF-κB (nuclear transcription factor-B,NF-κB)是一类关键性的核转录因子,通常以同源或异源二聚体非活性形式存在于几乎所有类型细胞的胞质 ,它与免疫细胞的活化、T和B淋巴细胞的发育 、应激性反应、细胞凋亡等多种细胞活动有关。NF-KB在VILI致肺水肿的发生中起了重要的作用。主要在信号转导中起“放大”作用。活化信号激活核因子NF-κB，增强TNF-α、IL-1、IL-6、IL-8、MIP-2、ICAM-1的转录，而TNF-α和IL-1，IL-8作为核因子NF-κB的细胞外刺激信号，再次激活核因子NF-κB，从而放大了初始的炎症信号。

（2）机械性损伤

机械通气所致的肺损伤，最直接的损伤来自容积伤及压力伤，可以诱导肺内上皮细胞及内皮细胞死亡或凋亡。肺维持正常的呼吸功能所需的潮气量在大鼠一般为6～10ml/kg，大于此潮气量的气体在相同的时间内进入肺组织内引起的容积及压力的增大是对肺组织有损伤的。肺生理学认为，肺组织有一定的顺应性，及在一定弹性阻力范围内可以自由呼吸运动。分子学研究表明，肺泡上皮细胞膜及血管内皮细胞膜本身具有一定承受牵张力作用的弹性变化幅度，即当对细胞进行3%幅度的牵拉时，约相当于正常呼吸时肺泡上皮细胞扩张的幅度，细胞膜展开其表面的皱褶，以增加表面积，不会对细胞膜造成损伤，且这个变化幅度不超过自身胞膜表面积的的3%～4%，牵张力大于此幅度，细胞将会发生应力衰竭（stress failure），即细胞膜断裂，细胞内容物外流。Hammerscbanidt试验证实，以较大幅度牵拉(表面积增加30%)体外培养的大鼠II型上皮细胞较小幅度牵拉(表面积增加13%)，细胞凋亡指数增加7%，Matuted等人亦论述了机械通气可以直接导致肺血管内皮细胞的凋亡。因此，机械力刺激作用直接作用于肺血管促使血管内皮细胞死亡或凋亡，为各种炎症细胞的渗出或漏出做了准备，也为炎症反应的进一步扩大提供了条件。

①屏障的破坏

肺组织内血-气屏障的作用除了参与肺泡气体交换外，内皮细胞、基底膜、表面活性物质组成肺内强大的抗拉力环。维持肺泡的正常通透性主要是由肺血管内皮细胞和肺上皮细胞间的致密连接（Tight junction，TJ）和粘附连接（Adherin junction，AJ）。而肺上皮细胞的致密连接对维持肺泡膜通透性更加重要[32]；有研究表明Occludin是第一个被发现的组成TJ最主要的成员；其与胞浆内ZO-1,2,3连接并相互作用后，才能使得相邻的细胞间occludin胞外环相互作用而形成TJ[33]。而VILI首先就是机械力牵张攻破肺泡膜屏障，继发引起细胞损伤或生物学损伤，肺水由血管内转移到肺泡腔内，加重水肿的发生，引起肺泡屏障的。

②机械力传导

近年来，有关研究机械牵张敏感的离子通道超家族—瞬时受体电位离子通道（transient receptor potential channals，TRPs）介导的机械通气致肺损伤[34-37]的机制越来越多。TRPs有六大类，其中研究最多的为TRPV（vanilloid）[38]，作用主要为在VILI致肺水肿的机制中感受机械牵张导致肺毛细血管通透性增加；TRPA1（ankyrin）亦为超家族中的一员，主要位于肺组织神经末梢，有研究称

其参与COPD或哮喘疾病中气道高反应性的形成。作为一种机械牵张敏感的离子通道，其是否参与机械牵张致肺损伤的发生机制尚有待探讨。

鸟嘌呤核苷酸交换因子（guanine nucleotide exchange factor，GEF）是一种G蛋白调节因子，参与细胞内微管蛋白的调节。Birukova等人发现体外机械牵张肺内皮细胞可以通过GEF-H1传递机械力刺激改变细胞骨架，导致内皮细胞屏障的破坏及肺水肿的发生[39]。

综上所述，对VILI的发生机制传统的认识虽说是因高气道压和(或)高容量通气导致吸气末肺组织过度扩张，以及萎陷的肺泡随机械通气发生周期性复张和萎陷所致，同时在肺机械性损伤的基础上肺内炎性细胞聚集，炎性介质释放和炎性反应信号转导的改变进一步促进了呼吸机相关肺损伤的发生和发展，早期机械牵张所致的肺损伤除机械性损伤外，还存在各种感受机械力刺激的信号转导途径的存在，导致早期炎症反应或早期肺泡膜结构环的器质性变化，进一步加重传统的炎症瀑布的爆发及肺水肿的发生。生物伤在VILI发生机制中作用固然重要，但是如果能遏制VILI的发生由机械伤进展到生物伤，阻断机械力损伤的进行，就能为机械通气致肺水肿的预防和治疗提出一种全新的方法。

参考文献

[1] Dreyfuss D, Saumon G. 1998. Ventilatorinduced lung injury: lessons from experimental studies. Am. J. Respir. Crit. Care Med. 157:294－323

[2] American Thoracic Society. 1999. International consensus conferences in intensive care medicine: Ventilator-associated lung injury in ARDS. Am. J. Respir. Crit. Care Med. 160:2118－24

[3] Tremblay LN, Slutsky AS. 1998. Ventilator induced injury: from barotrauma to biotrauma. Proc. Assoc. Am. Physicians 110:482－88

[4] Slutsky AS, Tremblay LN. 1998. Multiple system organ failure. Is mechanical ventilation a contributing factor? Am. J. Respir. Crit. Care Med. 157:1721－25

[5] Slutsky AS. 1999. Lung injury caused by mechanical ventilation. Chest 116:9S－15S

[6] Matthay MA, Eschenbacher WL, Goetzl EJ. (1984) Elevated concentrations of leukotriene D4 in pulmonary edema fluid of patients with the adult respiratory distress syndrome. J Clin Immunol 4: 479-483.

[7] Parsons PE, Fowler AA, Hyers TM, Henson PM. (1985) Chemotactic activity in bronchoalveolar lavage fluid from patients with adult respiratory distress syndrome. Am Rev Respir Dis 132: 490-493.

[8] Steinberg KP, Milberg JA, Martin TR, Maunder RJ, Cockrill BA, Hudson LD. (1994) Evolution of bronchoalveolar cell populations in the adult respiratory distress syndrome. Am.J.Respir.Crit Care Med. 150: 113-122.

[9] Abraham E, Carmody A, Shenkar R, Arcaroli J. (2000) Neutrophils as early immunologic effectors in hemorrhage- or endotoxemia-induced acute lung injury. Am J Physiol Lung Cell Mol Physiol 279: L1137-1145.

[10] Doerschuk CM, Allard MF, Martin BA, MacKenzie A, Autor AP, Hogg JC. (1987) Marginated pool of neutrophils in rabbit lungs. J Appl Physiol 63: 1806-1815.

[11] Tanaka H, Nishino M, Dahms TE. (2002) Physiologic responses to small emboli and hemodynamic effects of changes in deformability of polymorphonuclear leukocytes in isolated rabbit lung. Microvasc Res 63: 81-90.

[12] Doerschuk CM, Mizgerd JP, Kubo H, Qin L, Kumasaka T. (1999) Adhesion molecules and cellular biomechanical changes in acute lung injury: Giles F. Filley Lecture. Chest 116: 37S-43S.

[13] Drost EM, MacNee W. (2002) Potential role of IL-8, platelet-activating factor and TNF-alpha in the sequestration of neutrophils in the lung: effects on neutrophil deformability, adhesion receptor expression, and chemotaxis. Eur J Immunol 32: 393-403.

[14] Motosugi H, Graham L, Noblitt TW, et al. (1996) Changes in neutrophil actin and shape during sequestration induced by complement fragments in rabbits. Am J Pathol 149: 963-973.

[15] Hoegl S, Bachmann M, Scheiermann P.Am J Respir Cell Mol Biol. Protective Properties of Inhaled IL-22 in a Model of Ventilator-induced Lung Injury. 2010 May 12. [Epub ahead of print]

[16] Broccard AF, Feihl F, Vannay C, Markert M, Hotchkiss J, Schaller MD(2004) Effects of L-NAME and inhaled nitric oxide on ventilator-induced lung injury in isolated, perfused rabbit lungs. Crit Care Med 32:1872－1878

[17] Peng X, Abdulnour RE, Sammani S, Ma SF, Han EJ, Hasan EJ, Tuder R, Garcia JG, Hassoun PM (2005)Inducible nitric oxide synthase contributes to ventilator-induced lung injury. Am J Respir Crit Care Med

[18] Choi WI, Quinn DA, Park KM, Moufarrej RK, Jafari B, Syrkina O, Bonventre JV, Hales CA (2003)Systemic microvascular leak in an in vivo rat model of ventilator-induced lung injury. Am J Respir Crit Care Med 167:1627－1632

[19] Frank JA, Pittet JF, Lee H, Godzich M, Matthay MA (2003) High tidal volume ventilation induces NOS2 and impairs cAMP- dependent air space fluid clearance. Am J Physiol 284:L791－L798

[20] Ader F, Le Berre R, Lancel S, Faure K, Viget NB, Nowak E, Neviere R, Guery BP (2007) Inhaled nitric oxide increases endothelial permeability in Pseudomonas aeruginosa pneumonia. Intensive Care Med 33:503－510

[21] Beckman JS, Beckman TW, Chen J, Marshall PA, Freeman BA (1990) Apparent hydroxyl radical production by peroxynitrite: implications for endothelial injury from nitric oxide and superoxide. Proc Natl Acad Sci USA 87:1620－1624

[22] Michel CC, Curry FE (1999) Microvascular permeability. Physiol Rev79:703－761

[23] de Prost N, Dreyfuss D, Ricard JD, Saumon G (2008) Terbutaline lessens protein fluxes across the alveolocapillary barrier during high-volume ventilation. Intensive Care Med 34:763－770

[24] Patrucco E, Notte A, Barberis L, Selvetella G, Maffei A, Brancaccio M, Marengo S, Russo G, Azzolino O, Rybalkin SD, Silengo L, Altruda F, Wetzker R, Wymann MP, Lembo G,Hirsch E (2004) PI3 Kgamma modulates the cardiac response to chronic pressure overload by distinct kinase-dependent and －independent effects. Cell 118:375－387

[25] Perino A, Ghigo A, Damilano F, Hirsch E (2006) Identification of the macromolecular complex responsible for PI3 Kgamma-dependent regulation of cAMP levels. Biochem Soc Trans 34:502－503

[26] Lionetti V, Lisi A, Patrucco E, De Giuli P, Milazzo MG, Ceci S, Wymann M, Lena A, Gremigni V, Fanelli V, Hirsch E, Ranieri VM (2006) Lack of phosphoinositide 3-kinase-gamma attenuates ventilator-induced lung injury. Crit Care Med 34:134－141

[27] Chen CM, Penuelas O, Quinn K, Cheng KCProtective effects of adenosine A2A receptor agonist in ventilator-induced lung injury in rats. Crit Care Med. 2009 Jul;37(7):2235-41

[28] Eckle T, Grenz A, Laucher S. A2B adenosine receptor signaling attenuates acute lung injury by enhancing alveolar fluid clearance in mice. J Clin Invest. 2008 Oct;118(10):3301-15.

[29] Chiang CH, Pai HI, Liu SL. Ventilator-induced lung injury (VILI) promotes ischemia/reperfusion lung injury (I/R) and NF-kappaB antibody attenuates both injuries. Resuscitation. 2008 Oct;79(1):147-54. Epub 2008 Jun 26.

[30] Shikata Y, Rios A, Kawkitinarong K, DePaola N, Garcia JG, Birukov KG. Differential effects of shear stress and cyclic stretch on focal adhesion remodeling, site-specific FAK phosphorylation, and small GTPases in human lung endothelial cells. Exp Cell Res 304: 40－49, 2005.

[31] Finigan JH, Boueiz A, Wilkinson E,Activated protein C protects against ventilator-induced pulmonary capillary leak. Am J Physiol Lung Cell Mol Physiol. 2009 Jun;296(6):L1002-11. Epub 2009 Apr 10.

[32] Hartsock A, Nelson WJ. Adherens and Tight Junctions: Structure, Function and Connections to the Actin Cytoskeleton. Biochim Biophys Acta. 2008, 1778(3): 660－669.

[33] Seth A, Sheth P, Elias BC, Rao .Protein phosphatases 2A and 1 interact with occludin and negatively regulate the assembly of tight junctions in the CACO-2 cell monolayer. J Biol Chem. 2007, 282(15):11487-98.

[34] Pérez Fontan JJ.On lung nerves and neurogenic injury. Ann Med.2002,34:226-40. Review.

[35] Dib M, Zsengeller Z, et.al. A paradoxical protective role for the proinflammatory peptide substance P receptor (NK1R) in acute hyperoxic lung injury.Am J Physiol Lung Cell Mol Physiol. 2009,297:L687-97.

[36] O'Connor TM, O'Connell J, et.al. The role of substance P in inflammatory disease. J Cell Physiol. 2004,201:167-80. Review.

[37] Nassenstein C, Kwong KK, et al. TRPA1 expression and function in vagal afferent nerves innervating mouse lungs. J Physiol 2008,586:1595－604.

[38] Kazutoshi Hamanaka, Ming-Yuan Jian,et al. TRPV4 initiates the acute calcium-dependent permeability increase during ventilator-induced lung injury in isolated mouse lungs. Am J Physiol Lung Cell Mol Physiol 2007,293: L923－L932

[39] Birukova AA, Fu P, Xing J,Mechanotransduction by GEF-H1 as a novel mechanism of ventilator-induced vascular endothelial permeability. Am J Physiol Lung Cell Mol Physiol. 2010 Jun;298(6):L837-48. Epub 2010 Mar 26.

书讯

复旦大学附属肿瘤医院麻醉科陈志扬著的《临床麻醉难点解析》一书，已由人民卫生出版社出版，书中阐述了临床麻醉医生经常遇到的难点，如困难气管插管、硬膜外阻滞进展、双腔管原则、麻醉禁忌症（停手术）、麻醉与催眠术、心肺复苏失败的原因、把植物人唤醒、手术后猝死、癌痛治疗等。30元/本，汇款至200032，上海市徐汇区东安路270号复旦大学肿瘤医院麻醉科 陈志扬收

联系电话：18918818399

姚翔燕 张加强 孟凡民
河南省人民医院麻醉科 450003

摘要

仰卧位低血压综合征（supine hypotensive syndrome，SHS）是剖宫产术中常见的并发症，严重的低血压可能导致产妇恶心呕吐，甚至意识丧失，而且低血压还可以造成子宫胎盘血流灌注的急速下降，妨碍胎盘的血气交换，引起胎儿缺氧、酸中毒甚至中枢神经系统损伤等严重后果。本文就预防剖宫产术仰卧位低血压综合征的研究进展作一综述。

关键词：剖宫产；仰卧位低血压综合征；椎管内麻醉

责任作者及联系方式：孟凡民，E-mail：mfmsy@tom.com

预防剖宫产术仰卧位低血压综合征的研究进展

Progresses in the Research of Preventing Supine Hypotension Syndrome during Cesarean Section

Xiang-yan Yao, Jia-qiang Zhang, Fan-min Meng

Department of Anesthesia, the People's Hospital, Henan Province, China 450003

Abstract

Supine hypotension syndrome is a common adverse reaction during cesarean section after anesthesia. Anesthesia causes blood vessels dilate and blood vessels reflux disorder of lower body blood vessels. Severe hypotension may lead to maternal nausea, vomiting and even loss of consciousness. Hypotension can cause rapid decline of the utero-placental blood flow with the rapid decline, exchange of impede the placenta blood gas and serious consequences of fetal hypoxia, acidosis even the central nervous system injury. This review summarizes the current knowledge on this subject.

Key Words: Cesarean section; Supine hypotension syndrome; Intravertebral anesthesia

Corresponding Author: Fan-ming Meng,E-mail:mfmsy@tom.com

产妇于临产期取平卧位时发生仰卧位低血压综合征的约占50%，在椎管内麻醉下剖宫产术时发生率更高达55%～90%[1]。这不仅对产妇本身有不良影响，最重要的是产妇低血压会引起胎儿胎盘灌注降低，危害胎儿，引起胎儿缺氧、酸中毒甚至中枢神经系统受损[2,3,4]。因此，如何预防椎管内麻醉后低血压，在剖宫产手术中显得尤为重要，这也是近年来产科麻醉研究的一个热点。

一、体位干预

临床上最常用的方法是椎管内麻醉实施后手术床向左倾斜、向左推移子宫或产妇的腰椎下放楔形物[5]，从而使子宫向左侧倾斜，使子宫避开对下腔静脉、腹主动脉的压迫，增加回心血量，减轻低血压的程度。Mendonca[6]等人发现腰硬联合麻醉下左侧卧位与左侧倾斜12° 相比，低血压的发生率明显低于后者；但是Rucklidge等[7]对比了腰麻后产妇左侧卧位与左侧倾斜15° 15min，认为两种方法低血压的发生率、新生儿Apgar评分、脐带血PH值的差异没有统计学意义；于是有学者[7, 8, 9]通过改变产妇的纵向体位来预防仰卧位低血压综合征，认为头高脚低位可以防止麻醉平面过高，并且头高脚低位可以减少腹腔脏器对膈肌的挤压，从而减轻膈肌对肺的压迫，增加了肺的顺应性。但是这种体位会造成下肢静脉回心血量的进一步减少，从而使低血压的发生率和严重程度增加，并且头高足低位容易使麻醉平面过低，从而导致麻醉效果不满意。

国内外近几年集中于改变麻醉诱导时的体位来预防仰卧位低血压综合征，但是关于左侧卧位或右侧卧位的研究没有发现哪一种体位更有优势。而对比坐位与侧卧位，过去的研究单纯采用腰麻，蛛网膜给药后产妇即仰卧，由于注药与恢复到仰卧位的时间间隔极短，造成两种体位低血压的发生没有明显不同。Coppejans等[10]对比了在剖宫产CESA时采用侧卧位和坐位时对平面及血压的影响，结果显示坐位可减少严重低血压的发生率，这可能是由于蛛网膜下腔注药后要经过一段时间放置和固定硬膜外导管，从而影响腰麻的阻滞特征，进而影响低血压的发生率。但是这方面的研究结果并不一致，腰麻诱导时和腰麻后体位的不同对血流动力学的影响主要是腰麻阻滞平面和静脉回心血量两方面。坐位诱导可降低阻滞平面，使低血压的发生率降低，但是坐位也可能使下肢静脉回流受阻从而导致低血压的发生。所以腰麻诱导时和腰麻后哪种体位能更好的预防仰卧位低血压综合征还要根据麻醉医生采取的其他更有效的预防措施。

二、使用升压药

麻醉后当血压下降严重时往往需要用升压药维持血压，过去的研究是低血压发生后才静注血管收缩剂，但低血压稳定之前将不可避免的存在一段时间，对产妇或胎儿构成一定的威胁。近年来的研究认为麻醉前预先静脉注射升压药能降

低低血压的发生率，麻黄碱对α、β_1肾上腺受体均有激动作用，使心肌收缩力增强、心输出量增加、心率增快、血压升高。但近来国外研究发现麻黄碱可引起胎儿脐动脉血pH值下降和碱剩余的下降，而且有一定的剂量依赖性。另外麻黄碱快速耐药,低剂量时不能很好的预防低血压，而高剂量时又常常引起高血压，所以其仍不能成为一个最佳的选择。而且对于有妊娠高血压综合征、甲状腺功能亢进、心动过速、心脏疾患的孕妇应慎用或禁用麻黄素。

甲氧明是一种强力的α受体兴奋剂,可使小动脉收缩,全身血管阻力增加,心肌血流量增加,但是对心肌无兴奋作用,不使心肌耗氧量增加,这样有利于心脏的保护和心肌缺氧的改善。术中患者的低血压,恶心呕吐发生率降低,血压、心率平稳。不过随着甲氧明用量的加大,虽然血压更为平稳,但心率减慢的趋势更为明显,因此其临床应用剂量有待进一步探讨。

三、预扩容

以往大多数文献认为预防性输入晶体液为安全有效的方法,但输入大量晶体液预防低血压效果并不十分令人满意。Tamilselvan等[11]的研究结果是麻醉前预扩容，用多普勒测心输出量有所增加，但是不能预防腰麻后血压的下降。因为任何一种晶体液输入体内后约75%弥散进入组织间隙,在血管内半衰期不到15min,其扩容功效仅是一过性的,而且有学者的研究还表明大量输注晶体液可使部分产妇子宫收缩减弱。有人主张麻醉前预先输胶体液更能维持术中的循环稳定[12]，胶体液能明显增加循环血量、增加心输出量，对维持腰麻动力学的稳定非常有效，可减少腰麻后严重低血压的发生率。其扩容的优点主要反映在降低产妇很强的交感神经张力，降低子宫血管阻力，增加子宫胎盘血流。但是Teoh等[13]研究发现预充胶体液时，在麻醉后5min心输出量和每搏量是增加的，但是不能持续10min，并且产妇低血压的发生率与预充晶体没有显著差异。椎管内麻醉前预先输注一定量的晶体液或胶体液，是预防麻醉后低血压的常见措施，但并不能完全预防麻醉所引起的低血压[14]。不过合理的给予容量治疗可有效补充循环血量,维持生命体征相对平稳,降低仰卧位低血压的发生率。从理论上讲，为预防麻醉期间低血压,胶体液是更为理想的选择。

四、减少局麻药的剂量或采用等比重局麻药

布比卡因用于剖宫产给药剂量差别较大，根据报道从7.5mg至15.0mg之间不等。产妇生理结构发生改变:脑脊液蛋白质含量减少、密度下降，脊柱弯曲度改变,腹压与脑脊液压力升高,硬膜外腔和蛛网膜下腔容积缩小,以及对局麻药敏感性增加等，致使布比卡因常规剂量12mg脊麻时产生更为广泛的麻醉平面。多数研究者认为减少蛛网膜下腔局麻药的剂量，可以有效地减少产妇低血压的发生率。自从发现局麻药与吗啡类药物鞘内注射具有协同镇痛作用之后，已经证明了低剂量的布比卡因复合吗啡类药物腰麻能使腰麻后低血压的发生率显著降低，使麻醉效能增强。Van等[8]的研究结果显示，蛛网膜下腔注入高剂量布比卡因（9.5mg）的产妇低血压的发生率明显高于注入低剂量布比卡因（6.5mg）的产妇，由于两组产妇都复合了2.5μg的舒芬太尼，麻醉效果都满意，只是减少局麻药剂量缩短了有效麻醉维持时间，不过对于剖宫产手术来说时间也足够了，如果有意外需要延长手术时间，可以通过联合的硬膜外阻滞导管追加局麻药来完善麻醉效果。由此可知布比卡因剂量越小低血压的发生率越低。

重比重局麻药腰麻潜伏期短，阻滞完善，但其对血流动力学干扰过大，影响子宫胎盘血液灌流，影响胎盘的气体交换等。有研究证明[15,16,17]：脊麻等比重溶液与重比重液相比无上浮或下沉的特性，易于停留在麻醉药被注入部位的脊髓腔内,麻醉平面容易控制,病人的血流动力学稳定，这对产科病人是十分有利的。

五、减慢注药速度或改变麻醉药物

注药速度影响局麻药在蛛网膜下腔的扩散，从而影响阻滞平面，进而影响低血压的发生。腰麻的注药速率一般为1mL/5s,注药的速度越快,麻醉平面越广；相反,注药速度越慢,药物越集中,麻醉范围越小。减缓注药速率用于控制腰麻平面，从而预防低血压的报道已不少。Simon等的研究采用重比重布比卡因10mg+舒芬太尼2μg+吗啡200μg共4ml进行腰麻，结果显示，慢速注药组低血压的发生率明显低于快速注药组，并且麻黄素的使用量也明显少于快速组。但是Singh等[18]采用重比重布比卡因12mg+吗啡200μg共4ml进行腰麻，表明注药速度并不影响腰麻的阻滞平面和低血压的发生率。二者的研究快速注药组都是4s，但是慢速注药组Simon等的研究是120s，Singh等的研究是40s，由此提示注药速度只有慢到一定程度才可能预防低血压。

布比卡因是一种长效酰胺类局麻药，具有起效快、麻醉作用强、作用时间长等优点，是腰麻的常用局麻药，但布比卡因腰麻用于剖宫产术时，对血压影响较大，对产妇和胎儿都不利。罗哌卡因的化学结构及药理学特性与布比卡因相似，是一种新型长效酰胺类局麻药,半衰期短，脂溶性低，对中枢神经系统和心脏的毒性明显低于布比卡因，而且对新生儿也是安全的。腰麻时同等剂量的罗哌卡因和布比卡因相比，罗哌卡因低血压的发生率较低。提示罗哌卡因用于腰麻时大部分产妇的血流动力学改变较小，循环相当平稳， 可能与以下两点有关：运动阻滞起效时间长,对运动神经阻滞效果慢而弱， 完善的麻醉效果出现较迟[19]，有利于患者机体的代偿。

六、麻醉前预测或注药后低血压的早期检测

如果麻醉前能预测哪些产妇腰麻后容易发生仰卧位低血压综合征，就可以针对这些高危产妇积极地采取有效地预防措施。这就要求麻醉医生术前访视要询问患者孕期中舒适卧位，是否存在仰卧位低血压综合征,做到心中有数,如术前不了解清楚， 术中出现仰卧位低血压按常规处理,会导致严重后果，因为极少数孕妇子宫严重左旋,适合右侧卧位。产妇进入手术室麻醉前，最好分别测量左侧卧位和仰卧位的血压和心

率，仰卧位应激试验预测脊麻后低血压的敏感度是69%、特异度是92%[12]。如果连续两次测量产妇仰卧位的心率比侧卧位时的基础值增加快于10次/分，或者连续两次测量产妇仰卧位的收缩压比侧卧位时的基础值降低大于15mmHg,则可以诊断为仰卧位低血压综合征，就应该采取有效地干预措施。对于巨大子宫或经过常规综合处理无好转,应迅速果断地改为双手捧托子宫法，将整个子宫捧托起来(消毒铺巾后由手术助手协助完成),可迅速解除对大血管压迫,因为此手法易于疲劳，可由两人交替进行,直至胎儿娩出，此手法在严重仰卧位低血压综合征中极为重要,绝不可忽视。

脊麻从注药到发生仰卧位低血压有几分钟的时间间隔，而临床常用的间断无创血压监测存在明显的滞后性，如果能在注药后及时发现产妇低血压的早期征象，采取积极地措施进行处理就能避免出现严重的低血压。Berlac等采用经脑近红外线光谱分析法监测脑氧饱和度（cerebral oxygenation saturation，ScO_2）来早期发现脊麻后的低血压，研究结果表明，ScO_2降低5%可以作为一个很好的早期检测指标，从ScO_2降低5%到发生低血压（收缩压下降25%）的平均时间为81s,因此当ScO_2降低到5%时就立即采取预防措施，避免产妇发生仰卧位低血压综合征。

总之，任何一种麻醉方法和药物或预防措施都各有利弊、长短，对产妇和胎儿均可能会带来危险。因此如何使剖宫产麻醉达到效果确切，保证产妇的安全，同时对胎儿的抑制又最小，这是产科医生和麻醉医生所共同面临的一大课题。

参考文献

[1] Mercier FJ,Bonnet MP,Dela Dorie A,et al. Spinal anaesthesia for caesarean section: fluid loading,vasopressors and hypotension. Ann Fr Anesth Reanim,2007,26（7）:688-693.

[2] Cyna AM, Andrew M, Emmett RS, et al. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev, 2006, 18（4）: CD002251.

[3] Reynolds F,Seed P T. Anaesthesia for Caesarean section and neonatal acid-base status:a mate-analysis. Anaesthesia,2005,60（7）:636.

[4] Gonc é -Mellgren A,Tamayo-Rojas O, S á nchez-Martnez M, et al. Severe neonatal encephalopathy, secondary to a prolonged vasovagal episode in a woman 31 weeks pregnant. Rev Neurol, 2002,34（9）:833-835.

[5] Zhou ZQ, Shao Q, Zeng Q, et al. Lumbar wedge versus pelvic wedge in preventing hypotension following combined spinal epidural anaesthesia for caesarean delivery. Anaesth Intensive Care,2008,36（6）:835-839.

[6] Mendonca C, Griffiths J, Ateleanu B, et al. Hypotension following combined spinal- epidural anaesthesia for Caesarean section:left lateral position vs tilted supine position. Anaesthesia, 2003,58（5）:428-431.

[7] Rucklidge MW, Paech MJ, Yentis SM . A comparison of the lateral, Oxford and sitting for performing combined spinal-epidural anaesthesia for elective Caesarean section. Anaesthesia, 2005, 60（6）:535-540.

[8] Van de Velde M, Van Schoubroeck D, Jani J, et al. Combined spinal-epidural anesthesia for cesarean delivery: dose-dependent effects of hyperbaric bupivacaine on maternal hemodynamics.Anesth Analg, 2006, 1（103）:187-190.

[9] Russell R, Ropat M, Richards E, et al. Combined spinal-epidural anaesthesia for caesarean section: a randomezed comparison of Oxford, lateral and sitting positions. Int J Obstet Anesth, 2002, 111（3）:190-195.

[10] Coppejans HC, Hendrickx E, Goossens J, Vercauteren MP. The sitting versus right lateral position during combined spinal-epidural anesthesia for cesarean delivery: block characteristics and severity of hypotension. Anesth Analg, 2006,102（3）:243-247.

[11] Tamilselvan P, Fernando R, Bray J, et al. The effects of crystalloid and colloid preload on cardiac output in the parturient undergoing planned cesarean delivery under spinal anesthesia: a randomized trial. Anesth Analg, 2009,109（6）:1916-1921.

[12] Dahlgren G,Granath F,Wessel H,et,al.Prediction of hypotension during spinal anesthesia for Cesarean section and its relation to the effect of crystalloid or colloid preload.Int J Obstet Anesth,2007,16（2）:128-134.

[13] Teoh WH, Sia AT. Colloid preload versus coload for spinal anesthesia for cesarean delivery: the effects on maternal cardiac output. Anesth Analg, 2009,108（5）:1592-1598.

[14] Morgan DJ, HalPern SH, Tarahis J, et al. The effects of an increase of central blood volume before spinal anesthesic for cesarean delivery:a qualitative systennic review. Anesth-Analg, 2001, 92（4）:997-1005.

[15] King HK,Wood L, Steffens Z, et al.Spinal anesthesia for cesarean section: isobaric versus hyperbaric solution. Acta Anaesthesiol Sin,1999, 37（2）:61-64.

[16] Nasuhara H, Yokoyama K.The influence of baricity on differential blockade with 0.5% bupivacaine spinal anesthesia.Masui,2001,50（9）: 977-985.

[17] Malinovsky JM, Renaud G,Le Corre P, et al. Intrathecal bupivacaine in humans: influence of volume and baricity of solutions.Anesthesiology, 1999, 91（5）:1260-1266.

[18] Singh SI, Morley-Forster PK, Shamsah M,et al. Influence of injection rate of hyperbaric bupivacaine on spinal block in parturients: a randomized trial. Can J Anaesth,2007,54（4）: 290-295.

[19] Coppejans HC, Vercauteren MP. Low-dose combined spinal-epidural anesthesia for cesarean delivery: a comparison of three plain local anesthetics. Acta Anaesthesiol Belg, 2006,57（1）:39-43.

中国康复医学会第八届全国康复治疗学术年会

中国康复医学会第八届全国康复治疗学术年会定于2011年12月2-4日在四川省成都市召开。大会由中国康复医学会康复治疗专业委员会主办，川港康复中心及四川省八一康复中心共同承办。会议将围绕主题“抓住机遇，携手西部，团结进步，创新发展”进行学术交流，着重学习推广国际系统规范的康复治疗流程，了解国内外康复治疗新理念、新技术、新进展，届时将邀请国内外著名康复专家进行专题讲座。欢迎广大康复医学科、理疗科、骨科、神经内科、神经外科、老年医学科、儿科、创伤科、运动医学科、疼痛科、中医科、针灸科、推拿科及其他相关基础与临床学科的医师、治疗师、护士踊跃投稿参会。

一、征文范围

神经康复、脊柱与骨关节创伤康复、心肺康复、儿童康复、运动感觉功能障碍康复；残疾、神经电生理、言语和吞咽、认知功能和心理、心肺功能、日常生活自理和生活质量、康复结局预测与评定等；康复治疗技术与方法、治疗流程和机理研究；康复工程应用及相关研究、康复实践方面的成功经验;康复理疗仪器设备的研制与应用等研究；康复治疗师学历教育、在职培训及管理；康复护理及相关研究；社区康复、康复医学学科建设及康复网络建设等。

二、征文要求

提交不超过1000字的摘要。论文应为未公开发表的文章，应征论文必须具有科学性、先进性、实用性、创新性，数据真实可靠，文字准确精练，每篇论文应按照题目、作者、作者单位、摘要、关键词、正文的顺序撰写，如为基金项目，请在文后注明基金来源及编号。来稿请附个人简历（100字内）。

赵为禄 文 刚 雷恩骏
徐 琳 闵 佳
南昌大学第一附属医院麻醉科，江西南昌 330006

摘要

目的：探讨小剂量右美托咪啶应用于高龄患者全身麻醉的安全性，以及镇静效果。方法：100例ASAII～III级高龄患者，采用丙泊酚、芬太尼、阿曲库铵缓慢静脉注射进行麻醉诱导气管插管后，静脉输注小剂量右美托咪啶0.8～1ug/kg（输注时间＞10min）。记录患者的生命体征及苏醒时间。结果：静脉输注右美托咪啶后，患者SBP、DBP均有一定程度升高，与使用前比较差异无显著性（P＞0.05）；HR呈显著下降，与使用前比较差异有显著性（P＜0.05）；术中血流动力学稳定；麻醉苏醒期病人安静、耐受气管导管能力好，循环较稳定，无1例发生术中知晓和术后认知功能障碍。结论：小剂量右美托咪啶应用于高龄患者全身麻醉，镇静作用充分，可引起短暂血流动力学变化。

关键词：小剂量；右美托咪啶；高龄病人；全身麻醉；镇静

小剂量右美托咪啶用于100例高龄患者全身麻醉的临床观察

Clinical Observation on 100 Elderly Patients Underwent General Anesthesia with Small dose Dexmedetomidine

Wei-lu Zhao, Gang Wen, En-jun Lei, Lin Xu, Jia Min
Department of Anesthesia, the first hospital affiliated to Nanchang University, Nanchang, Jiangxi province, 330006

Abstract

Objective: To investigate the safety and the sedative effects of small dose dexmedetomidine used in elderly patients underwent general anesthesia.

Methods: 100 ASAII ~ III elderly patients underwent general anesthesia, after propofol, fentanyl, atracurium intravenous induction and tracheal intubation, intravenous infusion of small doses dexmedetomidine 0.8 ~ 1ug /kg (infusion time > 10min).

Results: SBP, DBP, had a certain degree of increase after intravenous infusion of dexmedetomidine, but not reach the statistical differences (P>0.05); HR was significantly decreased (P<0.05). During the recovery period, patients had high tolerance to the intubation, while without postoperative cognitive dysfunction.

Conclusion: Small dose of dexmedetomidine used in elderly patients underwent general anesthesia showed adequate sedation effect, with transient hemodynamic variability.

Key Words: small dose; dexmedetomidine; senile patient; general anesthesia; sedative

高龄患者全身麻醉后易发生认知功能障碍，成为临床麻醉难题之一。右美托咪啶具有良好的镇静、催眠和镇痛作用，其引起的镇静作用类似正常睡眠[1,2]，已广泛应用于临床镇静治疗。我院自2011年2月～2010年7月，对100例高龄全身麻醉病人于气管插管后小剂量缓慢静脉注射右美托咪啶（输注时间＞10min），取得了麻醉苏醒期病人安静、耐受气管导管能力好，循环较稳定，无术中知晓和术后认知功能障碍发生等效果。现报告如下：

一、资料和方法

1. 一般资料

选择无严重心脏疾病，高龄全身麻醉病人100例，ASA2～3级（ASA2级67例，ASA3级33例），男56例，女44例；年龄75-85岁，平均77.4岁。所有病例中35例合并一个或多个系统疾病；其中合并高血压病30例，糖尿病8例；慢性支气管炎并肺气肿7例；陈旧性脑出血2例；手术时间65.3±3.8min。

2. 麻醉方法

本组患者入手术室后，采用PHILIP监测仪常规监测收缩压（SBP）、舒张压（DBP）、心率（HR）、血氧饱和度（SPO_2）、心电图（ECG），常规建立静脉通路。麻醉诱导：丙泊酚1～1.5mg/kg、芬太尼2～3ug/kg、阿曲库铵0.6～0.8mg/kg。气管插管循环稳定后，将小剂量右美托咪啶（批号：10020334，江苏恒瑞医药股份有限公司）0.8～1ug/kg加入100ml生理盐水中静脉输注（输注时间＞10min）。麻醉维持：丙泊酚1.5～2.5mg/kg/h、瑞芬太尼8～10ug/kg/h、阿曲库铵0.4～0.5mg/kg/h微量泵静脉输注，术中依据病人对手术刺激的反应，酌情调整输注速度。手术结束前5min停止输注麻醉药物，手术结束后送入麻醉苏醒室，完全清醒后，拔除气管导管送回原病房。

3. 观察指标

监测麻醉前、右美托咪啶使用前、右美托咪啶使用后5min、麻醉苏醒期SPO_2、HR、SBP、DBP、ECG，麻醉苏醒时间。

4. 统计学处理

采用SPSS统计软件包进行统计分析，数据用均数±标准差（x±s）表示，组内比较采用t检验、P＜0.05为差异有显著性，计数资料以%表示。

二、结果

1.小剂量右美托咪啶静脉缓慢注射后与注射前BP、SPO_2、HR比较静脉输注小剂量右美托咪啶后，患者SBP、DBP均有一定程度升高，与使用前比较差异无显著性（P＞0.05）。HR呈显著下降，与使用前比较差异有显著性（P＜0.01）。SPO_2、各时段无显著变化（P＞0.05）。结果见表1。

2.小剂量右美托咪啶致循环严重变化例数，镇静效果以及术毕苏醒时间静脉输注小剂量右美托咪啶后2例（2%）发生严重短暂高血压；无1例发生术中知晓及术后认知功能障碍（0%），手术结束后10min内96例（96%）完全清醒；全部患者均顺利完成手术，无1例死亡。结果见表2。

表1 麻醉前、右美托咪啶使用前、右美托咪啶使用后5min、麻醉苏醒期SBP、DBP、HR、SPO_2变化

项目	麻醉前	右美托咪啶使用前	右美托咪啶使用后5min	麻醉苏醒期
SBP（mmHg）	125.3±11.63	113.8±11.36[1)]	138.2±15.75[1)]	118.2±10.61[1)]
DBP（mmHg）	77.3±8.31	72.8±9.69[1)]	88.68±11.65[2)]	69.65±8.63[1)]
HR（bpm）	72.3±7.4	69.1±10.3	53.8±7.8[2)]	66.9±8.2
SPO_2（%）	96.2±0.5	99.3±0.4	99.4±0.5	97.3±0.8

注：1）与麻醉前比较，差异无显著性，P＞0.05；2）与麻醉前比较，差异有显著性，P＜0.01

表2 术中严重高血压、严重低血压例数、术毕苏醒时间、术中知晓、术后认知功能障碍例数

	严重高血压	严重低血压	术毕10min内苏醒	术中知晓	术后认知功能障碍
100例	2	0	96	0	0

三、讨论

随着我国老龄化社会到来和医疗技术不断提高，高龄患者在全身麻醉下进行手术治疗越来越多，围术期并发症发生率相当高[3]，尤以发生认知功能障碍为常见[4]。但也有研究表明[5]高龄住院手术病人不是麻醉手术禁忌证，关键在于正确实施麻醉，围术期密切监测与处理，以及预防麻醉并发症。

右美托咪啶作用于脑干蓝斑核2A受体产生镇静作用，其镇静深度与血浆药物浓度呈正相关[6]。给药后可发生剂量依赖性心动过缓和剂量双向性血压变化，即大剂量时血管平滑肌收缩，呈高血压表现，小剂量时阻滞交感神经表现为低血压[7]。右美托咪啶降低了交感神经系统活性，在血容量过低、糖尿病或慢性高血压以及老年患者中可发生更多的血压过低和/或心动过缓、窦性停博[8]。本研究观察到即使小剂量、静脉缓慢注射右美托咪啶，患者短时间内仍可发生心率减慢甚至心动过　缓。但多数患者只发生短暂、轻度血压升高，并未发生严重低血压。因此，控制右美托咪啶的使用剂量和输注速度[9]对于高龄病人十分重要。

本研究采用气管插管后小剂量缓慢静脉注射右美托咪啶（输注时间＞10min），较好地预防了严重高血压和低血压的发生，有助于高龄患者循环的相对稳定。同时，针对发生的心动过缓、暂时性高血压，并未采用静脉注射阿托品和降压药物进行处理。因为小剂量右美托咪啶并未引起严重血流动力学改变，多在短时间内病人循环功能即可稳定。

丙泊酚镇静作用好，苏醒迅速而平稳，醒后无宿醉感、恶心及呕吐发生率低等优点[10]，且对认知功能无影响[10]。研究表明右美托咪啶与丙泊酚联合用药，患者情况稳定，无躁动，且明显加深患者的镇静程度，但苏醒时间会有所延长[12]。本研究观察到患者术后并未发生苏醒时间延长。可能与右美托咪啶小剂量使用，丙泊酚、瑞芬太尼、阿曲库铵快速代谢相关。多数患者麻醉苏醒后可继续良好睡眠状态，呼之能应，并未发生明显呼吸抑制。

综上所述，小剂量右美托咪啶应用于高龄患者全身麻醉，镇静作用充分，避免了术中知晓术后认知功能障碍的发生。但可引起心率减慢甚至心动过缓，以及短暂轻度的血压升高。

参考文献

[1] Nelson LE，Lu J，Guo T，Saper CB，Franks NP，Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003;98:428-436.

[2] Hsu YW，Cortinez LI，Robertson KM，Keifer JC，Sum-Ping ST，Moretti EW，Young CC，Wright DR，Macleod DB，Somma J. Dexmedetomidine pharmacodynamics: part I: crossover comparison of the respiratory effects of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology 2004;101:1066-1076.

[3] Eclited by Ronalod D Miller M.D Anaesthesia 5th edition Volum Sci-ence Press Harcourt Asia.Churchill Livingstone，2001，2140-2155.

[4] 王伟朋，李立环. 临床麻醉学[M]. 北京：人民卫生出版社，2004：1090.

[5] 古博,蒋夏.80岁以上高龄病人麻醉109例分析.中国麻醉与镇痛杂志[J].2000，（2）:94-97.

[6] Ebert TJ，Hall JE，Barney JA，et al. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology，2000，93(2):382-394.

[7] Paris A，Tonner PH. Dexmedetomidine in anesthesia. In: Paris A，ed. Curr Opin Anesthesiol[M]. Germang: lippincott Williams &Wilkins 2005:412-418.

[8] Bloor BC，Ward DS，Belleville JP，Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemo-dynamic changes. Anesthesiology 1992;77:1134-1142.

[9] Gomez-Vazquez ME. Hernandez-Salazar E，Hernandez-Jimenez A，et al. Clinical analgesic efficacy and side effects of dexmedetomidine in the postoperative period after arthroscopic knee surjery. J Clin Anesth，2007，19:576-582.

[10] Carlsson U，Grattidge P.Sedation for upper gastrointestinal endoscopy：a comparative study of propofol and midazolam［J］.Endoscopy，1995，27：240-243.

[11] 赵宏,孙艺丹,尹极峰. 丙泊酚用于无痛胃镜检查对认知功能的影响. 临床麻醉学杂志[J].2007，23（4）：283.

[12] 佘守章，李慧玲，许学兵，等. 右旋美托咪啶的镇静效应及其对全麻深度的影 响. 临床麻醉学杂志，2006，22（1）：10-12.

生物信息与生物医学工程国际学术会议

会议日期：2012.5.17-2012.5.20

中国 上海

主办单位：IEEE Eng. in Medicine and Biology Society, USA

会议主席：Prof. Kuo-Chen Chou

会议背景：第六届IEEE生物信息与生物医学工程国际学术会议将于2012年5月17日至20日在中国上海召开。会议由IEEE医学与生物工程学会、武汉大学、同济大学、戈登生命科学研究所、工程信息研究院等多所高校和研究机构共同举办。此次会议将聚集亚太、北美、欧洲乃至全世界知名专家及学者，共同探讨生物信息和生物医学工程领域的新成果及新议题。

ICBBE迄今已经成功召开五届，每届均在会后短期内被Ei核心检索。

余志中 万献尧

大连医科大学附属一院重症医学科 116011

摘要

目的：观察乳酸、D-二聚体、降钙素原（PCT）等指标在感染性休克患者中的变化和与急性生理和慢性健康评分（APACHE）Ⅱ的相关性及在预后评估中的作用。方法：回顾性分析2009年9月1日~2010年9月1日大连医科大学附属第一医院重症医学科收治的44例感染性休克患者入ICU时接受治疗前D-二聚体、乳酸、PCT等指标，并计算APACHEⅡ，统计患者病程中器官衰竭发生数目。比较生存组与死亡组APACHEⅡ、D二聚体、乳酸、PCT等指标有无差异，分析D-二聚体、乳酸与APACHEⅡ和最终器官衰竭数目的相关性。结果：44例感染性休克患者生存14例，死亡30例，病死率68.18%。两组患者APACHEⅡ、D-二聚体、乳酸经t检验差异均有统计学意义，PCT经两独立样本等级资料秩和检验差异也存在统计学意义，死亡组均高于生存组，APACHEⅡ及器官衰竭数目与乳酸、D-二聚体呈正相关。结论：患者入ICU时APACHEⅡ、乳酸、D-二聚体和PCT可用于评估病情并作为预后依据，乳酸、D-二聚体可用于预测多器官功能障碍发生的可能性。

关键词：感染性休克；乳酸；D二聚体；降钙素原

责任作者及联系方式：万献尧，E-mail:wanxianyao@gmail.com

感染性休克患者乳酸、D-二聚体、降钙素原变化与预后的关系

Changes and Prognosis of Lactic Acid, D-dimer, Procalcitonin from Patients with Septic Shock

Zhi-zhong Yu, Xian-yao Wan

First Affiliated Hospital of Dalian Medical University,central ICU,Dalian Liaoning 116011

Corresponding Author: Xiao-yao Wang, E-mail:wanxianyao@gmail.com

感染性休克是由微生物及其毒素等产物直接或间接的引起急性微循环灌注不足，导致组织缺氧、细胞损害、代谢和功能障碍，甚至多器官功能衰竭的危重综合征。国外报道其病死率达20%～63%，且耗费社会大量医疗资源，对患者家庭也造成极大的精神及经济负担。在临床工作中评估患者病情轻重及预后是必要的，可对医疗资源的投入进行适当调整，减小医疗资源的耗费。本文就目前临床常用的评估病情指标[急性生理和慢性健康评分（APACHE）Ⅱ、乳酸、D-二聚体和降钙素原（PCT）]对44例感染性休克患者进行回顾性分析，初步探讨其在病情预测及预后评估中的价值。

一、对象和方法

1. 对象

检索2009年9月1日～2010年9月1日大连医科大学附属第一医院重症医学科收治的诊断为感染性休克患者共54例，所有患者诊断均符合2001年美国胸科医师协会/美国危重症医学会（ACCP/SCCM）推荐的诊断标准[1]，入ICU后均参照集束化治疗原则，其中早期复苏目标为6h内中心静脉压达到8～12mmHg，平均动脉压达到65mmHg，尿量≥0.5ml/（kg·h），中心静脉血氧饱和度≥70%等[2]。以28天病死率为主要终点，其中排除9例因经济原因放弃治疗、1例怀疑脑出血加重形成脑疝导致死亡者，最后入选44例患者。基础疾病包括脑血管疾病后的肺部感染16例，慢性阻塞性肺疾病12例，白血病或淋巴瘤5例，外科术后4例，重症肺炎3例，流行性出血热2例，胆囊炎未行手术1例，不明部位感染1例。

2. 方法

44例患者以28天死亡为终点事件，分生存组和死亡组。收集每组患者入ICU时接受治疗前基本生命体征、肾功能、电解质、血气分析、血常规、D-二聚体、乳酸、PCT（采用半定量固相免疫测定法测定）等指标，并计算APACHEⅡ。统计患者病程中器官衰竭发生数目。器官功能功能障碍诊断标准参照1997年修正的Fry多器官功能障碍综合征诊断标准：①循环系统：收缩压低于90mmHg，并持续1小时以上，或需要药物支持才能维持循环稳定；②呼吸系统：急性起病，动脉血氧分压/吸入氧浓度(PaO_2/FiO_2)≤200mmHg（无论有否应用PEEP），X线正位胸片见双侧肺浸润影，肺动脉嵌顿压≤18mmHg或无左房压力升高的依据；③肾脏：血肌酐大于177μmol/L伴有少尿或多尿，或需要血液净化治疗；④肝脏：血胆红素大于34.1μmol/L，并伴有转氨酶升高，大于正常值两倍以上，或已出现肝性脑病；⑤胃肠：上消化道出血，24小时出血量超过400ml，或胃肠蠕动消失不能难受食物，或出现消化道坏死或穿孔；⑥血液：血小板计数小于50×10^9/L或降低25%，或出现弥散性血管内凝血；⑦代谢：不能为机体提供所需的能量，糖耐量降低，需要应用胰岛素，或出现骨骼肌畏缩无力等表现；⑧中枢神经系统：格拉斯哥昏迷评分小于7分。

3. 统计学方法

对两组患者APACHEⅡ、D-二聚体、乳酸等定量资料做两独立样本F检验和t检验，PCT为半定量资料故作两独立样本等级资料秩和检验。对D-二聚体、乳酸与APACHEⅡ和器官衰竭数目做两变量线性相关分析（Pearson检验）。所有统计学分析均应用SPSS13.0软件。

二、结果

44例患者存活14例，死亡30例。生存组中男性10例，女性4例；死亡组中男性20例，女性10例。病死率68.18%。

1.两组患者APACHEⅡ、D-二聚体、乳酸等计量资料如图1～3所示，经方差齐性分析及t检验差异存在统计学意义，死亡组均高于生存组（表1）[APACHEⅡ（F=0.411，t=4.882，P<0.05）、D-二聚体（F=1.949，t=4.247，P<0.05）、乳酸（F=2.167，t=8.649，P<0.05）]。

表1 两组患者APACHEⅡ、D-二聚体、乳酸比较

	APACHEⅡ	D-二聚体（μg/L）	乳酸（mmol/L）
生存组	25.85	621.85	3.76
死亡组	33.50	997.70	8.52
P	＜0.001	＜0.001	＜0.001

图1 两组患者APACHEⅡ比较

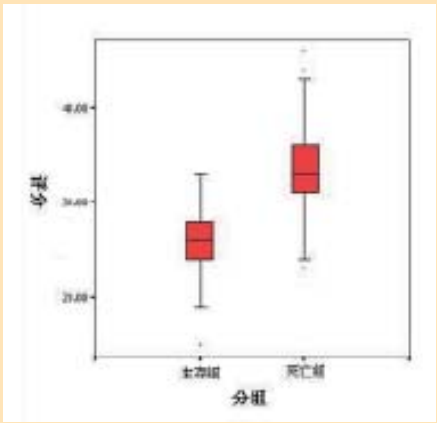


图2 两组患者D-二聚体比较

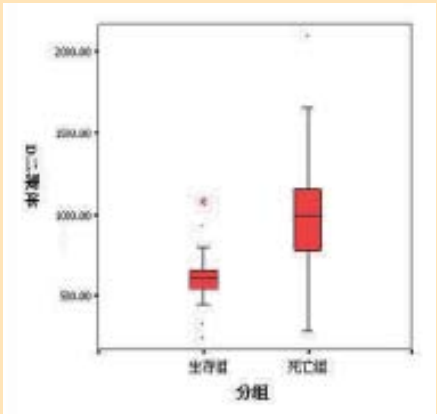
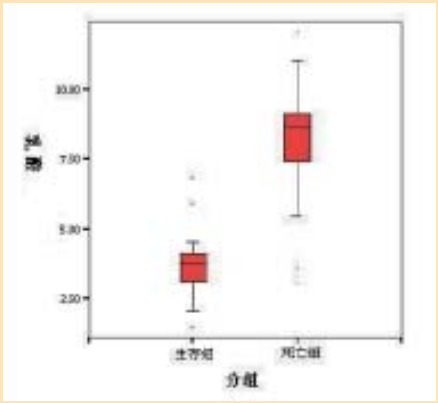


图3 两组患者乳酸比较



2.PCT为半定量资料，分为四组（分别为PCT＜0.5、0.5≤PCT＜2、2≤PCT＜10、PCT≥10），如表2所示，经两独立样本等级资料秩和检验（Z=2.831，P<0.05），发现死亡组高于生存组。

3.将乳酸、D-二聚体与APACHEⅡ及器官衰竭数目做两变量线性相关分析（Pearson检验），如表3所示，均明显相关（P＜0.05）。

4.因患者数较少，未能对各项定量资料行界限值分析及描绘受试者工作特征曲线。

表2 生存组与死亡组PCT比较

PCT（μg/L）	例数		合计	秩次范围	平均秩次
	生存组	死亡组			
PCT＜0.5	5	3	8	1～8	4.5
0.5≤PCT＜2	6	7	13	9～21	15
2≤PCT＜10	2	10	12	22～33	27.5
PCT≥10	1	10	11	34～44	39
合计	14	30	44	—	—

表3 乳酸、D-二聚体、APACHEⅡ与器官衰竭数目相关性

		器官衰竭数目					
		0	1	2	3	4	5
乳酸（mmol/L）	生存组	2.44	3.42	4.97	5.9	—	—
	死亡组	—	—	6.2	8.1	8.3	9.8
	均值	2.44	3.42	5.216	7.88	8.3	9.8
D-二聚体（μg/L）	生存组	522.1	611.3	639.5	1003	—	—
	死亡组	—	—	780	859.7	1018.5	1167.6
	均值	522.1	611.3	667.6	874.03	1018.5	1167.6
APACHEⅡ	生存组	23.2	25.9	27.9	28	—	—
	死亡组	—	—	28.9	31	33.7	37
	均值	23.2	25.9	28.1	30.7	33.7	37
生存组/死亡组人数		4/0	5/0	4/1	1/9	0/13	0/7

三、讨论

APACHEⅡ是目前国际上重症医学中应用最为广泛的评价病情危重程度的评分系统，是对危重病患者多项急性生理指标（包括基本生命体征、肾功能、电解质、血气分析及血常规等）和慢性健康状况的综合评分，多数研究认为病死率与APACHEⅡ呈正相关，并有报道APACHEⅡ达20分时其病死率超过50%，当超过30分时病死率高达100%[3]。此次收集的感染性休克总体病死率达68.18%，高于国外报道的20%～63%，分析其原因为该44例感染性休克患者APACHEⅡ平均高达31.06分，

死亡组甚至达33.5分，表明此次收集病例总体病情比较严重。对APACHEⅡ分段研究预计死亡危险度与临床实际病死率有统计学意义的相符，但低分值段的预测病死率比实际病死率稍高，而高分值段的预测病死率较实际病死率稍低[4]，因此临床应用该评分系统评价病情及预后时应对预计值做相应调整。

感染性休克时机体在末梢灌注不足、乏氧条件下，葡萄糖经过无氧酵解生成丙酮酸，后者在肌肉中转换为乳酸，这是乳酸主要的产生途径。乳酸在体内最主要的代谢途径为氧化利用和糖异生，其中糖异生的过程主要在肝脏发生。危重患者中影响乳酸代谢的主要因素有糖代谢异常、肝功能障碍、线粒体功能障碍等。由于动脉血乳酸水平受多种因素影响，故目前临床研究多倾向于以乳酸清除率来作为评价治疗措施对末梢循环、器官功能的改善及病情预后的依据[5]。一项同位素标记法比较心源性和感染性休克患者与正常人乳酸代谢差异，发现休克组与正常组乳酸清除率相当、休克组内源性乳酸产物较正常组明显增多、休克组内源性糖产物较对照组明显增多，且不受外源乳酸注入的影响。结论认为高乳酸血症主要是因为乳酸产物增多，而乳酸清除率并没有下降，乳酸盐产物增多伴随着高乳酸血症及糖代谢的加速，后者主要影响着乳酸代谢[6]。但该研究中入组患者少，且简化急性生理评分较低，平均分不到40。就如对混合静脉血氧饱和度能否作为目标指导治疗指标的怀疑一样[7]，感染性休克患者高乳酸血症系乳酸产物增多和组织乳酸清除率下降的双重影响，因感染性休克早期高氧耗时乳酸清除率可能正常甚至升高，而晚期可能存在着氧利用障碍，此时并存着乳酸清除的下降。本次回顾性分析未能统计患者乳酸清除率，仅仅以患者入ICU即时血乳酸水平作统计学分析，两组差异有统计学意义。

PCT是降钙素的一个前肽糖蛋白，由116个氨基酸组成。生理情况下，甲状腺C细胞可产生极少量的PCT，健康人的血清PCT水平通常测不到（PCT正常值约0.033μg/L）。在细菌引起的全身性感染或内毒素或促炎因子（如IL-1、TNF-α等）的刺激下，PCT水平会升高100～1000倍，该非激素产物数小时内出现在多种非甲状腺组织细胞中，而早期快速升高的特性使PCT可作为细菌感染的早期诊断工具[8]。但PCT在诸多非感染情况下（如严重创伤、烧伤、重症急性胰腺炎等全身性炎症反应重时）也会有明显升高[9]。此次收集患者中除一例不明部位感染外感染诊断均较为明确，因此可以认为两组患者PCT的升高均与感染有关，死亡组中PCT值升高明显高于生存组，可能比较支持死亡组感染情况较生存组重，如果能持续监测PCT动态变化，探讨其与感染控制情况及最终转归之间的关系则更能揭示感染是仅仅作为感染性休克发生发展过程中的一个始动环节还是贯穿于整个疾病过程。另外，在该44例患者感染相对明确的情况下，仍有8例PCT<0.5μg/L，这可能与其检测方法的灵敏度不太高有关。目前临床上检测PCT的方法多为半定量试验（LUMI test），其最大灵敏度为0.5μg/L，超过其正常值10余倍，这使得许多轻度升高者无法检测到[10]。

本次收集的44例患者中D-二聚体均明显升高，且死亡组血D-二聚体较生存组明显升高（P<0.05），可能系感染性休克时，微循环灌注不足、乏氧、微血管内皮细胞损伤、组织因子释放等因素而导致机体凝血和纤溶机制紊乱，启动内源性、外源性凝血系统导致微血栓形成，继发纤溶亢进、D二聚体升高，而D二聚体升高加重微循环障碍引起组织器官供血、供氧不足，最终导致多器官功能障碍。已有多项研究证实感染性休克患者存在凝血与纤溶紊乱，针对该机制指南建议在条件许可情况下应用人体活化蛋白C治疗重症感染性休克[2]。

乳酸和D-二聚体均能从不同意义上反映感染性休克患者微循环障碍情况，随着微循环障碍加重，多器官序贯出现功能障碍直至衰竭。30例死亡患者最终均死于MOF，按脏器功能衰竭发生频率以循环、呼吸、脑、肾常见。44例患者发生器官功能障碍的数目及APACHEⅡ评分与乳酸和D-二聚体呈正相关，如能进行大样本随机对照试验可研究乳酸和D-二聚体值是否可用于评估病情严重性及预测发生器官功能障碍。

参考文献

[1] Levy MM，Fink MP，Marshall JC，et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med，2003，31：1250-1256.
[2] 中华医学会重症医学分会. 成人严重感染与感染性休克血流动力学监测与支持指南（2006）. 中国实用外科杂志，2007，1:7-13.
[3] 孟新科，邓跃林. APACHEⅡ与SAPSⅡ评分系统对急诊内科危重患者病情评估价值的比较. 中国危重病急救医学，2001，13:751-755.
[4] Knaus WA，Draper EA，Wagner DP，et al. APACHEⅡ: a severity of disease classification system. Crit Care Med，1985，13:818-829.
[5] 杨从山，邱海波，黄英姿，等. 动态监测动脉血乳酸水平对感染性休克患者预后评价的前瞻性研究. 中华外科杂志，2009，17:685-688.
[6] Revelly JP，Tappy L，Martinez A，et al. Lactate and glucose metabolism in severe sepsis and cardiogenic shock. Crit Care Med，2005，33:2235-2240.
[7] 万献尧，黄伟. 对国际上有关全身性感染诊断标准与治疗指南的一些看法. 中华内科杂志，2007，46:709.
[8] Gabay C，Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med，1999，340:448-454.
[9] Becker KL，Snider R，Nylen ES. Procalcitonin assay in systemic inflammation，infection，and sepsis: Clinical utility and limitations. Crit Care Med，2008，36:941-952.
[10] Whang KT，Steinwald PM，White JC，et al. Serum calcitonin precursors in sepsis and systemic inflammation. J Clin Endocrinol Metab，1998，83:3296-3301.

2011年美国麻醉师学会(ASA)年会

会议地址：芝加哥，美国

会议时间：2011年10月15~19日

会议描述：美国麻醉师学会（ASA）成立于1905年，是集教育、研究、提高麻醉学标准和患者护理于一体的组织。60年来美国麻醉师学会（ASA）年会已经成为全球与麻醉相关的综合性大会，每年的年会会请来麻醉、疼痛医学与重症护理医学领域里最顶尖著名的教授出席。http://asahq.org/sitec

谢海辉 张 曙 倪新颖
李振花 陈笑红 蓝晓文
广东省东莞市人民医院总院麻醉科 523000

摘要

目的：研究盐酸右美托咪定(dexmedetomidine，Dex)在全麻诱导气管插管期间对老年冠心病患者自主神经系统功能的影响。方法： 98例择期腹部手术老年冠心病患者，随机分成盐酸右美托咪定（D组 n=49,诱导前给予负荷剂量右美托咪定0.7ug／kg，注射泵缓慢静脉注射，输注时间超过10 min，维持剂量以0.4ug／(kg·h)持续静脉注射）和安慰剂组（P组n=49，诱导前静脉注射等容量氯化钠溶液），分别于麻醉前（T_0），麻醉诱导后（T_1）及气管插管后（T_2）用心率变异功率谱分析(heart rate power spectrum analysis，HRPSA)技术观察患者的心率变异性（heart rate variability，HRV）改变。结果：麻醉诱导后，两组HRV总功率频段(TP)和其中低频段(LF)、高频段(HF)、LF/HF(低频／高频比)均显著降低(P<0.05)，组间比较D组LF低于P组(P<0.05)；气管插管后，两组LF、HF及TP均显著升高(P<0.05)，而D组的LF/HF较麻醉前（T_0）差异无统计意义，P组的LF/HF较麻醉前（T0）显著升高(P<0.05)；组间比较D组LF、TP升高程度显著低于P组(P<0.05)，HF组间差异无统计学意义。结论：盐酸右美托咪定能明显抑制插管操作引起的对植物神经功能的干扰，有利于维护老年冠心病患者围插管期心脏的自主神经调节功能。

关键词：盐酸右美托咪定；冠心病；心率变异性；气管插管
责任作者及联系方式：谢海辉，E-mail:xhh900@hotmail.com

盐酸右美托咪定对老年冠心患者全麻气管插管期心率变异性的影响

Effect of Dexmedetomidine on Heart Rate Variability of Elderly Coronary Heart Disease Patients During Intubation

Hai-Hui Xie, Shu Zhang, Xing-Ying Ni, Zhen-hua Li, Xiao-hong Chen, Xiao-wen Lan
Department of anesthesiology, the people Hospital of Dondguan, Guangdong Province, 523018,China

Abstract

Objective: To explore the effect of dexmedetomidine (Dex) on autonomic nervous system function during intubation in the elderly patients with coronary heart disease.

Methods: 98 patients undergoing abdominal surgery patients with coronary heart disease, were randomly divided into dexmedetomidine group(group D, n=49, the patients received intravenous in jection of Dex(0.7ug / kg)10 minutes before intuba tion,) and then received continuous in jection of Dex a t a rate0.4 ug / (kg·h) during the operation and placebo group (groupP, n=49 Before induction intravenous infusion of the same amount of normal sal ine), In pre-anesthesia (T_0), after the induction of anesthesia (T_1) and after intubation (T_2) the heart rate variability (HRPSA) was observed with power spectral analysis.

Results: After induction of anesthesia, both groups of total power of HRV spectrum (TP) and low-frequency (LF), high frequency (HF), LF / HF (low frequency / high frequency ratio) were significantly lower than before induction of anesthesia (P <0.05), inter-group comparison group D LF lower than group P (P <0.05); After tracheal intubation, two groups of LF, HF and TP were significantly higher than before tracheal intubation (P <0.05), D group of LF / HF were not significantly higher than before tracheal intubation,however,P group of LF / HF were significantly higher than before tracheal intubation(P <0.05),inter-group comparison Group D with LF, TP increased significantly lower than the group P (P <0.05), HF inter-group difference was not significant.

Conclusion: Dexmedetomidine inhibit the intubation stimulation on autonomic function. This is beneficial to maintain good cardiac autonomic nerve function for old patients with coronary artery disease during intubation.

Key Words: dexmedetomidine; Coronary heart disease; Heart rate variability; Tracheal intubatio

Corresponding Author: Hai-Hui Xie, E-mail:xhh900@hotmail.com

心率变异性（heart rate variability,HRV）分析是测定连续正常心动周期之间的时间变异数，反映心率的变化程度，临床上常用于无创伤地反映植物性神经系统的功能状况，是定量测定交感和副交感神经张力的指标。近年来，不少研究表明，冠心病患者的心率变异明显高于正常人，可能与冠心病患者靶器官损害有关，HRV对冠心病的预后判断有重要价值[1-2]。心率变异功率谱分析（heart rate power spectrum analysis, HRPSA）技术是一种无创定量反映自主神经功能及其对心血管系统调节作用的方法。盐酸右美托咪定(dexmedetomidine,Dex) 为新型高选择性a_2肾上腺素能受体激动剂, 具有剂量依赖性的镇静催眠作用,还具有镇痛、抑制交感活性、改善手术期心血管稳定性及抑制围术期的应激反应等作用[3-5]，目前国内外关于其对围术期应对气管插管引起心率变异变化影响的报道较少见。本研究应用HRPSA技术观察盐酸右美托咪定在全麻诱导气管插管HRV的变化，探讨盐酸右美托咪定在全麻诱导气管插管时对冠心病患者自主神经

功能的影响，为临床麻醉用药提供参考。

一、材料与方法

1. 一般资料

本研究经本院医学伦理委员会批准，所有患者均知情同意并签署知情同意书。选择我院普外科与肿瘤外科2010年3月-2011年3月收治冠心病老年患者98例（根据1979年国际心脏病学会关于冠心病诊断标准或冠状动脉造影确诊为冠心病），择期行中上腹部手术，其中男65例，女33例，年龄67±9岁，体重43kg±16kg，ASAⅡ～Ⅲ、心功能Ⅰ～Ⅱ级，心电图检查均示有不同程度ST段改变，排除有不稳定型心绞痛，慢性阻塞性肺部疾病、过度肥胖（BMI≥30）房室传导阻滞患者，另外，气管插管操作超过一次或气管插管时间超过60秒的患者在统计分析时被排除。采用McLeod改良Wichmann-Hill伪随机数发器生成的随机序列。患者被双盲随机分为盐酸右美托咪定组(D组n=49)和安慰剂组(P组n=49)，两组患者的年龄、性别、身高、体重、ASA分级、心功能、手术持续时间等差异无统计学意义(P>0.05)。

2. 麻醉方法与观察指标

麻醉前30min肌注盐酸戊乙奎醚0.01mg/kg，咪达唑仑0.02mg/kg，患者入室后，开放静脉通路,监测BP、SpO_2、PET CO_2、RR，用PM-6000多功能监测仪(深圳迈瑞生物医疗电子股份有限公司,中国)连续记录HRV及低频(LF)、高频(HF)、低频/高频比值(LF/HF)和总功率谱(TP)，患者静卧5min后记录上述参数作为基础值。D组麻醉诱导采用芬太尼2μg/kg，依托咪酯（宜妥利，生产批号:B7471C33, 沈阳Braun公司）0.3mg/kg，顺式阿曲溴铵0.2mg/kg；并于麻醉诱导前给予负荷剂量右美托咪定(江苏恒瑞医药股份有限公司，批号：09081232，国药准H20090248) 0.7ug/kg，kg，注射泵缓慢静脉注射，输注时间超过10min，维持剂量以0.4ug/(kg·h)持续静脉注射；P组麻醉诱导采用芬太尼2μg/kg，依托咪酯0.3mg/kg，顺式阿曲溴铵0.2mg/kg均依次缓慢静注，诱导前10min缓慢泵注安慰剂(等容量氯化钠溶液)；给药者对所注射的药物为右美托咪定或安慰剂并不知情。每50次心搏记录一次HRV有关参数值。同时监测无创血压和脉搏血氧饱和度。分别于麻醉前(T_0)，负荷剂量右美托咪定或生理盐水输注后5min（麻醉诱导后，插管前T_1)及气管插管后15min(T_2)各时间点记录上述指标持续5min。

3. 统计学方法

所有数据均采用SPSS13.0。统计软件包处理，以均数士标准差($\bar{x}\pm s$)表示。组内比较采用配对t检验，组间比较采用单因素方差分析，计数资料比较采用X^2检捡,P<0.05为差异有统计学意义。

二、结果

1.麻醉诱导后（T_1），D组LF和TP，P组LF，HF，LF/HF及TP均显著降低(P<0.05)，组间比较D组LF低于P组(P<0.05)而D组HF高于P组 (P<0.05)；气管插管后（T_2），两组LF，HF及TP均较麻醉前（T_0）显著升高(P<0.05)，而D组的LF/HF较麻醉前（T_0）差异无统计意义，P组的LF/HF较麻醉前（T_0）显著升高(P<0.05)；组间比较D组LF、TP升高程度显著低于P组(P<0.05)，HF组间差异无统计意义，见表1。

表1 两组患者麻醉前、麻醉诱导后及气管插管后心率变异性变化（x±s, n=49）。

参数	组别	T_0	T_1	T_2
LF(ms^2/Hz)	D	391±282	219±183*	503±293#
	P	386±279	287±181*☆	631±267#☆
HF(ms^2/Hz)	D	159±139	137±113	246±191#
	P	153±138	89±43*☆	239±188#
LF/HF	D	2.7±1.5	2.5±1.3	3.0±1.7
	P	2.6±1.4	2.0±1.1*	5.8±2.1#☆
TP(ms^2/Hz)	D	956±599	756±535*	1266±781#
	P	959±587	760±462*	1389±632#☆

注：与T_0比较，*P<0.05；与T_0比较，#P<0.05；与D组比较，☆P<0.05

2.麻醉诱导后，两组HR，SP，DP均显著降低（P<0.05）；组间比较，D组HR，SP，DP降低程度显著高于P组(P<0.05)，D组有1例患者给药后出现显著的心动过缓,HR低至41次/min，经给予阿托品0.5mg后恢复至正常,其他病例均未出现明显的低血压、心动过缓。气管插管后，两组HR，SP，DP较麻醉诱导后均显著升高(P<0.01)。组间比较发现，气管插管后D组HR、SP及DP升高程度显著低于P组(P<0.05)，见表2。

表2 两组患者麻醉前、麻醉诱导后及气管插管后心率和血压变化（x±s, n=49）。

参数	组别	T_0	T_1	T_2
HR(次/分)	D	81.0±19.0	65.0±11.0*	69.0±13.0#
	P	83.0±17.0	73.0±13.0*☆	90.0±16.0#☆
SBP(mmHg)	D	116.5±11.4	91.3±10.3*	97.7±9.8#
	P	115.8±11.4	113.6±11.6*☆	131.8±9.8#☆
DBP(mmHg)	D	73.3±8.4	57.8±7.6*	71.2±6.3#
	P	72.8±9.3	71.5±6.8*☆	97.7±7.7#☆

注：与T_0比较，*P<0.05；与T_0比较，#P<0.01；与D组比较，☆P<0.05

三、讨论

全麻诱导气管插管期间可刺激交感神经，引起心动过速、血压增高及儿茶酚胺释放，从而增加心肌耗氧量。尤其是高血压、冠心病患者容易增加心脏负担、影响心脏氧供需平衡,增加心率失常及心脑血管意外的可能。而HRV是指逐次心搏间期之间的微小差异,它产生于自主神经系统对心脏窦房结自律性的调制，主要反映心脏自主神经的功能状态。HRV降低表明植物神经对心脏的调节功能下降。HRPSA是一种常用的HRV分析方法，其LF主要反映交感神经活性对心脏的调节功能；为副交HF则通常作感神经心脏活性的指标；LF/HF则反映植物神经对心脏调节的平衡状态，LF+HF则反映植物神经总的张力[6]。HRV在冠心病患者中发生改变，甚至早在冠心病出现症状前即已经出现下降[7]。在伴有心脏事件的心绞痛患者中LF/HF比值显著增高，提示该群体中自主神经功能失调,以交感活性的增高为显著,而交感神经过度激活可导致致命性心律失常的发作。因此,自主神经系统与术中急性心肌缺血后恶性心律失常，心性猝死密切相关。HRV和室性心动过速同为在院期间不稳定心绞痛住院期间病死率和中期病死率的独立的预报因子。由急性冠状动脉阻塞引起的致命性心律失常是心性猝死的主要原因。在此过程中，交感神

经张力的增高有重要作用[8]。因此，在了解了药物对植物神经的影响情况后,麻醉中通过监测HRV来掌握静脉麻醉药和镇痛药的应用时机,从而达到既取得良好的麻醉质量,又避免过度抑制冠心病患者的心血管调节能力,提高麻醉的安全性。

右美托咪定是一种新型的α$_2$肾上腺素能受体激动剂。α$_2$肾上腺素能受体激动剂抑制中枢交感神经发放冲动，使交感神经张力降低及迷走神经活动性增强， 并激动交感神经末梢的突触前α$_2$受体,抑制去甲肾上腺素的释放及降低血浆中儿茶酚胺浓度[9]。在药效学上主要表现出血压和心率下降,提示α$_2$受体激动药物有助于维持术中患者心血管能的稳定。本研究表明，右美托咪定静注后LF和TP降低，可能与右美托咪定通过增加中枢脑干蓝斑核副交感神经的输出,减少交感神经输出有关，而HF，LF/HF下降不明显，说明其对植物神经功能无明显干扰,对心脏调节平衡状态无显著影响,与其循环变化相一致。气管插管后，D组的LF明显低于P组，且气管插管前后LF/HF无显著变化，说明右美托咪定能明显抑制插管操作引起植物神经功能的干扰，有利于维护老年冠心病患围插管期心脏自主神经调节功能。由于LF受外周压力反射调节，而研究结果显示静注右美托咪定比对照组LF的影响比较显著，这可能与右美托咪定降低循环中儿茶酚胺水平,从而一定程度抑制压力反射有关。气管插管后两组HRV指标均显著性升高，提示气管插管可使交感、迷走神经活性、交感/迷走均衡性及植物神经总张力显著升高；就控制气管插管引起的自主神经作用而言静注右美托咪定明显强于对照组。

上述自主神经系统的功能改变与患者血压心率变化基本一致。两组患者麻醉诱导后血压、心率均显著降低。静注右美托咪定组患者降低血压、心率的作用显著大于对照组。气管插管后，两组患者血压、心率均显著升高，说明气管插管可使血压、心率显著升高；静注右美托咪定组血压、心率升高显著低于对照组，说明静注右美托咪定能抑制插管引起的心血管反应。

综上所述，静注右美托咪定能明显抑制插管操作引起植物神经功能的干扰，对老年冠心病患围插管期心脏调节平衡状态有保护作用，并能一定程度抑制插管引起的心血管反应。

参考文献

[1] 王宏志. 冠心病患者心率变异性分析. 中国医师进修志, 2006, 29(9): 32-33.
[2] Doulalas AD, Flather MD, Pipilis A, et al. Evolutionary pattern and prognostic importance of heart rate variability during the early phase of acute myocardial infarction. int J cardiol, 2006, 82(2): 169-176.
[3] Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine:a review of clinical applications. Curt Opin Anaesthesiol,2008,21(4) :457-461.
[4] 杨伟 邵建林右美托咪定用于腹腔镜胆囊切除术中的临床观察. 临床麻醉学杂志, 2011,27(1):47-48.
[5] 许忠玲, 徐兴国, 崔松勤. 盐酸右美托咪定对食管癌根治术患者围术期血糖、β-内啡肽、TNF-a及IL-6表达的影响. 第二军医大学报,2010,31(12):1130-1132.
[6] 程华春, 杭燕南. 心率、心率变异性与麻醉. 国外医学麻醉学与复苏分册, 2000, 20(2): 94-96.
[7] Kop WJ, Verdino RJ, Gottdener JS, et al. Changes in heart rate variability before ambulatory ischemic events. J AM Coll cardiol, 2001, 38(2): 742-749.
[8] Copie X, Lamaison D, Salvador M, et al. Heart rate variability before ventricular arrhythmias in patients with coronary disease and an implant- table cardioverter defibrillator. Ann Noninvasive Electrcaroil, 2006, 11(3): 179-185.
[9] 马立刚，王哲银. 右美托咪定对腹腔镜子宫切除术患者循环及应激反应的影响. 广东医学,2011,32(4):489-491.

第九届胸腔麻醉亚洲会议（2011 ASCA）

时间：2011年9月30日至10月2日
台湾省台北市臺大醫院國際會議中心
主办单位：National Taiwan University
会议主席：Rick S.C.Wu
联系电话：+886-2-8226-2785
会议网站：http://www.asca2011.org/index.html
大会欢迎词：

我謹代表第9屆亞太心胸麻醉醫學年會之籌備委員會，很榮幸邀請您參加2011年9月30日至10月2日於臺灣台大醫院國際會議中心舉辦的「2011年第9屆亞太心胸麻醉醫學年會」(2011 ASCA)暨第七屆國際華人心血管麻醉論壇、第十一屆臺灣心臟麻醉醫學會年會，及第一屆全球華人經食道超音波課程及認證。

依循先前成功的會議經驗，本年會是以結合臨床、學術之研究，改善現今心臟手術之麻醉醫療診療技術，降低手術之風險，提升醫療品質為宗旨及促進國際交流為目標。藉由本年會，您將結識來自世界各地相關領域的專家學者，並進行深度知識交流。

本年會三天的議程中，包括了講述近年心胸麻醉主要發展的主題演說、摘要、海報展示及促進與會者交流的小組討論會議。

今年適逢台灣慶祝建國一百歲生日，在這意義深遠的一年，有關單位規劃了一系列的慶祝活動，本年會籌備委員會誠摯地邀請您參與第9屆亞太心胸麻醉醫學年會，期待您的出席和全程參與，將使本年會更加成功！

第九屆亞太心胸麻醉醫學年會籌備委員會主席

Assessment of Continuous Celiac Plexus Block (CCPB) Outcomes and Technique in the Management of Refractory Visceral Cancer Pain

Feng-Rui Yang, Bai-San Wu, Guang-Hui Lai, Qi wang, Li-Qiang Yang, Ming-Wei He, Jia-Xiang Ni

Department of Pain Medicine, Xuan Wu hospital of capital medical university, Beijing, China

Abstract

Objective: MTo assess outcomes and safety of continuous celiac plexus block (CCPB).Design. Retrospective clinical data analysis.Setting. Three pain department, academic medical center.Patients. 12 patients with terminal visceral (mostly pancreatic) cancer who failed conservative measures. Interventions. 12 Celiac plexus alcohol neurolytic procedures done for pain control after a positive diagnostic block.

Materials and Methods: 12 patients with terminal visceral (mostly pancreatic) cancer thos failed conservative measures was managed by continuous celiac plexus block guided by computed tomography at the pain department of xuanwu hospital from January 2005 to June 2010. The study evaluated continuous celiac plexus block efficacy efficacy with regard to pain relief, its adverse effects/complications.

Results: Continuous celiac plexus block efficacy with regard to pain relief was exhibited by a marked decrease in the visual analog score and in opioid consumption, with preprocedural mean values dropping from (8.7±1.0) and (155±56)mg/d of morphine to (1.8±1.1) and (0) mg/d at the first postprocedural visit, respectively. These results persisted during the 6-month follow-up period or until death. Minor adverse effects (moderate diarrhea and mild hypotension) were frequent (n=3, and n=4, respectively), and severe complications occurred in 1 patient with a transient paraparesis (n=1). No procedure-related mortality was observed.

Conclusions: Continuous celiac plexus block is a technique that provides analgesia and the alleviation of the secondary undesirable effects of analgesic drugs resulting from the decrease of morphine consumption in patients with upper abdominal malignancies. In experienced teams, the reliability of its analgesic effects is high, with a low rate of severe complications.

Key words：Cancer Pain; Nerve Block; Sympathetic Block

Introduction

Celiac plexus neurolysis (CPN) has been performed for almost 100 years to treat pain of pancreatic origin and a variety of techniques, routes and chemical agents have been used to maximize efficacy and minimize complications [1-3]. Traditionally, CPN has been most commonly performed percutaneously under fluoroscopic or CT guidance using for single block and studies have confirmed the efficacy of the procedure and highlighted potential advantages over opioid therapy [4,5]. Single CPB, the role of alcohol concentration in the nerve fibers decreased rapidly due to absorption, often leads to mild nerve damage, therefore less effective in long-term effects [6-9]. This study is to assess outcomes and safety of continuous celiac plexus block (CCPB).

MATERLALS AND METHODS

This clinical observation study aims to assess the efficacy and safety of continuous celiac plexus block in the treatment of cancer pain. After permission to conduct this study was granted by the Ethics Committee of Xuan wu hospital, a maintained database containing the medical records of 18 patients who undervent CCPB between January 2005 and June 2010 was examined. Inclusion criteria included unrespectable abdominal malignancy; moderate or severe abdominal and/or back pain poorly controlled with pharmacotherapy, and underwent CCPB. Exclusion criteria were ntreated coagulopathy, unstable medical illness, and cognitive impairment that precluded an accurate response assessment. And 6 patients only received the continuous celiac plexus block, never received the alcohol neurolysis, so they were excluded from the analysis. All procedures were performed by professor Ni at a university-based pain treatment center. And we followed up for 1 month, 3 month, and 6 month.

Assessment of the Patients and of the Procedure

Before the procedure, Recorded the intensity of the

pain with the visual analog scale (VAS) and the use doses of analgesics (i.e., morphine dosage).

After the procedure, recorded and followed up the patient at prescheduled dates (the first day, the first week and the first, third and sixth month) of until death. We recorded and evaluated the following:(1:1) the degree of analgesia obtained according to the VAS, (2) the daily morphine consumption (mg/d, per os), (3) any complications of the procedure.

Statistical Analysis

The results were reported by means of descriptive statistics (mean±SD and percentages) and statistical analysis. The main effectiveness outcome of UAS was tested trough both a Student t test and a linear generalized model (with analysis of variance [ANOVA] of repeated measures) to probe consistency across these multiple measures over time.

Technique

Day of surgery, patients stop taking pain medicine, open intravenous access before surgery, intravenous infusion of Ringer's solution, routine continuous monitoring of blood pressure, heart rate, pulse oxygen saturation. Position, CT guided vertebral plane will T12/L1 aortic puncture target is set, the use of CT scanning to determine the needle entry site and the path of needle, using 15cm long 18G epidural needle puncture from the side to corresponding target, after successful puncture, turn the needle to middle side, then insert the 20G catheter through the needle. After the scan is correct inject 1% lidocaine and iohexol mixture of 20ml, observe the spread of contrast medium and the pain of patients, when the VAS score dropped to 50% the preoperative diagnostic block is positive. Catheter position confirmed by contrast, after subcutaneous tunnel and fixed the catheter. Half an hour later, if no local anesthetic toxicity, spinal anesthesia, intractable severe hypotension and abnormal spinal nerve block, then inject 100% alcohol 20ml, after that connect the patients with patient controlled analgesia pump (open it when VAS≥4), and then order patients 6 hours of prone position after the procedure.

RESULTS

Patients' Demographics

12 patients with upper abdominal cancer were included in the study, a group composed of 5 women and 7 men. The age of the patients ranged from 46 to 77 years, with a mean age of 64±11 years. The neoplasms were pancreatic in 9 patients, hepatic in 2 patients, gastric in 1 patient. The overall survival rate at 6 months was 3 of 12 patients.

Evaluation of the procedure

TABEL 1.Preprocedural and Postprocedural Behavior of the Studied Population

Time	Assessed	Lost to follow-Up	VAS mean	P	Morphine, mg/d	P
Before	12	0	8.7±1.0	155±56		
After procedure						
1 day	12	0	1.8±1.1 <0.001	0	<0.001	
1 wk	12	0	19.±1.0 <0.001	0	<0.001	
1 mo	9	3	2.3±1.2 <0.001	30±39	<0.05	
3 mo	3	6	3.2±1.0 <0.05	42±44	<0.05	
6 mo	3	6	3.3±1.5<0.05	40±35	<0.05	

Figure 1: insert catheter and inject contrast medium

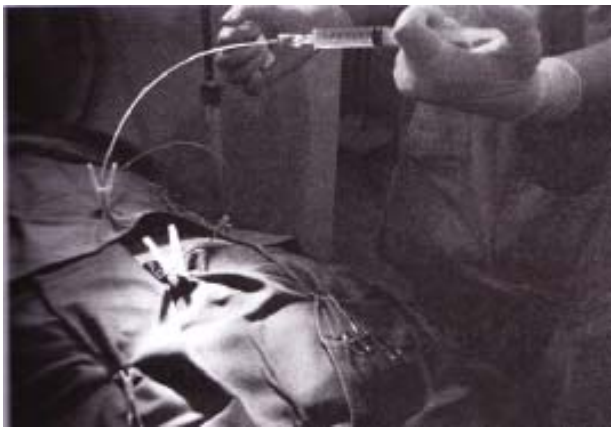
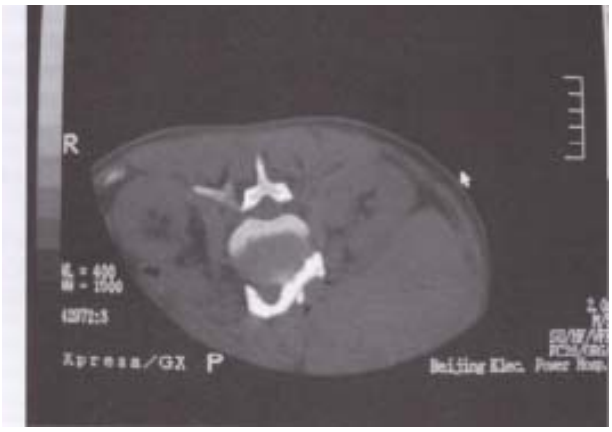


Figure 2: contrast medium spread



Adverse Effects and Complications

Minor adverse effects included diarrhea (n = 3, 25%), hypotension (n = 4, 33%). Diarrhea and hypotension in these cases were mild, without any hydroelectric or hemodynamic disturbances. Severe complications occurred in 1 patient with a transient paraparesis (n = 1, 8%). No mortality was observed.

DISCUSSION

Single celiac plexus block for visceral cancer pain, its effective analgesia can be maintained 4 to 6 weeks or longer, the immediate and short-term analgesic efficiency up to 85%. But the role of alcohol concentration in the nerve fibers decreased rapidly due to absorption, and often causes only mild nerve damage, therefore less effective for long-term pain relief.

Our department believe that sent a special catheter with tip of many openings to the celiac plexus, the injection of contrast agent shows the spread of better distribution in the celiac plexus, then we can do several times of chemical damage, therefore can make broader and more thorough destruction of celiac plexus, and achieve the purpose of long-term pain relief, so we made this study.

There are also several limitations to our study, which mostly revolve around the retrospective nature. The lack of standardization limits the conclusions one can draw. The data for the procedures reviewed were also not uniformly charted, and in some instances were absent. Finally, although statistical significance was detected for some variables, the power for detecting other differences may not have been sufficient, such as quality of life.

Future study might consist of a prospective study which would allow for a more complete gathering of some other variables. Ideally, such a study would be powered to obtain statistical significance from major variables of interest.

In conclusion, continuous celiac plexus block is a technique that provides analgesia and the alleviation of the secondary undesirable effects of analgesic drugs resulting from the decrease of morphine consumption in patients with upper abdominal malignancies. In experienced teams, the reliability of its analgesic effect is high, with a low rate of severe complications.

REFERENCES

[1] Caraceni A, Portenoy RK. Pain management in patients with pancreatic carcinoma. Cancer 1996; 78:639−53.
[2] Malfertheiner P, Dominguez−Munoz JE, Buchler MW. Chronic pancreatitis:management of pain. Digestion 1994; 55(Supp1.1):29−34.
[3] Ward EM, Rorie DK,Nauss LA, et al.The celiac ganglia in man:normal anatomic variations. Anesth Analg 1979; 58:461−5.
[4] lillemoe KD, Cameron JL, Kaufman HS, et al. Chemical splanchnicectomy in patients with unresectable pancreatic cancer. A prospective randomized trial. Ann Surg 1993;217:447−57.
[5] kawamata M, Ishitani K, Ishikawa K, et al. Comparison between celiac plexus block and morphine treatment on quality of life in patients with pancreatic cancer pain. Pain 1996;64:597−602.
[6] Eisenberg E, Carr DB, Chalmers TC, Neurolytic celiac plexus bloc k for treatment of cancer pain: A meta−analysis. Anesth Analg, 1995, 80:290−295.
[7] Mercadante S, Nicosia F, Celiac plexus block: a reappraisal. Reg Anesth Pain Med, 1998, 23:37−48.
[8] Polatj E, Finco G,Gottin L, et al. Prospective randomized double−blind trial of neurolytic celiac plexus block in patients with pancreatic cancer. Br J Surg, 1998, 85:199−201.
[9] Vranken JH, Zuurmond WW, de lange JJ. Increasing the efficacy of a celiac plexus block in patients with severe pancreatic cancer pain. J Pain Symptom Manage, 2001, 22:966−977.

Current Treatment of Central Pain

Xiang-mo Yan

Department of Anesthesiology and Pain Medicine, Yuquan Hospital, Tsinghua University,Beijing,China.

Abstract

Pain Clinic has become independent medical department in China.Central pain caused by a lesion or disfunction in the central nervous system(CNS),it is definitioned by IASP.This paper expound the causes, mechanism, characteristics, diagnostic standard, method of current treatment, especially introduce neurleptadenolysis of pituitary gland(NALP)+Relevant place nerve block(RPNB) for central pain, get good results, finally also mention drugs Therapy and other mentods.

Key words: Central pain, Nerve block, Neuroadenolysis pituitary gland, Treatment.

Introduction

Pain Clinic has become in dependent medical department in China. Modern pain clinic in China were started at 1970. After that time many hospitals were launched the pain clinic. In 2007, ministry of health of the people's republic of China were published a official that ministry of health Number 227 of 2007, decided among the "medical clinical subjects List" increase "department of pain", the code name number is 27. All of above grade Ⅱ hospitals, can be launch the pain practice. In 2007, held first Chinese chapter symposium for the world society of pain clinicians in Beijing. In the meeting president of 13th international pain clinic WSPC, professor Sang Chul Lee declared Chinese chapter for the WSPC were established, and about 600 pain clinicians were registered the society, professor Jiaxiang Ni was elected the president. The 14th world pain clinic Congress & the 1st Asian Congress on pain will be held in Beijing at Oct. 29-Nov. 1st, 2010, Chins.

NEW CONCEPT OF CENTRAL PAIN(CP)

The International Association for the study of pain (IASP) has defined central pain as pain caused by a lesion or dysfunction in the central nervous system (CNS). The core is caused by a primary process in the CNS, it means that brachial plexus avulsion, phantom pain is not central pain. But thalamic pain and pseudothalamic pain is sometimes used for central pain in general. Dysaesthetic pain can have either central or peripheral causes (fig 1).

Clinically, thalamic pathological changes is central pain. 'anesthesia dolorosa' happened from head and face neurogenic pain that sometimes develops after neurosurgical lesions of the trigeminal nerve or ganglion, or after destructive nerve blocks carried out to treat trigeminal neuralgia, It has also been used for central pain in an anesthetic region caused by neurosurgical brain lesion created in the treatment of sever pain.

The term 'deafferentation pain' is used for similar conditions, but it is more commonly used in patients with lesions of spinal nerves..

CAUSES OF CENTRAL PAIN

Vascular lesions in the brain and spinal cord
infact; hemorrage; vascular malformation
Multiple sclerosis
Traumatic brain injury
Syringomyelia and syringobulbia
Tumours abcesses

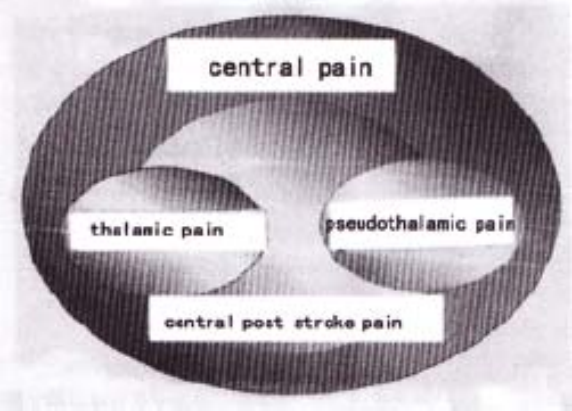


Figure 1: New concept of central pain

Inflammatory diseases other than MS; myelitiscaused by viruses, syphilis

Epilepsy

Parkinson's disease

Central post stroke pain

There are large differentes in the prevalence of central pain among the disorders that may lead to such pain(Tble 1).

CHARACTERISTICS OF CENTRAL PAIN

1.Pain location: It is usually started wich considerable emphasis that central pain is diffusely located. This notion appears to be largely derived from the fact that central pain often extends over large areas of the body, whole body, whole right or left side, lower half of the body, or involve one hand only, or just the ulnar or radial side of the hand or one face the location of the lesion determines the location of the pain (Table 2)

2.Quality of pain: central pain can have any quality, and the variation between patients is great, although some qualities are more common than others(Table 3). The different pain can coexist in a body region, or may be present in different parts of the body. Patients with central post stroke pain(CPSP), for instance, may have burning and aching pain in the leg & arm, and burning & stinging pain in the face.

3.Intensity of pain: central pain ranges from low to extremely high. However, even if the pain is of low or moderate intensity the patients assess the pain as severe because it causes much suffering due to its irritating character and constant presence.

4.Onset and other temporal aspects. CP may start almost immediately after occurrence of the lesion, or it may be delayed for up to several years, This delay may he as long as 2-3 years, but most patients the pain starts within a couple of weeks of the stroke.

5.Stimuli affecting of CP: cutaneous stimuli, body movements, visceral stimuli, emotions & changes in mood, allodynia evoked by touch, light pressure moderate heat or cord.

6.Neurological symptoms & signs: CP caused by perturbat ions of the somatosensory systems. Somatosensory abnormalities is important for diagnosis, such as hypoaesthesia, hyperaesthesia, paraesthesia or dysaesthesia, numbness, radiation, prolonged reponse

Table 1.with Central Pain (CP) in the USA 1989(250million)

Disease	Total patients(No)	Patients with cp(No)	Patients with cp(%)
Spinal cord injury	225000	68000	30
Multiple sclerosis	150000	42000	28
Stroke	2000000	168000	8.4
Epilepsy	1600000	44800	2.8
Parkinson's disease	500000	50000	10

Form Bonica 1991 and osterberg & Boivie, in preparation

Table 2.Common location of central pain

Stroke(Fig 2and 3)	All of one side All of one side except the face Arm and /or leg on one side Face on one side, extremities on the other side The face
Multiple sclerosis	Lower half of the body One or both legs Arm and leg on one side Trigeminal neuralgia
Spinal cord injury (Fig.4)	Whole body below the neck Lower half of the body One leg
Syringomyelia	Arm and thorax on one side One arm Thorax on one side One leg in addition to one of the above

From Jorgen boive; Bonica:Textbook of pain p888

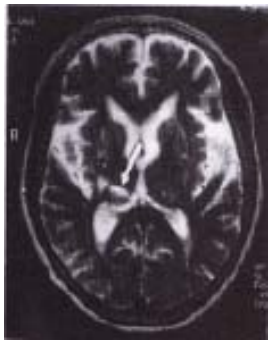


Figure 2: face and oral. Cavity pain from stroke CP, 5y, 75y. o,F.(MRI)

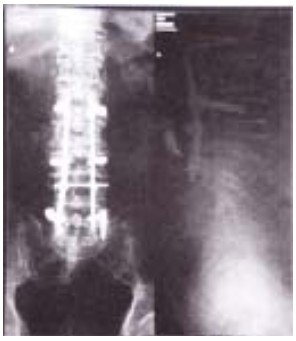


Figure 4: Spinal cord injury

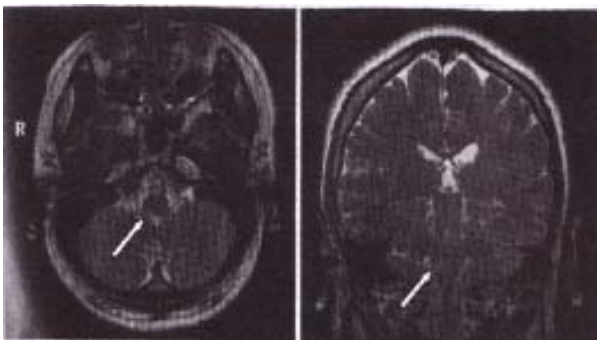


Figure 3:left clental pain from right externdal medulla oblongata infarction.25 y.o,F,(MRI)

latency, after sensations summation.

DIAGNOSIS OF CENTRAL PAIN

The definition of CP states that it is caused by a lesion or dysfunction in the CNS. Diagnostic step is first, therefore to ensure that the patient has a CNS disorder, for example, stroke or multiple sclerosis (MS), moderate spinal trauma, or suspected minor stroke. Secondary, A detailed history of the neurological symptoms and a neurological examination, Thrd, laboratory examination include CT scan, or MRI, assays of the cerebrospinal fluid (CSF), neuro physiological examination and other tests.

Recently, international headache commite suggested diagnostic standard of central post stroke pain (CPSP), (Table 4 and 5).

CURRENT TREATMENT OF CENTRAL PAIN

In the book "Textbook of pain" (Edited by Wall PD, Melzack R), Jorgen Boivie writed "because no universally affective treatment is available for central pain." "othen lasting for the rest of patients lives."

According to my practice of treatment for central pain patients, above mentation were net overall, I suggest that opposite conclusion, after through treatment for central pain were can be complete cured, can't continous until the rest of patients lives.

Table 3.Qualities of Central Pain (CP) patients

Burning※	Shooting	Stabbing
Aching※	Squeezing	Cramping
Lancinating※	Throbbing	Smarting
Pricking	Cutting	Pulling
Lacerating※	Crushing	Sore
Pressing※	Splitting Stinging	Icy feeling

※indicates the most common qualities

Table 4.Diagnostic standard of Central Post Stroke Pain※

A	One-side face pain and par aesthesia Pink, temperature, toach, along them have any one Sense disappear were appeared and have C and D
B	Among the next item, conform to number 1 or 2 ①blood vessel pathological changes (stroke) were appeared medical record ②appears blood vessel pathological changes on the CT or MRI
C	Pain and par aesthesia sere appeared at 6 month after stroke
D	Can't explain pathological changes of trigeminal nerve

※from international headache commite

Table 5.Diagnostic Standard of Face Pain by Multiple Sclerosis※

A	Pain were appeared on the one-side or both-sides, companion or not companion paraes thesia
B	There have evidence the patients suffer frome a multiple sclerosis
C	Appeared pain & par aesthesia, times of pons and trigeminal nerve thalamic (V) demyelinate were consist, maintained by MRI
D	Can deny other reasons

※from international headache commite

Treatment of central pain with minimally invasive

1.Neuroleptadenolysis of pituitary gland (NALP) under C-arm plus relevant place nerve block (RPNB) were very effective for central pain.

2.Cases example

①Case 1.

Cui xx, Male. 73-years-old, Diag. –parkinson's disease, both knee and leg's obstinate pain. Pethidine etc drugs were no effect. Narch-24-2005; NALP, after that pain score with VAS, from 10 come down to zero.

②Case 2.

Liu xx, Male, 61-years-old, Diag: syringomyelia obstinate pain at neck, sould, chest, arm. Occipital pain, in X hospital, cerebellar hermia were performed repair. December. 1st-200 NALP-after that, pain score with VAS from 10 come down to zero, next day raise up to 5, and then performed RPNB, cured.

③Case 3.

Park xx, Female, 54-years-old, Diag: central post stroke pain, right side of body and right leg pain. Treatment, NALP+RPNB, April, 22-2006, pain were complete disappear, pain score with VAS frome 10 come down to 2, May 19, 2006: psoas compartment block + Naosan's therapy, June 5, 2006, recover leave hospital.

Clinical application of NALP

1.Anatomic &physicologic consider

①position of pituitary glomd in brain (Fig 5)

②Left and right of sella turcica, there are sponge vein sinus internal caroted, abducens nerve, oculo-motor nerve,

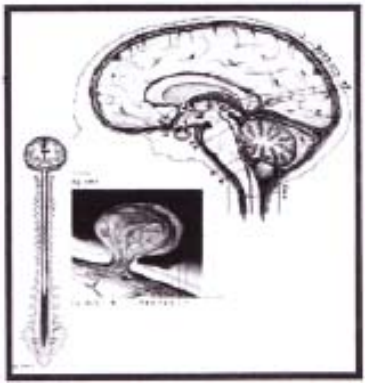


Figure 5:Position of Pituitary gland in bram

opthalamic nerve, maxillary nerve.

2.Contraindication of NALP

①the patients suspected will be died before 2 weeks

②infection of cavity of nos or sphenoid sinus

③calcification of sphenoid sinus

④bleeding of sphenoid sinus

3.Technique of NALp

①According to the results of examination, selece left or right nasal cavity; The patient laid in a spine position on the C-arm table; following general anesthesia, under C-arm fluoroscopy, double needle for NALP was injected to confirm the correct position; 1.8-2.0 ml of dehydrated alcohol or 5-10% phenol glycerine was injected into the pituitary.(Fig. 6A and B).

4.The effect of treatment with NALP

The degree of pain relief was assessed by the pain score with VAS. Excellent (0-2):116 cases (78.8%), Good (3-5):25 cases (17.8%), Excellent + Good were account for 96.6%, Moderate (6-8): 5cases (3.4%), No effect (9-10): o cases (0%). Table 6 shows kind of intractable pain disease by NALP.

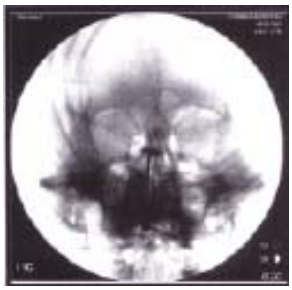


Fig.6. (A) Neuroleptadnolysis of pituitary Gland (NALP) radiograph of the anterior-posterior view of the needle located in middle line.

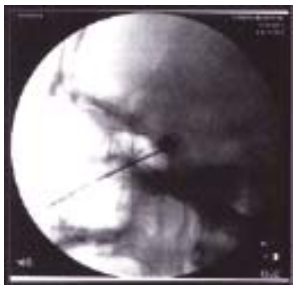


Fig.6. (B) NALP rediograph of the lateral view of the needle inserted into near pituitary.

Table 6.kind of intractable pain diseases by Neuroleptadenolysis of Pituitary Gland (NALP)

Kind of intractable pain diseases	Number of cases
Cancer pain	77
Whole body obstinate pain	11
Post operative pain syndrome	9
Whole body analogue rheumathritic pain	8
Failed back surgery syndrome (FBSS)	10
Neuropathic pain	3
Complex regional pain syndrome (CRPS)	4
Central pain	16
Brachial plexus injure pain	1
Viscera obstinate pain	5
Phantom limb pain	2
Low limbs pain of Parkinson's disease	1
Syringomyelia	2
Total	149

Drugs therapy

Treating central pain is no easy task, most treatment regimens for central pain are empirical and based on clinical experience.

1.Antidepression drugs:①amitriptyline 50-100 mg/d, Bid, or 10-20 mg/d,②doxepine.

2.Antiepileptic drugs:①Carbamazepine 400-800 mg/d, Bid, 4 weeks,②chlorzepam.

3.Antiarrhythmic drugs, local anaesthetics:①lidocaine,I. V.1 mg/kg, 30 min, iv gtt,②mexiletine.

4.Analgesics:①morphine,②codeine.

5.Adrenergic drugs:①colonidin 50μg, for epidural bl ock,②physostigmine,③pyridostigmine,④naloxone 25-50 mg.

Others

1.TENS:50-100 Hz, or 1-4 Hz

2.Spinal cord stimulation

3.Deep brain stimulation

4.Surgical therapy: Tasker suggest nerve root cutting, in the any level of spinal cord to cerebral cortex damage surgery, but no avail. Spinal antero-lateral cord incision were effective for pain of sacrum coccyx injury, but easy to relapse.

5.Sympathetic nerve block: stellate ganglion block (SGB) and other sympathetic ganglion block have definite effective.

REFERENCES

[1] Ministry of hygiene. Documents of health ministry.Chines Journal of Pain Medicine. 2007,13(5):1.
[2] Xiangmo Yan, Shuji Piao, Ning Fang. Treatment of cancer pain and obstinate pai n by neuroadenolysis of the pituitary gland. Chinese Journal of Anesthesiology, 1994,14(5):362.
[3] Xiangmo Yan, Shuji Piao, Ming Fang. Clinical application fo neuroadenolysis of the pituitary gland, Chinese Journal of Pain Medicine, 1995;1(1):23−5.
[4] Boivie J. Central pain .In Textbook of pain. Edited by Wall PD, Melzack R: − Churchill Livingstone, Harcourt Brace & Company 1994, pp 879−914.
[5] Yanagida H. Pituitary gland alcohol block. See: Bunkichi Wakasugi. Surgery Mook, No. 36−Tokyo, Ganahara publish Co.
[6] Xiangmo Yan. Present status of pain clinicians in china. 11th International Pain Clinic World Society of Pain Clinicians (IPCWSPC). Tokyo Japan. 2004; 7(11):111−2.
[7] D. Bruce Scott. Techniques of Regional Anaesthesia. Medglove S.A. Callifornia. 1989, pp 189−92.
[8] Eguchi C, Euchiyama H, Kitzumura N. A case report of chemical hypophysectomky wich showed remarkably long−term effect on a patient with recurrent breast cancer. Pain Clinic. 1987;8(1):93−6.
[9] Chai Mei, Yan Xiangmo. Treating cancer and non−cancer pain with neuroadenolysis of pituitary gland (NALP) and relanted changes in blood hormone level, Chinese Journal of Pain Medicine. 2005,11(6):340−5.
[10] Imai N,Ikawa M. Noboru Imai, et al. Central orofacial pain. Pain Clinic. 2007;28(6):791−800.
[11] Xiangmo Yan. Clinical Painology. Yanji, Yanbianpublishing. Co. 1996.209−16.

The effect of NMDA receptor antagonists on thalamocortical sensory processing in rat

Jiaheng Wang, Chaoping Wang, Tian Yu*
Zunyi Medical College, ZunYi, GuiZhou, China
*Corresponding Author, E-mail: zyyutian@21cn.com

N-methyl-D-aspartate receptors (NMDARs) are excitatory ionotropic glutamate receptors which are widely expressed in the central nervous system[1]. Many intravenous anesthetics are known as NMDA receptor antagonists[2], but the local effects of these drugs on NMDA receptors whether or not effect the sensory processing in thalamocortical circuit remain an open issue. In this study, we investigate the changes of tactile sensory processing in primary somatosensory cortex (S1) of rats by locally blocking the NMDA receptors in ventral posteromedial nucleus (VPM).

The study included 24 rats. During experiment procedure, anaesthesia was induced and maintained by infusion propofol. After surgery an extracellular tungsten electrodes were inserted into S1 for recording spontaneous local field potentials (sLFPs) and whiskers stimulation-evoked field potentials (eFPs) and a micro glass electrode was inserted into VPM for infusions of the NMDA receptor antagonist D,L-2-amino-5-phosphonovaleric acid (AP-5) 5ug/1ul[3], ketamine 25ug/1ul, 12.5ug/1ul and saline solution 1ul. An extracellular AC amplifier was used and the raw electric signals were collected via an CDE 1401 interface to a personal computer. Whisker stimuli were performed by deflections of the optimal whisker on the contralateral face. spontaneous sLFPs power spectrum and eFPs were analysed before and after administration of NMDA receptor antagonists.

After administration of AP-5 1ul（5ug/ul），the amplitude of eFPs were reduced and α (8-12Hz), β (12-25Hz) and γ (25-60Hz) powers of sLFPs decreased significantly. After administration of ketamine 1ul（25ug/ul）and (12.5ug/ul), the amplitude of eFPs was reduced and β (12-25Hz) and γ (25-60Hz) powers of sLFPs decreased significantly. After administration of saline solution 1ul there was no significant deviation on sLFPs and eFPs than before infusion.

The findings indicate that locally blocking NMDA receptor in VPM can reduce the excitability of primary somatosensory cortex which may result in a loss of information capacity..

Keywords: general anaesthetics, NMDA receptor antagonist, sensory processing, cerebral cortex, thalamocortical circuit, thalamus.

Acknowledgements: This work was supported by grants from the National Natural Science Foundation of China(No. 81060266), and State Key Laboratory of Neuroscience, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences

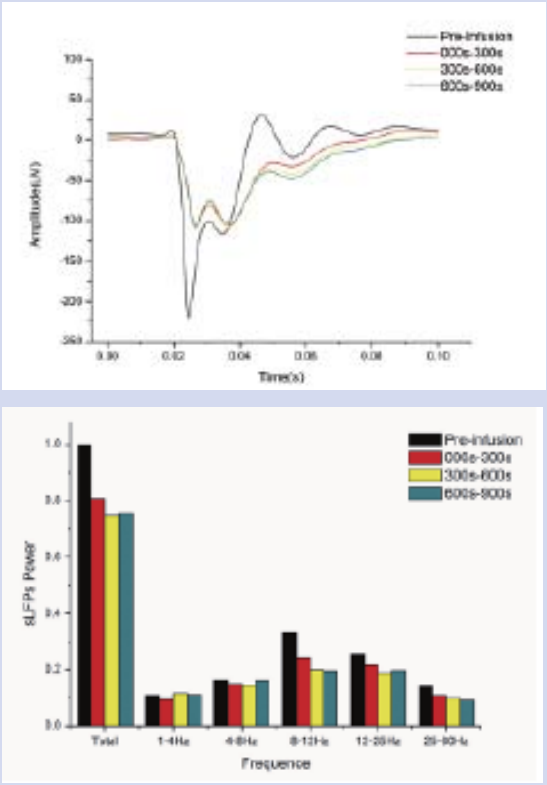


Fig1. After administration of AP-5 1ul（5ug/ul），the amplitude of eFPs were reduced and α (8-12Hz), β (12-25Hz) and γ (25-60Hz) powers of sLFPs decreased significantly.

References

1.Paoletti, P. and J. Neyton, NMDA receptor subunits: function and pharmacology. Curr Opin Pharmacol, 2007.

7(1): p. 39-47.

2.Alkire, M.T., A.G. Hudetz, and G. Tononi, Consciousness and anesthesia. Science, 2008. 322(5903): p. 876-80.

3.Hsu, E. and M.G. Packard, Medial prefrontal cortex infusions of bupivacaine or AP-5 block extinction of amphetamine conditioned place preference. Neurobiol Learn Mem, 2008. 89(4): p. 504-12.

Antibody variance about the anaphylactic shock induced by cystic echinococcosis in patients

Yimei Li , Hong Zheng*, Meiling Gu, Zaoling Liu, Tao Liu

Department of Anesthesiology, The First Affiliated Hospital of XinjiangMedical University, Urumqi 830054, China

*Corresponding Author, E-mail:xyzhenghong@yahoo.com.cn

Classification and level variation of specific antibody was important point of anaphylactic shock. IgE was one of the index estimated whether or not high sensitive state[1]. At a great extent, parasite antigen cause anaphylactic shock depending on IgG and IgG1 besides IgE in host[2]. We adopted prospective case-control study and discussed the changed feature of IgE、IgG、IgG1 in anaphylactic shock caused by cystic echinococcosis in patients. There was practical significance for raising safe and enlarging cure indication and improving prognosis and reducing mortality.

The Internal Review Board of the First Affiliated Hospital of Xinjiang Medical University granted permission for this study. The research had undertaken prospective case control study the records of 33 patients with cystic echinococcosis who were treated surgically at the first affiliated hospital of Xinjiang medical university between January 2008 and March 2010.we designated the 11 patients with anaphylactic shock as Group I and the 22 patients without anaphylactic shock as Group Ⅱ, and the two groups were matched according to 1：2.We collected respectively venous blood at preoperation, encyst ruptured instant time, shock instant time, a hour after encyst ruptured time, a day after encyst ruptured time, and a week after encyst ruptured time. We adopted quantitative assay to IgG,IgG1,and IgE by ELASA.

IgE, IgG1and IgG almost were twice higher in group I than in group II. there were statistically significant between group I and group II. For IgE/IgG1,there were not statistically significant between group I and group II.

Higher level of IgE,IgG and IgG1 predicted easy occurrence of anaphylactic shock after hydatid fluid flew over.IgG1 may be specific antibody of allergic reaction in cystic echinococcosis[3] and the level of IgG1had referred significance for the prognosis of anaphylactic shock induced by cystic echinococcosis.

Key words: cystic echinococcosis, anaphylactic shock, antibody

Acknowledgments of Funding source: This work was supported by National Natural Science Foundation of China(No.30960367, 2009)

References

1.Macglashan D Jr. Ann N Y Acad Sci,2005,10(50):73-88

2.Miyajima I,Dombrowicz D,Martin TR,et al. J Clin Invest,1997; 99: 901-914.

3.Carol L. Liebeler, Saonli Basu, et al. Hum Immunol. 2007; 68(2): 113–121.

Effects of Moderate Hyperventilation on Jugular Bulb Gases under Propofol or Isoflurane Anesthesia during Supratentorial Craniotomy

Fang Luo, MD, phD, Nan Ji, MD, phD, Tao Wang, MD, *Shuqin Li, MD, Jizong Zhao, MD, Ruquan Han, MD, phD, Jingjing Lu, MD

Department of Anesthesiology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100050, China

The purpose of this study was to investigate jugular bulb

gases during propofol or isoflurane anesthesia in patients undergoing craniotomy for removal of supratentorial brain tumors, and to clarify the effects of hypocapnia or normocapnia on those variables. Our ultimate goal was to determine whether the optimal ventilated status under total intravenous or inhalation anesthesia respectively in neurosurgical patients with supratentorial tumor is almost similar or not. Twenty adult patients were randomly assigned to receive a propofol infusion followed by isoflurane anesthesia after a 30-min stabilization period or isoflurane followed by propofol. Patients were also randomized to one of two treatment sequences: hyperventilation (arterial carbon dioxide tension, $PaCO_2$ = 272 mm Hg) followed by normoventilation ($PaCO_2$ = 372 mm Hg) or normoventilation followed by hyperventilation during isoflurane or propofol anesthesia respectively. Ventilation and end-tidal CO_2 tension were kept constant for 20 min. Radial arterial and jugular bulb catheters were inserted for blood gas sampling. Mean arterial blood pressure (MAP) and heart rate (HR) were monitored continuously. At the end of each study period, we measured the change of arterial and jugular bulb blood gases. The mean value of jugular bulb oxygen saturation (SjO_2) significantly decreased and oxygen extraction ratio (O_2ER) significantly increased under isoflurane or propofol anesthesia during hyperventilation compared with those during normoventilation, respectively. SjO_2 significantly decreased and O2ER significantly increased under propofol anesthesia as compared with those under isoflurane anesthesia during moderate hypocapnia. However, no significant change in SjO_2 and O_2ER was observed under propofol as compared with isoflurane during normocapnia in the study. Our results suggest that the optimal ventilated status under total intravenous or inhalation anesthesia in neurosurgical patients should be different. When hyperventilation was performed, the $PaCO_2$ under total intravenous anesthesia should be adjusted to somewhat higher level compared with that under inhalation anesthesia in neurosurgery in order to maintain an improved balance between cerebral oxygen supply and demand.

Keywords: Isoflurane – Propofol – neuroanesthesia - hyperventilation.

Breath pentane as a potential biomarker for survival in hepatic ischemia and reperfusion injury – a pilot study

CS Wang[1], JH Shi[2], B Sun[1], DS Liu[1], P Li[1], YL Gong[1], Y He[1], SJ Liu[1], AL Luo[2], EY Li[1]*

1.Department of Anesthesiology, the First Affiliated Hospital of Harbin Medical University, Harbin, China

2.Department of Anesthesiology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Background: Exhaled pentane, produced as a consequence of reactive oxygen species-mediated lipid peroxidation, is a marker of oxidative stress.1 Propofol is widely used as a hypnotic agent in intensive care units and in the operating room. Moreover, this agent has been reported to inhibit lipid peroxidation by directly scavenging reactive oxygen species.2 In this study using a swine liver ischemia-reperfusion injury model we have evaluated the hypothesis that high concentrations of breath pentane is related to adverse outcome and propofol could reduce breath pentane and improve liver injury and outcome of swine in this situation.

Methods: Twenty male swine were assigned to two groups: propofol (n=10) and chloral hydrate groups (n=10). Hepatic ischaemia was induced by occluding the portal inflow vessels. Ischemia lasted for 30 min followed by reperfusion for 360 min. Pentane in breath and blood were preconcentrated by means of solid phase microextraction. A gas chromatogram-mass spectrogram equipped with a GS-GasPro plot column was used for pentane assay.

Results: Exhaled and blood pentane concentration in the chloral hydrate group markedly increased 1 min after reperfusion and then decreased to baseline. Breath and blood pentane concentrations in the propofol group increased 1 min after reperfusion but were significantly lower than in the chloral hydrate group. A negative correlation was found between breath pentane levels and survival in the chloral hydrate group. The median overall survival was 251 min after reperfusion (range 150-360

min) in chloral hydrate group. All swine were alive in the propofol group.

Conclusions: Monitoring of exhaled pentane may be useful for evaluating severity of hepatic ischemia-reperfusion injury and benefit in predicting the outcome, propofol may improve outcome in this situation.

Key words: breath; pentane; biomarker; propofol; oxidative stress; hepatic ischemia and reperfusion injury;

Acknowledgement: Financial support by grants from the National Natural Science Foundation of China (No. 30571783 and 30972839) and Doctoral Fund of Ministry of Education of China (No. 20092307110005) are gratefully acknowledged.

References

1.Scholpp J, Schubert JK, Mleklsch W, et al. Clin Chem Lab Med 2002;40:587-94.

2.Kamada N, Kanaya N, Hirata N, et al. Can J Anaesth 2008;55:595-605.

The clinically commonly used dose of fentanyl vs. remifentanil for anesthetic induction with etomidate

Guohua Zhang, Li Sun

Department of Anesthesiology, Cancer Institute & Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

Background: Etomidate was proved to have a less inhibitory effect on the pharyngolaryngeal reflex. 1-3Hence, blunting the responses to endotracheal intubation is more dependent of opioids for etomidate induction. This study was to investigate the hemodynamic and conscious level changes during anesthetic induction with etomidate and fentanyl or remifentanil.

Methods: Sixty ASA Ⅰ-Ⅱ patients scheduled for elective surgery were allocated in a randomized, controlled and doubled blinded fashion to the two groups of 30 individuals each, Groups F and R. In group R, the patients received a remifentanil bolus of 1 ug/kg over 60s, followed by a continuous infusion of 0.15 ug·kg-1·min-1 .In groups F, fentanyl was given at a bolus dose of 3 ug/kg over 60s. Two minutes after initial bolus doses were given, etomidate 0.3mg/kg was administrated over 30s. After another two minutes interval, rocuronium 0.6mg/kg was given to facilitate endotracheal intubation. Opioid-induced sedation was assessed and two induction times, from administration of etomidate to loss of eyelash reflex and to a decrease in BIS to 50 were recorded .SBP, DBP and HR were also recorded immediately before intubation (T0), at intubation (T1), and 1min (T2),3min(T3) and 5 min (T4) after intubation. The average maximum changes of SBP [(|maximal or minimal measuring value-baseline|/baseline)×100%]for each group during observation period were calculated.

Results: There were four and two patients in groups R(13%) and F(6%), respectively, showing different degrees of sedation (P=0.0389).The time to loss of eyelash reflex was significantly longer in group F (75.4±26.7s) than in group R(60.6±22.3s)（P=0.023）. The times to a decrease in BIS to 50 were comparable between groups (P=0.19). SBPs were significantly lower in group R than in group F at each of observation time points(T0-T4) （P<0.001）. DBPs were also significantly lower in group R than in group F at T1-T4 time points （P<0.05）. HR was more effectively inhibited at T1 and T2 time points in group R compared with group F. The average maximum changes of SBP were（17±6）% and（12±7）% in groups R and F, respectively（P=0.004）.

Conclusions: Both remifentanil and fentanyl combined with etomidate can provide a clinically acceptable condition for endotracheal intubation with a relatively stable hemodynamics. Although remifentanil was likely to produce greater blood pressure changes than fentanyl, it was of no clinical relevance. BIS may not real-time reflect the sedation state during anesthetic induction using opioids and etomidate.

References

1.Uzun S, Gözaçan A, Canbay O,et al. J Int Med Res 2007;35:878-85;

2.Ulsamer B, Raps M. Anaesthesist 1988;37:517-21;

3.Schou J, Kübler J, Knaack-Steinegger R. Anaesthesiol Reanim 1992;17:67, 70-6.

Intensive insulin therapy and glycemic control to alleviate acute lung injury in cardiac surgery under cardiopulmonary bypass

No authors and address

Background: Insulin has been shown to have anti-inflammatory effects and also reducing the systemic inflammation during cardiopulmonary bypass (CPB), whereas hyperglycemia is known to increase the proinflammatory cytokines. In this study we aimed to assess the effect of Intensive Insulin Therapy(IIT) on cardiopulmonary bypass induced acute lung injury during cardiac surgeries.

Methods: Patients (n=40) undergoing elective cardiac surgery with median sternotomy under cardiopulmonary bypass were selected and were randomly divided into 2 groups, group C and group T. Group c (n=20) was the control group of the study and did not receive any intensive insulin therapy. Group T (n=20) was the Intensive Insulin Therapy with patients receiving insulin therapy throughout the operation according to the ALGIP protocol. Bio markers: High Mobility Group Box-1, Tumor Necrosis Factor-alpha, Neutrophil Elastase, and Myeloperoxidase levels were measured at different timing point.

Results: Bio markers levels were found to be lower in group T compared to group C. There was a significant decrease in the blood markers at two timing point in group T. High Mobility Group Box-1 had a biphasic increase in both groups but with values lower ($p<0.05$) 10 mins and 2 hours after unclamping of aorta. The same tendency was observed with Tumor Necrosis Factor-alpha, Neutrophil Elastase, and Myeloperoxidase levels at same timing points but with a monophasic increase.

Conclusion: Our results show that Intensive Insulin Therapy has a beneficial effect on the suppression of some of the inflammatory markers associated with acute lung injury during cardiopulmonary bypass.

Key words: Cardiopulmonary bypass, Lung injury, Insulin, Hyperglycemia, Inflammation.

Table 1: Demographic and clinical characteristics of patients			
Characteristics	Group C (n=20)	Group T (n=20)	p
Sex (M : F)	8:12	7:13	0.74
Age (year)*	46.9 ± 1 1.7	44.7 ± 8.2	0.49
Weight (kg)*	56.8 ± 9.7	58.9 ± 11.0	0.51
Body surface area (m2)*	1.71 ± 0.17	1.67 ± 0.16	0.44
Left ventricular ejection fraction (%)*	59.2 ± 4.8	58.9 ± 5.2	0.82
Cardiopulmonary bypass time (min)*	99.8 ± 35.7	101.6 ± 46.3	0.74
Cross-clamping time (min)*	68.5 ± 28.9	70.0 ± 38.2	0.77
Types of operation (number)			
Mitral valve replacement	11	12	0.75
Aortic valve replacement	1	1	1
Mitral and aortic valve replacement	8	7	0.74

No significant difference between the two groups (p>0.05)
Group C-control group, group T- Intensive Insulin Therapy group
*Mean ± standard deviation

Table 2: Comparisons of blood markers at different timing points between Group IIT and Group C							
Markers	Groups	T1	T2	T3	T4	T5	T6
HMGB 1	Group C#	4.5±1.5	12.2±2.7	14.1±3.4	10.8±2.6	12.9±3.6	15.5±4.4
(ng/ml)	Group IIT#	4.4±1.4	9.6±2.3*	10.4±2.5*	8.7±2.3	11.2±3.4	13.3±4.1
TNF-α	Group C#	25.5±9.6	84.6±29.3	98.4±38.5	67.1±23.7	46.2±18.9	-
(pg/ml)	Group IIT#	26.8±10.4	68.3±21.7*	80.7±30.9*	56.2±20.8	38.5±17.3	-
NE	Group C#	144.8±34.9	343.1±66.0	392.8±55.7	295.2±62.9	238.8±47.5	
(μg/L)	Group IIT#	154.1±38.8	250.9±62.6*	287.8±73.2*	229.7±74.1	194.2±46.2	
MOP	Group C#	10.6±4.9	32.6±16.3	46.5±21.6	31.8±18.8	25.2±17.9	
(μg/L)	Group IIT#	10.7±5.1	25.3±14.7*	35.1±19.8*	27.5±20.6	20.9±16.3	

*P<0.05
Data represented as mean ± SD
HMGB-1:High Mobility Group Box-1, TNF-α: Tumor Necrosis Factor-alpha, NE: Neutrophil Elastase, MOP: Myeloperoxidase

Table 3: Postoperative Complications			
Characteristics	Group C (n=20)	Group T (n=20)	p
Perioperative Hypoglycemia	0	1	0.31
Atrial fibrillation	5	4	0.71
Acute renal failure	0	0	
Superficial wound infection	1	1	1
Respiratory Tract Infections	1	0	0.31
Length of intubation (hours)*	26.1 ± 7.3	22.9 ± 3.9	0.13
In-hospital mortality	0	0	

No significant difference between the two groups (p>0.05)
*Mean ± standard deviation

Fig 1A. The evolution of HMGB-1 levels

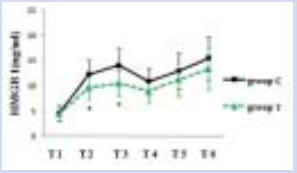


Fig 1B. The evolution of TNF-α levels

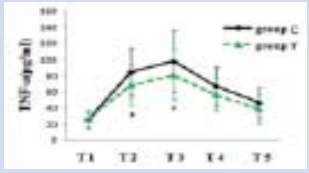


Fig 1C. The evolution of Neutrophil Elastase levels

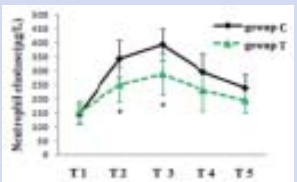


Fig 1D. The evolution of MOP levels

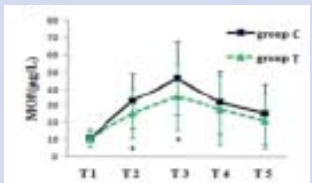


Fig 1A-1D: * P<0.05. A- plasma levels of HMGB, B- plasma levels of TNF-a, C- plasma levels of NE, D- plasma level of MOP. Group C: the control group. Group T: the Intensive Insulin Therapy (IIT) group. T timing; T1-Post induction of general anesthesia, T2- 10 minutes after unclamping of aorta, T3- 2 hours after unclamping of aorta, T4- 6 hours after unclamping of aorta, T5- 24 hours after unclamping of aorta, T6- 72 hours after unclamping of aorta. *P<0.05 for T2 and T3 for all serum markers when comparing IIT group T with the control group C

Comparison of propofol effect on patients with different blood groups

Yu Jianshe, Shi Haixia

Department of Anesthesiology, Affiliated Hospital of Inner Mongolia Medical College, Hohhot, 010050, China

Objective: To compare the effect of propofol on patients with different blood groups.

Methods: 80 ASA I or II patients, aged 40～60 yr, weighing 50～75kg，scheduled for selected general anesthesia，were enrolled in this study. According to ABO blood-group system, the patients were divided into 4 groups(n＝20):group A, group B, group AB, group O. After the patients in operation room coordinated 10 minutes, record the values of MAP, HR, BIS before administrating propofol (T0), then Propofol was administrated by TCI at an effect-site concentration of 4.0μg/ml initially，the target effect-site concentration was 6μg/ml. Record the values of MAP, HR, BIS at different time points of propofol effect-site concentration respectively, such as 4μg/ml(T1), 4.5 μg/ml(T2), 5μg/ml(T3), 5.5μg/ml(T4). Measured the value distance (Δ) of MAP, HR, BIS at each time point, compared with T0 as baseline.

Results: ΔMAP、ΔHR was the highest in group B($P<0.01$)，the second in group($P<0.05$),and group A and group B has no significance. Between T3 and T4, ΔBIS in group A was higher than the other blood groups.

Conclusion: The effect of propofol is different on patients with different blood groups.

Key words: ABO blood-group system; Propofol; Sedation

Effects of different depths of anesthesia assessed by the bispectral index on early postoperative cognitive dysfunction in elderly patients undergoing hip replacement surgery

Yue Shi, Hong Ma

Department of Anesthesiology, First Affiliated Hospital, China Medical University, Shenyang, China

Objective: This study, with bispectral index(BIS) monitoring depth of anesthesia, is about to value effects of different depths of anesthesia in elderly patients who undergoing hip replacement surgery of early postoperative cognitive dysfunction (POCD)during total intravenous anesthesia or inhaled anesthesia.

Methods: eighty ASA I-II patients with age≥55 undergoing hip replacement surgery were randomly allocated into one of four groups: lower BIS regimen group or higher BIS regimen group maintained by intravenous anesthetics or inhalation anesthetics . Routine anesthesia introduction was performed ,and BIS was maintained with 40-50 in lower BIS regimen group and maintained with 50-60 in higher BIS regimen group. The patients' cognitive status was assessed with a cognitive test battery to recognize if the POCD or delirium takes place.

Results: The incidence of POCD in lower BIS regimen group or higher BIS regimen group did not differ between the two groups.

Conclusion: Depth of anesthesia assessed by the bispectral index is not related to postoperative cognitive dysfunction in elderly patients undergoing hip replacement surgery.

Keywords: Postoperative cognitive dysfunction（POCD）; bispectral index（BIS）;depth of anesthesia; hip replacement surgery ;delirium

References

1.Newman S, Stygall J, Hirani S et al. Anesthesiology 2007; 106: 572-590.

2.Hudetz JA, Iqbal Z, Gandhi SD, et al. Anesthesiology 2007; 106: 423–430.

3.Bekker AY, Weeks EJ. Best Pract Res Clin Anaesthesiol 2010; 17: 259–272.

4.Rasmussen LS, Steentoft A, Rasmussen H et al. Br J Anaesth, 1999; 83 (4) : 585-592.

5.Moller JT, Cluitmans P, Rasmussen LS et al. Lancet, 1998; 351(9) : 857-861

6.Marcantonio ER, Goldman L, Mangione CM, et al. JAMA 2010; 271:134–139.

7.Bekker AY, Weeks EJ. Best Pract Res Clin Anaesthesiol 2003; 17:259-272.

Hyperalgesia of Remifentanil in postoperative patients: a study of MTD10 using continual reassessment method

He Wang, Xiao-Qian Li, Jun Wang, Hong Ma

Department of Anesthesiology, The First Hospital, China Medical University, Shenyang, Liaoning, P.R. China.

Remifentanil is a new synthetic ultra-short opioid receptor agonist. recent clinical observations suggested a possible role for remifentanil to frequently elicit an increased sensitivity to noxious stimulus withdrawal. It is still unclear what extent for clinical use not prone to inducing hyperalgesia as it was demonstrated dose-dependent The Continual Reassessment Method (CRM) was originally used to rapidly determine the maximum tolerated dose of the new drug for chemotherapy. With advantages of fewer samples without double-blind, nowadays, the CRM has also been used in general clinical studies10-13. Therefore, the current study was firstly designed to estimate remifentanil-induced postoperative hyperalgesia and to determine its MTD10 (or dose leading to any other probability of success) using the CRM with advantages of markedly reduced sample size and the probability of severe side effects occurred.

With ethical committee approval and informed consent obtained from patients, eight dose levels were chosen before the study was started: 0.05 μg $kg^{-1}min^{-1}$, 0.10μg $kg^{-1}min^{-1}$, 0.15μg $kg^{-1}min^{-1}$, 0.20μg $kg^{-1}min^{-1}$ 0.25 μg $kg^{-1}min^{-1}$, 0.30 μg $kg^{-1}min^{-1}$, 0.35 μg $kg^{-1}min^{-1}$ and 0.4 μg $kg^{-1}min^{-1}$. Recruited patients in a cohort were allocated to the same dose of remifentanil, determined by the responses (the existence of hyperalgesia) of previous patients. Remifentanil-induced hyperalgesia was defined as statistical differences in pain detection threshold or pain tolerated threshold tested by transdermal electrical stimulator at any time within 24h compared with baseline measurements.

Thirty patients divided into 10 cohorts were enrolled in this study. During the trail procedure, one cohort received 0.05 μg·kg^{-1}·min^{-1}, three cohorts received 0.20 μg·kg^{-1}·min^{-1} and the remaining six cohorts were assigned 0.15 μg·kg^{-1}·min^{-1} of the dose. Of which the12th, 18th and 18th patients in the fourth cohort, sixth and seventh cohort with the does level of 0.20 μg·kg^{-1}·min^{-1}, 0.20 μg·kg^{-1}·min^{-1} and 0.15 μg·kg^{-1}·min^{-1} respectively, were indicated the occurrence of acute postoperative hyperalgesia, and posterior response probability of the situation described was then computed and analyzed by application of BPCT software in a sequential logistic model. Based on seven stopping criteria of CRM, the maximum tolerated dose in 10% of patients was 0.15 μg·kg^{-1}·min^{-1} calculated by with a final estimated posterior response probability of success 8.4% closest to the target (95% credibility interval, 0.020-0.227). During the titration period, there was a significant curve relationship between dose level and posterior response probability. From which we can figure out the dose needed to induce hyperalgesia in 10% patients was 0.16 μg $kg^{-1}min^{-1}$ calculated by inverse solution from the predicted dose-probability curve, larger than clinical routine use.

According to our study, remifentanil administrated with the clinical routine dose in a short term is not associated with the development of acute postoperative hyperalgesia for almost patients, may be a perfect and safe choice of anesthesia.

Keywords: Breast cancer surgery, Continual Reassessment Method, general anesthesia, hyperalgesia, maximum tolerated dose, remifentanil

Table 1: Dose allocated, corresponding responses observed and posterior probability of acute postoperative hyperalgesia associated with each administrated dose

Cohort (No)	Patients cases (n)	Dose (μg.Kg^{-1}.min^{-1}g)	Cases associated with postoperative hyperalgesia (n)	All dose levels of remifentanil(μg.kg^{-1}.min^{-1}g) 0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40 predicted probability of postoperative hyperalgesia associated with each dose level(%) 10 15 30 40 55 70 90 99 posterior probability of postoperative hyperalgesia associated with each dose level(%)							
1	3	0.05	0	1.5	3.1	12*	21.8	42.7	68	95	99
2	3	0.15	0	0.3	0.8	5.0	11.9*	33	66.2	97.2	100
3	3	0.20	0	0.1	0.22	2.2	6.6*	25.4	64.6	98.4	100
4	3	0.20	1	0.6	1.4	7.4*	15.7	37.1	67	96.4	100
5	3	0.15	0	0.4	1	5.7	13*	34.3	66.5	97	100
6	3	0.20	1	0.8	1.8	8.5*	17.3	38.7	67.3	96	99.9
7	3	0.15	1	1.6	3.3	12.5*	22.4	43.1	687.1	94.8	99.9
8	3	0.15	0	1.2	2.6	10.7*	20.1	41.3	67.7	95.4	99.9
9	3	0.15	0	0.9	2.1	9.3*	18.4	39.8	67.5	95.8	99.9
10	3	0.15	0	0.8	1.7	8.3*	17.0	38.4	67.2	96.1	100

Dose allocated, corresponding responses observed and posterior probability of acute postoperative hyperalgesia associated with each administrated dose in each cohort. *Dose was chosen to administrated in the next cohort with posterior probability calculated was closest to the target (10%).

References

1. Joly V, Richebe P, Guignard B, Fletcher D, Maurette P, Sessler DI, Chauvin M. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. Anesthesiology 2005; 103(1):147-155

2. O'Quigley J, Zohar S.Retrospective robustness of the continual reassessment method. J Biopharm Stat 2010 Sep; 20:1013-1025.

Sufentanil limits the myocardial infarct size by preservation of the phosphorylated connexin 43 in rat in vivo

Y Wu[1,2], EW Gu[1], WP Fang[1], Y Zhu[1], L Zhang[1], XQ Liu[1]

1.Dept of Anesthesiology, The First Affiliated Hospital of Anhui Medical University，Hefei, China;

2.Dept of Anesthesiology, The Second Affiliated Hospital of Anhui Medical University，Hefei, China

Myocardial ischemia reperfusion injury (MIRI) was obviously limited by ischemic postconditioning[1-2]. The opioids could also protect the rats heart from MIRI when aiministered after myocardial ischemia[3-4]. While sufentanil, with little hemodynamic instability, has been used widespreadly, especially in the cardiovascular surgery. In the present study, we investigated whether sufentanil can mimic the effect of ischemic postconditioning and evaluated the function of gap junction proteins, connexin 43 (Cx43) in the cardioprotection effect of sufentanil.

All experiment protocol was approved by the local committee for the use of live animals in teaching and research. Forty-eight male Sprague-Dawly rats weighing 230～330 were randomly allocated to eight groups for infarct size determination. All animals were subjected to 30 min of left coronary artery occlusion and 120 min of reperfusion except group sham in which rats underwent perfusion without ischemia. 1ml of normal saline or sufentanil with the dose of 0.1, 0.3, 1, 3, 10 μg/kg were administered at the 25 min of ischemia (group control, CON; group 0.1～0.3 sufentanil postconditioning, 0.1～0.3 SpostC), and rats underwent 3 intermittent cycles of 10 s reperfusion alternating with 10 s ischemia immediately at the onset of reperfusion (group ischemic postconditioning, IpostC). The infact size (IS) and the area at risk (AAR) were measured by 2,3,5-triphenyltetrazolium staining (TTC). MIRI was determined by IS/AAR. Another twelve hearts were collected at the 5 min of reperfusion in group CON, IpostC and the optimal dose of sufentanil which has the maximal reduction in the IS/AAR and together with group sham at the 35 min of perfusion for Cx 43 western blot analysis.

Both ischemic and sufentanil postconditioning reduced the myocardial infarct size compared with group CON. IS/AAR was significantly decreased in the treatment groups except group 0.1SpostC compared with group CON, and 1 μg/kg of sufentanil has the optimal protective effect in the sufentanil postconditioning groups ($P < 0.05$). Increasing the dosage could not afford further cardioprotection. The sigmoidal equation of the dose-effect curve was Y=0.374 9+0.487 2/（1+101.502-X），ED50 was 0.03174μg/kg. Cx43 underwent dephosphorylation in response to ischemia-reperfusion measured by Western blot at the anterior myocardium tissues of left ventricle while ischemic and sufentanil postconditioning preserved the phosphorylation of Cx 43.

Sufentanil postconditioning can protect myocardium against ischemia reperfusion injury in rat hearts in vivo which is comparable to ischemic postconditioning, and the effect is dosage-dependent and ceiling-effective, 1μg/kg of sufentanil has the optimal protection. Increasing the dosage could not afford further limitation of IS/AAR. Preservation of phosphorylation of connexin 43 plays an important role in the cardioprotection.

Keywords: sufentanil, ischemic postconditioning, ischemia reperfusion injury, myocardium, connexin 43

References

1. Zhao ZQ, Corvera JS, Halkos ME, et al. Am J Physiol Heart Circ Physiol 2003; 285: H579-88

2. Yellon DM, Opie LH. Lancet 2006; 367: 456-8

3. Chen Z, Li T, Zhang B. J Surg Res 2008; 145: 287-94

4. Wong GT, Li R, Jiang LL, et al. Acta Anaesthesiol Scand 2010; 54: 510-8

Effect of morphine preconditioning on myocardium against ischemia-reperfusion injury with chronic heart failure in vivo

YX Wu[1], Y Zhang[1],Y Li[1], XW Hu[1],LJ Weng[1],F Jiang[2]

1.Department of Anesthesiology, Second Affiliated Hospital of Anhui Medical University, Hefei 230601, China;

2.Department of ultrasonography, Second Affiliated Hospital of Anhui Medical University, Hefei, 230601, China ;

Background: Previous studies have suggested that morphine preconditioning can mimic cardioprotective effect of ischemic perconditioning in rat heart. However, it is intriguing to note that there are some pathological conditions such as aging, cardiac hypertrophy. The aim of this study is to investigate the effect of morphine preconditioning on myocardium ischemia-reperfusion(I/R) in rats heart with chronic heart failure in vivo. Methods Healthy male SD rats weighting 220-250g were administered adriamycin 2.0 mg/kg for six weeks at a total dose of 12mg/kg by tail vein injection as the chronic heart failure model group1. Transthoracic echocardiography was performed to measure left ventricular diameters at 8 weeks after the first infusion. Then all the rats in the model group were randomly divided into 10 groups(n=6 each): group Ⅰ sham operation was performed (S);group Ⅱ myocardial I/R(I/R); group Ⅲ (ischemia precondition) the animals were subjected to three cycles of 5-min occlusion and 5-min reperfusion before ischemia (IPC) and group Ⅳ and Ⅴ and Ⅵ(different dose of morphine precondition)morphine was given by vein in 3 repeated total dose of 0.045,0.09,0.15mg/kg respectively at 5 min intervals before 30 min ischemia(MPC1, MPC2, MPC3); naloxone(the non-selective opioid receptor antagonist) and wortmannin(PI3-kinase inhibitor) were given in groupⅦ and groupⅧ at a dose of 3.0mg/kg and 0.3mg/kg before MPC with the better protective effect (Nol+MPC*,Wor+MPC*); In groupⅨ and Ⅹ, naloxone and wortmannin were respectively given at 40 min before ischemia. Myocardial I/R was induced by 30 min occlusion of left anterior descending branch of coronary artery followed by 120 min of reperfusion in all groups2 except group Ⅰ.HR and BP were monitored and recorded at 15 min after surgery procedures (T0) after ischemia preconditioning or morphine preconditioning (T1), 30min after regional ischemia(T2), 2h after reperfusion(T3). Rat –pressure product(RPP) were calculated. All the animals were killed and the hearts were removed at the end of reperfusion to measure the area at risk(AAR) and infarct size(IS), IS/AAR ratio was calculated. Results HR, BP and RPP were significantly decreased in all groups as compared with the baseline values. In group Ⅴ and Ⅵ,infarct size as a percentage of area of risk was significantly reduced (n=6,P<0.05,P<0.01) in adriamycin induced heart failure rats but not in group . This effect was stopped by pretreatment with naloxone or wortmannin; infarct size as a percentage of area of risk was not reduced significantly in group Ⅲ than in group Ⅱ.

Conclusions: MPC can confer cardioprotection in adriamycin induced heart failure rats; morphine precondition with 0.15mg/kg produces better effect than 0.09 mg/kg. This effect maybe was mediated through cardiac opioid receptor. Meanwhile, PI3K signaling pathway may involved in this process. The cardioprotection effect induced by IPC in healthy rat heart was abolished in heart with chronic heart failure.

Key words: chronic heart failure, myocardial reperfusion injury, morphine, precondition, rat

Acknowledgement

This study was supported by National Science Foundation of China(No.30672032).And we thank ZW Chen, PhD, for his helpful suggestions in making the heart failure model.

References

1.SY Xu, RL Bian, X Chen. Pharmacology Experiment Methodology 2002:1079-96

2.R Li, GT Wong, TM Wong, et al. Anesth Analg 2009,108:23-9

The incidence and risk factors of postoperative residual curarization after

general anesthesia in a post-anesthesia care unit

M. Xie, D.X. Wang, and Z.Y. Geng

Department of Anesthesiology and Surgical Intensive Care, Peking University First Hospital, No. 8 Xishiku Street, Beijing100034, China

Postoperative residual curarization (PORC) after the use of neuromuscular blocking drugs (NMBDs) remains a clinical problem. Even though intermediate-acting NMBDs are using widely, PORC still commonly occur.1-3 The aim of this study was to determine the incidence of PORC in a post-anesthesia care unit (PACU) during daily work and to analysis the risk factors of PORC.

This was a prospective observational cohort study. General anesthesia was performed as routine practice. Train-of-four ratio (TOFR) was examined when patients were admitted to and discharged from the PACU. PORC was defined when TOFR was less than 0.9. Multivariate logistic regression analyses were performed to identify risk factors of PORC in the PACU.

Five hundred and sixty-nine patients were enrolled, among them 542 finished the study. On arrival at PACU, TOFRs less than 0.7 and 0.9 were observed in 166 (12.9%) and 376 (30.6%) patients, respectively. Multivariate logistic regression analysis showed that increasing age (OR 1.211, 95% CI 1.068-1.374, P = 0.003), hypothermia on arrival at PACU (OR 1.693, 95% CI 1.138-2.520, P = 0.009), and combined use of two kinds of non-depolarizing NMBDs (OR 1.778, 95% CI 1.043-3.032, P = 0.035) were the independent risk factors of PORC on arrival at PACU. On the other hand, prolonged duration from the last dose of NMBDs to arriving at PACU (OR 0.326, 95% CI 0.215-0.496, P < 0.001) and the use of NMBDs antagonist at the end of surgery (OR 0.341, 95% CI 0.164-0.709, P = 0.004) decreased the risk of PORC. The duration of stay in PACU was significantly prolonged in patients with PORC than those without PORC (38.6±21.5 min vs. 34.7±20.7 min, P = 0.045). The incidence of adverse events was significantly higher in patients with PORC than in those without PORC (16.3% vs. 9.6%, P = 0.025).

PORC is common in patients on arrival at PACU. Increasing age, hypothermia on arrival at PACU, and combined use of two kinds of non-depolarizing NMBDs were associated with increased risk of PORC, while prolonged duration from last dose of NMBDs to arriving at PACU and use of NMBDs antagonist at the end of surguery decreased the risk of PORC. The presence of PORC caused prolonged duration of stay in PACU and increased incidence of adverse events.

Keywords: Postoperative residual curarization, Post anesthesia care unit, Train-of-four ratio

References

1.Kim KS, Lew SH, Cho HY, et al. Anesth Analg 2002;95:1656-60.

2.Debaene B, Plaud B, Dilly MP, et al. Anesthesiology 2003;98:1042-8.

3.Cammu G, De Witte J, De Veylder J, et al. Anesth Analg 2006;102:426-9.

The incidence of dreaming during propofol short-term sedation

GH Xu[1,2], XS Liu[1], EW Gu[1], J Zhang[1], K Wang[2]

1.Department of Anesthesiology, First Affiliated Hospital, Anhui Medical University, 218 Jixi Road, Hefei, Anhui 230022, China

2.Department of Neurology, First Affiliated Hospital, Anhui Medical University, 218 Jixi Road, Hefei, Anhui 230022, China

Dreaming, a clinical sign of light anesthesia, is more common after propofol-based sedation1,2. A few studies focus on the relationship between the dreaming and anesthetic depth3. However, the dreaming of short- term sedation remains elusive. In this paper, we investigated the dreaming ratio, dreaming contents in gastroscope and first-trimester surgical abortion with propofol short- term sedation.

All patients wrote the informed consents and this study was approved by Anhui Medical University ethics committee. 100 patients presenting for elective outpatient

gastroscope and 100 patients presenting for first-trimester surgical abortion were sedated with propofol. Patients were interviewed immediately after they emerged from sedation using the modified Brice questionnaire1. If dreaming was reported, and the dreamers were immediately asked to complete a five-point Likert scales regarding the dream4. The ultimate goal was a report of dreaming during propofol short-term sedation.

In case of the similar recovery time, there was a significant difference in the incidence rate of dreaming between gastroscope group (18%) and first-trimester surgical abortion group (33%) ($p< 0.05$). Most of dreamers could remember the last thing and the first thing of modified Brice questionnaire, and the thing was related to surgical and anesthetic topics or events occurring during anesthesia. Few dreamers could recall anything between the first thing and the last thing. But there were no significant differences between the two groups. Furthermore, most dreams were simple and pleasant, and no influence on patients' satisfaction.

Recovery time of patients from propofol short-term sedation is not decisive factor to the incidence of dreaming during. The dream occurs need some degree the depth of anesthesia and is not related to the lower doses of anesthetic drug. The incidence of dreaming is associated with physical stimuli of different type of operation, and sexual nature of the procedure may be increasing the incidence of dreaming. But the content is unrelated to surgery and no influence the followed satisfaction of patients.

Key words: Dreaming, Propofol, Short-term sedation.

Acknowledgements

Support by Youth Culture Program of First Affiliated Hospital, Anhui Medical University, China (2009kj09).

References

1.Brice D, Hetherington R, Utting J: A simple study of awareness and dreaming during anaesthesia. Br J Anaesth. 1970; 42:535-42.

2.Eer AS, Padmanabhan U, Leslie K. Propofol dose and incidence of dreaming during sedation. Eur J Anaesthesiol. 2009; 26: 833-6.

3.Leslie K, Skrzypek H, Paech MJ, Kurowski I, Whybrow T. Dreaming during anesthesia and anesthetic depth in elective surgery patients: a prospective cohort study. Anesthesiology. 2007; 106: 33-42.

4.Marsch SC, Schaefer HG, Tschan C, Meier B. Dreaming and anaesthesia: total i.v. anaesthesia with propofol versus balanced volatile anaesthesia with enflurane. Eur J Anaesthesiol. 1992; 9: 331-3.

Experimental Study of the Ozone Oxidative Preconditioning on Hippocampal Neurons in Rat Forebrain Following Endotoxemia

Li Rui-hua[1], Cai Da-sheng[1], Pei Ling[1*]

2nd department of anesthesiology, the first affiliated hospital of China medical university

Objective: To investigate the protective effect of ozone oxidative preconditioning on hippocampal neurons in rat forebrain following endotoxemia .

Methods: Thirty health adult male SD rats weighing 200~220g were randomly divided into 3 groups (n = 10 each), group Ⅰ Endotoxin; group Ⅱ ozone oxidative preconditioning (OP); groupⅢ Control Group. Rats in Group Ⅱ were accepted the mixture of ozone and oxygen 1mg/kg(concentration：50μg/ml) by intraperitoneal injection on the same time daily, Rats in Group Ⅰ were accepted the same volume oxygen ,once a day , continuing 5 days, Rats in Group ⅢⅢwere not accepted any treatment. To establish the model of endotoxic rats in Group Ⅰ and Group Ⅱ accept 10% LPS 12.5 mg/kg by intraperitoneal injection on the same time daily 24 hours after ozone preconditioning was on the last time. Blood was get before all rats were put to death 6 hours after LPS injected. The hippocampal neurons of rats and the content of MDA , SOD in serum were recorded.. The changes of apoptotic factors caspase-3，bcl-2 and the changes of the hippocampal neurons in electronmicroscope were recorded.

Results: Pretreatment with ozone before endotoxemia enhanced the activities of bcl-2, but attenuated the activities of caspase-3 and the activity of SOD in serum is

increased, but the content of MDA in serum is decreased, meanwhile the injured level of hippocampal neurons in ozone pretreatment group is significantly attenuated compared with that in control group.

Conclusion: Ozone pretreatment can protect the hippocampal neurons in rat against endotoxemia .

Key words: endotoxemia; zone oxidative preconditioning; apoptotic factors; SOD MDA.

Impact of CYP2C9 polymorphism on the metabolic rate of ketamine in human liver microsomes

Yun-hui Zhao, Hong Ma, Jun-ke Wang

Department of Anesthesiology, First Hospital of China Medical University, Shenyang , China

Ketamine is a N-methyl-D-aspartate receptor antagonist used in clinical practice for its anesthetic, sedative, and analgesic properties. It is frequently used for induction of anesthesia in short term surgical operations. In recent years, there is increasing evidence of ketamine abuse, many cases of illegal ketamine consumption and dependence was reported1, 2. Ketamine is N-demethylated by cytochrome P450 (P450) enzymes in the liver into norketamine. The identification of the enzymes responsible for ketamine metabolism is of great importance in clinical practice. Yanagihara3 et al investigated the metabolism of ketamine in human liver microsomes at clinically relevant concentrations. They demonstrate that CYP2B6 is the principal enzyme responsible for ketamine N-demethylation in human liver microsomes at therapeutic concentrations of the drug. In another study, the human liver microsomal enzyme CYP2C9, CYP2B6 and CYP3A4 were identified as the main P450 isoform responsible for the N-demethylation of ketamine in pooled human liver microsomes obtained from 20 donors, at a ketamine concentration of 0.005 mM4. CYP2C9 catalysed 12 percent of clinically common used medicine. Genetic polymorphism, inhibition and conduction of enzyme and physiological factors could change activities of P450, so that pharmacokinetics and potency of drugs would be changed and interactions of drugs occurred5-7. In light of these studies, and in the view of the growing interest of ketamine both as a therapeutic agent and as a drug of abuse, the knowledge of the identity and the contribution of P450 enzymes to N-demethylation of ketamine in humans, at clinically relevant concentrations, are highly desired. The research about modulation of CYP2C9 expression at gene level was needed. It was helpful to elucidate mechanism of ketamine pharmacokinetics and predict individual difference.

With ethical committee approval and informed consent, two hundred and three cases were chosen, who were picked up for hepatic partial excision under general anesthesia in the General Department of the General Hospital of Shenyang Command of PLA, the First Affiliated Hospital and Shengjing Affiliated Hospital of China Medical University from March, 2006 to March, 2007. Human liver microsomes were also obtained from the cases mentioned above. Liver microsomes were prepared by the differential centrifugation and then stored at refrigerator(−70℃).Protein content of microsomes were measured with modified Lowry's method. The change of ketamine concentration in an incubation mixture with human liver microsomes was determined by high performance liquid chromatography (HPLC), to calculate the rate constants of metabolism of ketamine. The correlation of these rate constants with rates of metabolism of CYP2C9 selective substrate tolbutamide, and the effect of CYP2C9 specific inhibitor sulfaphenazole on ketamine metabolism were examined. The mobile phase: acetonitrile: KH2PO4: triethylamine (40:60:0.02). The flow rate was 1ml/min. Fluorescence detection wavelength was 211nm.Two-milliliter venous blood was taken after anesthesia for DNA estration and genotyping. Genotyping was performed by multiplex polymerase chain reaction (PCR) and restriction enzyme digestion with NsiI. Two different groups were created according to genotype, wild-type and mutation-type. The content of P450 and activities of CYP2C9 were compared for the two groups. Compare the metabolic rates of ketamine in the two groups. Ketamine metabolism test in the hepatic microsomes was performed as that of mentioned above.

All PCR products were specific 170bp fragments. PCR products of CYP2C9 mutant type (CYP2C9*3) had one NSiI catalytic site, and was separated into 140bp and 30bp segments by enzymolysis. Therefore wild type had one segment 170bp, the mutant heterozygote had three segments 170bp, 140bp and 30bp, and the mutant homozygote had two segments 140bp and 30bp. In the two hundred and three cases, one hundred and ninety-six cases belonged to wild type; seven cases belonged to mutation heterozygote and mutation homozygote was not detected. The range of content of P450 was 0.4-1.0nmol/mg it fitted the demand of content of P450. For the group of wild type, the content of P450 was 0.76nmol/mg and for the other group, mutation group, was 0.81nmol/mg. ($P>0.05$) For the two groups (wild type group and mutation group), the metabolic rate of tobutamide was 1.7nmol·min-1·mg-1 protein and 0.6nmol·min-1·mg-1 protein respectively. ($P<0.01$) The metabolic rate of ketamine was 7.9nmol·min-1·mg-1 protein for the wild type group and 5.3 nmol·min-1·mg-1 protein for the mutation group. ($P<0.05$) The present study showed that CYP2C9 polymorphism had no effect on the content of P450 in human liver microsome. CYP2C9 polymorphism decreased activity of CYP2C9. CYP2C9 polymorphism had an effect on metabolism of ketamine in human liver microsomes. CYP2C9 polymorphism was an important genetic factor to produce individual differences of ketamine pharmacokinetics.

Key words: CYP2C9; gene polymorphism; ketamine; pharmacokinetics

References

1.Jansen K , Darracot-Cankovic R. J Psychoactive Drugs 2001; 33:152–158

2.Moore KA, Sklerov J, Levine B, et al. J Anal Toxicol 2001; 25:583–588

3.Yanagihara Y, Kariya S, Ohtani M, et al. Drug Metab Dispos 2001, 29: 887-890

4.Hijazi Y, Boulieu R. Drug Metab Dispos 2002; 30: 853-858

5.Takanashi K, Tainaka H, Kobayashi K, et al. Pharmacogenetics 2000; 10: 95-104

6.Niemi M, Cascorbi I, Timm R, et a1. Clin Pharmacol Ther, 2002, 72(3): 326-332

7.Leung YH,Chow CH,Lie KW,et a1.Blood 2001, 98: 2584-2587

Role of GABAB receptors in spinal dorsal horn neurons in the development of diabetic neuropathic pain

Xiu-li Wang, Yue-xian Guo, Rui Dong, Yan-tao Liu, Jiang-hong Ma

Department of Anesthesiology, The Third Hospital of Hebei Medical University, Shijiazhuang 050051, China

Correspongding author: Xiu-li Wang,E-mail: wangxl301@yahoo.com.cn

Background: Diabetic neuropathic pain(DNP) is a common clinical problem and remains difficult to treat with classic analgesics. Most studies have focused on the changes of primary afferents in rats with DNP. However, it remains poorly undersood as to whether GABAB receptors in spinal dorsal horn neurons is altered in DNP. We explored the role of GABAB receptors in spinal dorsal horn neurons in the development of DNP in this study.

Methods: Rats with DNP were induced by single intraperitoneal injection of streptozotocin(STZ, 50mg/kg). Twenty-four rats with DNP(D group) were randomized into 3 groups according to 3,5,7weeks after STZ injection(D3,D5,D7,n=8 each group). Similarly, as a control group, twenty-four normal rats (C group) were randomly assigned into 3 group who received the equal volume saline injection(C3,C5,C7 n=8 each group). Blood glucose level and paw withdraw threshold(PWT) were medsured at 3,5,7 weeks of STZ/Saline injection. We used immunohistochemistry and western blotting to detect GABAB receptors expression at 3,5,7 weeks of STZ/Saline injection. The whole-cell voltage-clamp patch was used to record the glutamatergic mEPSCs of lamina II neurons and the baclofen(GABAB receptor agonist) effect only at 3 weeks after injection both two group(D3, C3group).

Result: The mean blood glucose levels in rats of

D groups were siginificantly higher than that in rats of C groups, while values of PWT in D groups were significantly lower than that in rats of C groups. In parallel and based on immunohistochemical semi-quantification , 3 weeks after STZ injection, D3 group exhibited siginificant increase in GABAB1 receptor's immunoreactivity in spinal dorsal horn compared with C3 group: 27.17±10.07 vs 83.33±12.42 , n=4, p<0.05, respectively, there was no siginificant difference in it among three(D3,D5,D7) groups; while values of GABAB1 receptors derived from western blotting quantification were remarkable attenuation in D5 group compared with C5 control group: 3.52±0.69 vs 2.09±0.30 , n=4, p<0.05, respectively. The baseline frequency of glutamatergic mEPSCs was siginificant higher in diabetic D3 group(7.18±0.42Hz, n=12neurons) than in control rats of C3 group(4.06±0.35Hz, n=9neurons, p<0.05). 1-50 uM baclofen dose dependently decreased the frequency but not the amplitude of mEPSCs both two groups, and caused a significantly greater decrease in the frequency of mEPSCs in the control(C3 group) than in diabetic rats(D3 group).

Conclusion: Reduced GABAB receptor's sensitivity at glutematergic neurons in spinal dorsal horn increases glutamate neurotransmitter release, which may contribute to the development of diabetic neuropathic pain.

Key words: diabetic neuropathic pain; spinal dorsal horn; GABAB receptor; mEPSCs; glutematergic

Sevoflurane-induced postconditioning protect cardiomyocytes from ischemia and reperfusion injury via Akt-eNOS signaling

LIU Y, DONG ZM

Department of anesthesiology,Second Clinical Hospital, Hebei Medical University,Shijiazhuang, 050000, China

Sevoflurane-induced postconditioning have a cardioprotective effect and limit myocardial infarct size. The activation of the PI3-kinase-Akt- endothelial nitric oxide synthase (eNOS) signalling pathways in reperfusion following ischemia was found to play a key role in myocardial protection by ischaemic postconditioning. The aim of the present investigation was to evaluate whether sevoflurane -induced postconditioning is dependent on Akt-eNOS signalling.

Using a model of regional myocardial ischaemia and reperfusion, Wistar rats were subjected to 30 min of regional myocardial ischaemia followed by 120 min of reperfusion. The rats were randomly assigned to one of the following five experimental groups: sham-operated controls (S group,n=10); ischaemia and reperfusion controls (I/R group,n=10); sevoflurane(2.5%) postconditioning (Spo group,n=10); a PI3K inhibitor, LY294002(0.3 mg kg(-1) i.v.) + sevoflurane (Spo+LY,n=10); and 0.02%DMSO+ sevoflurane (Spo+DMSO,n=10). Myocardial injury was assessed by measuring the serum concentration of the MB fraction of creatine kinase (CK-MB), Lactate dehydrogenase (LDH) and Troponin I(CTnI). Infarct size was assessed by Evans blue and 2,3,5-triphenyl tetrazolium chloride staining. Myocardial expression of Phosphorylation of Akt/total Akt and phosphorylated eNOS/total eNOS, a downstream target of PI3K. were assessed by western blotting.

The levels of CK-MB,LDH and CTnI were decreased in Spo group compared with I/R group(801+/-78 U/L, 724+/-79 U/L, 1.46+/- 0.76 ng/ml vs 957+/-69 U/L, 864+/-55 U/L, 2.66+/- 1.00 ng/ml, P<0.05). Myocardial enzymes were increased significantly in Spo+ LY group compared with Spo group (949+/-58 U/L, 920+/-66 U/L, 3.54+/-0.80 ng/ml,P<0.05).

Sevoflurane -induced postconditioning was seen as reduced infarct size compared with I/R group: 29.62+/-3.34% and 50.26+/-4.80% respectively (P<0.05). LY294002 abolished this cardioprotective effect with myocardial infarct size at 49.84+/-4.26% compared with Spo group (P<0.05). There were no differences in total Akt (t-Akt) and total eNOS. Akt and eNOS phosphorylation were increased after sevoflurane -induced postconditioning, but administration of LY294002 blocked this effect.

Our data demonstrate that sevoflurane-induced postconditioning protects the myocardium from ischaemia reperfusion injury could be partly through activation PI3-

kinase-Akt-eNOS signalling pathways.

Key words: sevoflurane; postconditioning; myocardial ischemia reperfusion; Akt-eNOS

Isoflurane induces apoptosis via endoplasmic reticulum stress response in rat pheochromocytoma neurosecretory cells

WANG Qiu-jun[1],ZHAO Juan[2], ZHAI Wen-hui[1],WANG Xiu-li[1],HUO Shu-ping[1],CHEN Xu-guang[1]

1.Department of Anesthesiology,Third Hospital of Hebei MedicalUniversity, Shijiazhuang 050051 ,china

2.Department of Cell Biology, Hebei MedicalUniversity, Shijiazhuang 050081 ,china

BACKGROUND: Isoflurane, a commonly used inhaled anesthetic, induces apoptosis by an unknown mechanism. Therefore, we investigated the mechanism of cytotoxicity in rat pheochromocytoma neurosecretory cells (PC12). We wished to ascertain if The mechanism of this local toxicity is via endoplasmic reticulum (ER) stress response.

METHODS: PC12 cells in vitro incubation with nerve growth factor (NGF) for 7 days.were treated with equivalent of 1 MAC of isoflurane for 12 h.MTT assay and flow cytometry were used to measure the cell viability and the rate of cells apoptosis at different times. .The expressions of caspase-12 were determined by immunohistochemistry.We also determined the effects of inositol 1,4,5-trisphosphate receptor (IP3R) (an intracellular Ca2+ channel in the ER) antagonist xestospongin C on isoflurane-induced cytotoxicity in PC12 cells.

RESULTS: soflurane at 1 MAC for 12 h induced cytotoxicity in PC12 cells, and also caused the increase of apoptosis index (AI) and calcium concentration ([Ca2+] i), Isoflurane did not induce significant changes of mitochondiral membrane potential (MMP), but increased The expression of caspase-12 protein. Xestospongin C significantly attenuated isoflurane cytotoxicity and inhibited the increase of apoptosis index (AI) , calcium concentration ([Ca2+] i) and expression of caspase-12 protein.

CONCLUSION: Isoflurane activates the ER membrane IP3 receptor, producing excessive calcium release and expression of caspase-12 protein , then triggering apoptosis. Isoflurane induces apoptosis via endoplasmic reticulum stress response in PC12 cells.

Funding:This work was supported with National Natural Science Foundation（30972832） and Hebei Natural Science Foundation (C2009001187）.

Comparison study of the difference of sedation level between epileptic and non-epileptic patients under general anesthesia with TCI of propofol when using BIS monitoring

Lili Yang, Tianlong Wang

Deprtment of anesthesiology，Xuanwu hospital，Capital Medical University

Background: BIS is widely used in clinical anesthesia to monitor the sedation level now. BIS monitoring is based on the results of normal brain electrical information processing. The epileptic patients always have had antiepileptic drugs for a long time before operation .It is reported that when BIS is used to monitor the sedation level of the epileptic patient there would be something abnormal1,2.However the systematic study about the credibility of BIS monitoring when it is used to monitor the sedation level of the epileptic is lacking. In our study ,we investigate the difference of sedation level （BIS）between the epileptic and non-epileptic patients under general anesthesia with TCI of different target concentrations of propofol.

Methods: Forty patients (ASA Ⅰ～Ⅱ) undergoing elective surgery were divided into 2 Groups: Group epileptic (n=20) and Group non-epileptic (n=20).The patients were anesthetized with target-controlled infusion of propofol. The initial target plasma concentration of propofol (Cp) was set at 1μg/ml. When the target effect-site concentration of propofol (Ce) had been equaled with the target plasma concentration of propofol for 5minutes,

the mean BIS values in the sixth minutes were recorded. Then, the target plasma concentration was changed to 2μg/ml. With the same method，the mean BIS values were also recorded when the Ce=Cp=2μg/ml，3μg/ml，4μg/ml，5μg/ml.The correlation analysis of the different target concentration of propofol and BIS value is made. The spectral index (BIS) of the epileptic with that of non- epileptic patients under different propofol target concentration were compared.P<0.05 is considered that the difference has statistically significant.

Results: 1.The BIS values were significantly decreased as Cp increased[r:0.935(the epileptic group) vs 0.958(the non-epileptic group)，P<0.01];2.At the same Cp and Ce，BIS values were higher in group non-epileptic than in group epileptic. The difference was statistically insignificant.

Conclusion:1. The BIS values were highly correlated with the target concentration of propofol. The BIS values can accurately reflect the actual level of consciousness of epileptic people under general anesthesia with TCI of propofol. 2. Under general anesthesia with TCI of propofol,the value of BIS between epilepsy and non-epilepsy patients has no significant difference, the requirement of propofol has no significantly difference between them under general anesthesia with TCI of propofol.

Key words: Epilepsy Anesthesia level Monitoring BIS Propofol TCI

Reference

1.Sophie Hamada, MD, Pierre-Antoine Laloë, MD,et al. Seizure After Aortic Clamp Release: A BISpectral Index Pitfall. J Cardiothorac Vasc Anesth 2008;22(1):119-121

2.Chinzei M,Sawamura S,Hayashida M,et al Change in BISpectral index during epileptiform electrical activity under sevoflurane anesthesia in a patient with epilepsy. Anesth Analg 2004;98(6):1734-1736

Heme oxygenase-1 fused to TAT-PTD transduces and alleviates ischemia/reperfusion injury in liver of rats

Na GUO[1], Yan-li ZHAO[1], Jing CHEN[2], Li-hui YUE[1], Da-ru LU[2]

1.Anesthesia Department, HeBei General Hospital, ShiJiazhuang 050051, China

2.State Key Laboratory of Genetic Engineering, School of Life Science, University of Fudan, Shanghai 200433, China

Heme oxygenase-1 (HO-1) is a stress-responsive enzyme that acts as the rate-limiting step in the catabolism of heme, yielding equimolar amounts of iron (Fe), biliverdin, and the gas carbon monoxide (CO). HO-1 has been described as a protein capable of cytoprotection via antiinflammatory, antioxidant, antiapoptosis, maintenance of microcirculation. The aim of this study was to analyze whether the induction of HO-1 by protein transduction in ischemia and reperfused liver of SD rat could result in cell protection and improved in vivo functional performance of liver.

We produced the fusion protein TAT-PTD-HO-1 and the model of liver ischemia/ reperfusion injury of SD rat. SD rats were given the purified TAT-HO-1 protein 10mg/kg by tailvein injection 4 h before ischemia. The level of ALT, AST, SOD, MDA, MPO protein and tunel assay were measured, and the histopathology was investigated.

We demonstrated that the fusion protein TAT-HO-1 was highly efficient in transducing into the cultured PLC/PRF/5 cells and significantly inhibited TNF-a/CHX induced apoptosis. The TAT-HO-1 treated rat showed better liver function. Oxidative stress, inflammatory and apoptosis index were significantly reduced compared with IRI group and HO-1 group. And the TAT-HO-1 treated rat liver showed better histopathology.

These results demonstrated that TAT-HO-1 protein pretreatment leads to attenuation of hepatic I/R injury through antiinflammatory, antioxidant, antiapoptosis. Thus, HO-1 induction by protein transduction would be a novel therapeutic strategy to combat hepatic I/R injury.

Acknowledgement:National Nature Science Foundation of China 30672024

Keywords: Protein transduction domain; TAT; Heme oxygenase-1; reperfusion injury

浦璎修 黄绍强
复旦大学附属妇产科医院麻醉科 上海 200011

摘要

报道一例产前超声诊断胎儿颈部肿块，成功进行剖宫产同时施行子宫外产时治疗(EXIT)的麻醉处理。关注术中麻醉管理，保障EXIT的施行确保母婴安全。

分娩期子宫外产时治疗的麻醉一例

Anesthesia for the Ex Utero Intrapartum Therapy Procedure

Ying-xiu Pu, Shao-qiang Huang
Department of Obstetrics and gynecology hospital affiliated to Fudan University, Shanghai 200011

Abstract

We present the case of a mother carrying a fetus of 37 weeks' gestation with a cervical mass who underwent the Ex Utero Intrapartum Therapy (EXIT) procedure for fetal airway access. This discussion will focus on the anesthesia management issues and concerns to be contemplated before embarking on the care of a pregnant mother whose child may need surgery shortly before delivery to ensure neonatal survival.

当胎儿伴有致命性的原发性或继发性气道梗阻时，新生儿在娩出后无法及时建立气道可导致缺氧、窒息甚至新生儿死亡。现代影像医学技术使产前宫内诊断和宫内治疗干预成为可能，从而提高新生儿的存活几率。子宫外产时治疗（EXIT），也称胎盘支持下胎儿产时手术(OOPS)，即在保持胎儿胎盘循环的同时进行胎儿手术。EXIT的成功需要产科、新生儿和儿外科、麻醉科、耳鼻喉科及医学影像学等多学科的通力协作综合治疗。适用于胎儿患有如先天性膈疝的严重病例、颈部巨大淋巴瘤或畸胎瘤、先天性高气道阻塞综合征、胸部异常及其他如胸脐联体婴儿等，以及先天性高位气道阻塞综合征(CHAOS)。我们报道一例我院进行的EXIT手术，并讨论该类手术麻醉与常规剖宫产手术麻醉的不同点。

病例报道

孕妇，31岁。三胎一产，有一次剖宫产术史，现孕37周。产前B超检查发现胎儿颈部前方肿块62×58×68mm，无回声，内见光带。考虑为淋巴管瘤可能（食管气管受压可能）。经产科、新生儿和儿外科、麻醉科、耳鼻喉科及医学影像学等多学科会诊讨论准备在行剖宫产时实行EXIT。方法:剖腹产前，在超声指导下确认胎盘位置和胎儿体位；然后打开子宫，暴露胎儿上半身，气管插管建立人工气道确保气道通畅，充分氧合后，结扎脐带，再将胎儿从母体分离。

孕妇术前一般情况良好，ASAⅠ级，各项血生化指标均在正常范围。术前产妇禁食禁饮8小时。产妇入室后，常规监测EKG，NIBP，SPO_2。开放右侧上肢静脉，静脉持续输注乳酸林格注射液。手术医生进行术前消毒铺巾。

麻醉诱导：静脉注射艾司洛尔25mg，丙泊酚2mg/kg，琥珀胆碱100mg快速顺序诱导插管。插管成功即切皮开始手术。

麻醉维持：吸入5%异氟醚，新鲜气流量6L/min，静脉持续推注丙泊酚4mg/kg/h，直至胎儿完全娩出，间断给予顺式阿曲库铵维持肌肉松弛。手术从切皮到胎头娩出历时5分钟，胎头娩出到胎儿完全娩出断脐历时3分钟。在这3分钟期间子宫保持松弛状态，麻醉医师成功进行了胎儿气管插管。新生儿在确保气道通畅的情况下转入儿科监护室，一周后顺利了进行颈部肿块切除术。

胎儿娩出后麻醉维持：手术中断脐前异氟醚呼气末浓度达到2.2%，断脐后立即关闭异氟醚，静脉给予舒芬太尼30μg，丙泊酚调整至6mg/kg/h。同时在麻醉回路内串联入一次性麻醉气体吸附器。停用吸入麻醉药后5分钟呼气末异氟醚浓度降到0.3%，停止吸入后6分钟将新鲜气流量降至1L/min。手术临近结束前静脉给予氟比洛芬酯50mg。手术结束时呼气末异氟醚浓度已经降为0。手术共历时35分钟。术后产妇转入麻醉后苏醒室。整个手术中$PetCO_2$维持在30-34mmHg，SPO_2维持在99-100%。术中出血量200ml，尿量80ml。

手术结束后4分钟，产妇开始出现自主呼吸，5分钟后产妇自主呼吸恢复良好，呼之睁眼，吸净少量口腔和气道内分泌物，拔除气管导管，改用面罩吸氧5L/min。约35分钟后产妇完全清醒，无不适主诉，停用面罩吸氧。产妇吸空气状态下血流动力学平稳，予送回病房。

术后产科医师检查认为产后子宫收缩良好，产后恶露少。术后第五天产妇顺利出院。

讨论

当胎儿伴有致命性的原发性或继发性气道梗阻时，可通过分娩期子宫外产时治疗（EXIT）的方法获得气道通畅或切除肿块。颈部巨大肿块是子宫外产时处理最好的适应证，常见有畸胎瘤和淋巴管瘤，患儿由于出生后肿块压迫气道，无法通气，导致出生后新生儿窒息及脑损伤。此时如能在胎儿胎盘循环状态下，先进行气管插管或气管切开，建立气道通气，再断脐，接着处理肿块，如此就能挽救患儿的生命。[1,2]

这样的手术和治疗对麻醉提出了与普通剖宫产不同的特

殊要求。见表1。[3]

表1 子宫外产时治疗（EXIT）与剖宫产的比较

比较	EXIT	剖宫产
子宫张力	目标：胎儿娩出前：最大限度的子宫松弛以部分娩出和胎儿治疗：胎儿娩出后：迅速恢复子宫张力	目标：最低程度的子宫松弛以及分娩后快速恢复高张力
首选麻醉方式	全身麻醉	区域麻醉
麻醉深度	深	尽可能浅以防胎儿镇静
宫内灌注温热液体	需要	不需要
麻醉医师数量	2：母儿各一位	1：母亲的一位

针对需要进行EXIT治疗的剖宫产手术，麻醉选择静脉吸入复合的全身麻醉。借助吸入麻醉药剂量依赖性的抑制子宫平滑肌收缩作用，引起子宫的松弛。高剂量的吸入麻醉药有利于保证最大限度的子宫松弛给EXIT的进行提供最佳条件。在EXIT结束后用静脉麻醉药丙泊酚维持手术，丙泊酚在血浆浓度较低时不会影响子宫平滑肌的收缩，只有达到10μg/ml才会对子宫平滑肌的收缩造成影响。[4]临床应用丙泊酚的血浆浓度一般为2-5μg/ml。使用静脉麻醉药维持，迅速降低吸入麻醉药的影响，配合使用子宫收缩剂逆转子宫的松弛状态以免产科手术中过度失血。

本例胎儿在产前检查中除外发现颈部肿块会对气道造成机械性梗阻外，未发现其他发育异常，因此产时治疗主要是建立新生儿通畅的气道。麻醉诱导在手术医师准备完善后开始。以高流量无重复吸入麻醉尽快达到胎头娩出进行EXIT的最佳条件，缩短断脐前胎儿暴露于深麻醉下的时间，减少麻醉药对胎儿可能产生的不良影响。手术中麻醉科和手术医师充分沟通配合，使本例手术产妇和胎儿暴露在高浓度吸入麻醉药的时间小于10分钟，产妇血流动力学平稳，新生儿在建立气道的情况下呼吸建立良好，没有出现呼吸抑制。

EXIT结束后以高流量新鲜气体辅以麻醉气体吸附器快速洗出吸入的异氟醚，短时间内异氟醚浓度降到苏醒肺泡气浓度以下，给予静脉药物维持手术，配合宫体注射缩宫素类药物使得产妇的术中和术后出血与常规剖宫产产妇无异。

在胎儿完全娩出前没有应用麻醉性镇痛药，为了维持血流动力学的平稳和麻醉深度，手术开始阶段的麻醉维持在吸入高浓度异氟醚的同时仍复合一定剂量的丙泊酚，初衷是避免麻醉性镇痛药对胎儿可能造成的呼吸抑制。总结病例后我们认为，这种非常规的剖宫产与常规手术相比，胎儿在断脐前就建立了气道，有利于对新生儿进行辅助通气，麻醉性镇痛药对胎儿可能产生的呼吸抑制的风险反而降低了。今后此类手术可以使用超短效的阿片类镇痛药如瑞芬太尼诱导维持，复合高流量吸入麻醉来完成胎儿娩出前的麻醉，后期使用静脉麻醉药替代吸入麻醉药。娩出后的新生儿即使存在呼吸抑制也可以通过辅助通气避免产生缺氧，必要时可以直接转运至儿科手术室进行手术。

吸入性麻醉药对于发育中的大脑的影响一直是关心的焦点，由于EXIT还是一项比较新的技术，需要更长时间的经验数据的积累。虽然在动物实验中发现吸入麻醉药作用于未成熟的大脑可能造成细胞凋亡引起以后的学习障碍，但是这类证据不足以证明对人类的影响。[5]接受EXIT治疗的婴儿需要后续的神经病学评估随访，目前还没有结论。这将是需要进一步研究的领域。

充分掌握麻醉药的药理特性，灵活合理应用，加上多科室协作使得对患有致命性气道梗阻的胎儿进行EXIT成为可能，进而获得最佳的围产儿结局。

参考文献

[1] M Ogamo, T Sugiyama, Y Maeda, et al. The ex-utero intrapartum treatment (EXIT) procedure in giant fetal neck masses [J]. Fetal Diagn Ther, 2005,20(3):214-218.

[2] Stevens GH, Schootb BC, Smetsc MJ, et al. The ex-utero intrapartum treatment (EXIT) procedure in fetal neck masses: a case report and review of the literature [J]. Eur J Obs & Gynec and Repro Bio, 2002, 100(2):246-250.

[3] Priscilla J, Garcia, M.D., M.H.A., et al. Case Scenario: Anesthesia for Maternal-Fetal Surgery The Ex Utero Intrapartum Therapy (EXIT) Procedure [J]. Anesthesiology, 2011, 114(6):1146-1150.

[4] Shin YK, Kim YD, Collea JV. The effect of propofol on isolated human pregnant uterine muscle [J]. Anesthesiology, 1998, 89(1): 105—109.

[5] Wilder RT. Is there any relationship between long-term behavior disturbance and early exposure to anesthesia? [J]. Curr Opin Anaesthesiol, 2010, 23(3):332-336.

第三届（上海）国际减灾与安全博览会暨长三角急救、危重、灾害医学论坛

第三届（上海）国际减灾与安全博览会暨长三角急救、危重、灾害医学论坛将于2011年10月12日至14日在上海世博主题馆2号馆隆重举行。

急诊、重症、灾害医学范畴广泛，从院前急救、复苏、中毒、创伤到危重病、灾害和急诊医疗服务体系，并且与国家的公共卫生突发事件和应急救援体系密切相关。急诊急救和灾害重症救治工作的及时、妥善与否，直接关系到急性重症病人和受灾害人群的安危和预后，急诊、重症、灾害医学作为新兴的跨多个临床医学专业的学科群，越来越受到重视和关注。

急诊重症灾害医学目前在我国正处于一个迅速发展的时期，从国家卫生部将急诊医学列为我国首批专科医师培训和认证的试点专业以及把重症医学列为首批卫生部重点专科建设专业学科，到长三角地区包括上海市多年前就把急诊医学（含重症医学）列为医师晋升高级职称的单独系列，这个学科群已进入发展的成熟时期，广大从事急诊急救、危重病救治和灾害应急救援的医务工作者也越来越多的得到了社会的尊重和承认。然而，我国急诊重症灾害医学在迅速发展的同时也面临着诸多的挑战，如何建设快捷有效的院前急救系统，如何加强医院急诊科（室）及ICU的建设和医院对突发事件的应急能力，如何从灾害医学的角度研究提升政府和社会对各类灾害的应急救援能力，以及对于急诊危重病医学的专业人才和队伍的培养等等，都是我们必须探讨和研究的问题

白洁 张晓琴 薛荣亮
西安交通大学第二附属医院麻醉科 西安 710034

新生儿咽壁畸胎瘤麻醉处理一例

Anesthesia Management for One Case of Neonate Pharyngeal Wall Teratoma

Jie Bai, Xiao-qing Zhang, Rong-liang Xue

Department of Anesthesiology,the second Affiliated Hospital of Xi'an Jiaotong University

Corresponding Author: Jie Bai, E-mail: baijie520@gmail.com

一、临床资料

患儿为出生2天女婴，体重3.35kg。喂水发现吞咽困难，呛咳，未好转就诊于我院。患儿足月顺产，无家族遗传病及传染病史。患儿一般情况尚可，平卧位呼吸困难明显，哭闹时加重。查体发现口腔中肿物，位置大小判断不明。颈部CT示咽侧壁囊肿。各项实验室检查均无异常，胸部x检查未见异常。心电图示：心电图大致正常。积极完善术前准备，出生6天拟在全麻下行侧壁囊肿切除术。术前三十分阿托品0.05mg肌注。入室后患儿平卧位，平静时呼吸困难，哭闹时呼吸困难明显，三凹征阳性。吸氧SpO2 93%，心率150次/分。麻醉开始前准备好吸引器，备好气管切开包，将患儿头侧向一侧，充分吸氧去氮后吸入浓度6%七氟醚诱导二分钟，患儿停止哭闹，意识消失，呼吸减慢变深，遂小儿喉镜轻柔暴露声门，尽量避免触碰肿物，2%利多卡因表麻咽壁、声门后插入3.0气管导管，后静脉推注芬太尼10ug，顺阿曲库胺0.3mg，吸入1.5%七氟烷，行机械通气，麻醉管理中严防脱管。手术进行20分钟，术中所见：肿物表面为皮肤组织，内为脂肪样物。手术结束后待患儿自主呼吸恢复，送ICU监护。次日拔管，安送病房。术后病理报告：病检号：2011-7669 1749179肿瘤形态码：M90800/1肉眼所见：灰白灰红色肿物2.5×1.8×1.6cm，表面光滑，切面淡黄色颗粒状。病理诊断：左咽侧壁脂肪组织瘤样增生，表面少许皮肤及附件，符合畸胎瘤。患儿术后恢复良好，两天后出院。

二、讨论

1.畸胎瘤是来源于性腺或胚胎剩件中全能细胞肿瘤,由二到三个胚层组织构成。畸胎瘤常见部位按发生频率依次为卵巢、睾丸、前纵隔、腹膜后、骶前和尾部, 偶见于颅底、松果体和甲状腺附近。本例患儿原发于口腔咽壁的畸胎瘤极少见[1]。

2. 麻醉难度

（1）患儿年龄小，不能配合，口腔肿物的大小、位置、性质不能探查，插管困难程度不能评估。

（2）口腔空间狭小，较大的肿物占位增加了气管插管困难，并不排除麻醉后无法通气，缺氧而危及患儿生命。

（3）术前肿物性质不明确，尝试插管过程中可能出现肿物破裂致气道梗阻甚至窒息可能。

（4）该患儿呼吸抑制后通气困难发生可能性大，并且若行气管切开对患儿术后的恢复影响极大。该病例罕见，无成功经验可循，故加大了麻醉的风险性。

3. 药物选择

氯胺酮麻醉时喉反射有抑制，并且用于新生儿麻醉极易引起新生儿呼吸抑制[2]。γ-羟丁酸钠是一种催眠性静脉麻醉辅助药，对呼吸系统没有明显影响，很少发生呼吸抑制，曾在我国使用很多，但因其睡眠时间长，可控性差，目前已逐渐被取代。七氟烷血气分配系数低，诱导及苏醒迅速，对呼吸道无刺激性，麻醉深度易于控制，很适合小儿麻醉，并能够保留患儿自主呼吸[2]。单用七氟烷进行小儿麻醉诱导和维持其在诱导期苏醒期兴奋躁动发生较多，高的肺泡七氟烷浓度可能致癫痫样作用[3],同时七氟烷与钠石灰相互作用可产生肾毒性代谢产物，所以我们选择高浓度七氟烷诱导，静吸复合维持麻醉。

4. 麻醉方法

我们术前进行了细致的分析和充分的准备，首先询问病史，详细了解病儿熟睡时呼吸状态，以便在麻醉时选择合适的体位尽量使儿呼吸通畅，选择七氟烷吸入麻醉，维持患儿自主呼吸，以避免不能预测的通气困难，充分的咽腔声门表面麻醉，减轻患儿插管应激，备好吸引设备，以备探查插管过程肿物破裂内容物阻塞气道，同时备好气管切开包以备插管失败通气困难之需，插管时轻柔置入小儿喉镜片，一边暴露一边推进，尽量不触碰肿物，暴露声门后完成插管，使手术顺利进行。

参考文献

[1] 李风芝，胡光春，徐华林，胎儿口腔上腭未成熟畸胎瘤一例. Chin J Pathol, August 1998, Vol 27, No. 4.250.

[2] 庄心良，曾因明，陈伯銮，现代麻醉学[M].人民卫生出版社,2009.1422.

[3] Constant I, S eeman R, Murat I. Sevoflurane and epileptiform EEG changes. Paediatr Anaesth , 2005, 15: 266-274.

徐巧莲 万献尧

大连医科大学附属一院重症医学科 辽宁大连 116011

摘要

目的：了解中国大连地区ICU患者中低钙血症发生率，并对低钙血症危险因素进行分析。方法：选择自2010年9月14日至2010年9月30日间入住大连市8家三级医院ICU的患者。入院当日采集以下资料：血总钙、血磷、乳酸、动脉血气pH、白蛋白，并记录性别、年龄、诊断、日照情况。结果：入选44例患者中低钙血症患者20例，低钙血症发生率为45.4%。根据血钙水平将患者分为低钙血症组和正常血钙组，两组间性别、年龄、pH值差异无统计学意义，而血磷、乳酸水平、白蛋白水平以及日照时间具有统计学意义。全身性感染患者18例，低钙血症发生率为61.1%；心血管疾病、神经系统疾病、创伤及其他疾病（急性药物中毒、过敏性休克、肝性脑病、DIC等）低钙血症发生率分别为40.0%、12.5%、40.0%、50.0%。结论：①ICU患者中低钙血症发生率高。②低钙血症与蛋白水平、血磷水平、乳酸水平以及日照时间长短相关，与年龄、性别、动脉血气pH值无关。③各种疾病中全身性感染低钙血症发生率最高，随后依次为其他疾病、心血管疾病、创伤和神经系统疾病。

关键词：低钙血症；危险因素；ICU

责任作者及联系方式：万献尧，E-mail:wanxianyao@gmail.com

ICU患者低钙血症发生率调查与危险因素分析

Incidence and Risk Factors of Hypocalcemia in Intensive Care Unit

Qiao-lian Xu, Xian-yao Wan

First Affiliated Hospital of Dalian Medical University,central ICU,Dalian Liaoning 116011

Abstract

Objective:To investigate incidence and risk factors of hypocalcemia in ICU of DaLian city.

Methods:Patients admitted in intensive care unit of eight tertiary hospitals in DaLian from 09-14-2010 8:00AM to 09-30-2010 07:59 AM.Patients' age、sex、diagnosis、serum total calcium、lactate, arterial blood gas、albumin、time expourse to sun were recorded at the first day they admitted.

Results:20 patientsamong 44 were found hypocalcemia.Incidence of hypocalcemia was 45.4%(20/44), Patients were divided into two groups based on serum total calcium level.There was no difference in age、sex and arterial blood gas PH between two groups.Lactate、albumin,time expourse to sun were different between two groups.18 of 44 patients were diagnosised sepsis,and incidence of hypocalcemia of sepsis、cardiovascular disease 、trauma、nervous system disease and other diseases were 61.1%, 40.0%, 40.0%, 12.5%, 50.0%.

Conclusion:①Hypocalcemia in ICU paitents were common.②Risk factors of hypocalcemia were Lactate、albumin、time expourse to sun.③Incidence of hypocalcemia of sepsis was higher than other disease.

Key Words：Hypocalcemia; Risk factors; ICU

Corresponding Author: Xiao-yao Wang, E-mail:wanxianyao@gmail.com

低钙血症在危重症患者中常见，文献报道发生率15%～88%[1-6]，尤其是全身性感染患者，且有资料显示低钙血症与疾病严重程度、ICU住院时间、ICU病死率具有相关性[5-7]，然而低钙血症在临床上并未引起足够的重视。筛查危重症患者低钙血症的发生率及相关的危险因素有利于临床医师在具体工作中提高对低钙血症的认识进而采取有效措施进行干预，对于降低危重患者因低钙所导致的神经系统或心血管系统的严重并发症具有重要意义。为此我们采用横断面调查的方法对大连地区新入急诊ICU或综合ICU的患者低钙血症发生率进行调查并对其相关因素进行分析。

一、对象与方法

1. 对象

选择大连市8家三级甲等医院自2010年9月14日8时00分至2010年9月30日7时59分16日间入住急诊ICU或综合ICU的患者。排除标准：年龄＜15岁或≥80岁；合并甲状旁腺疾病者；合并慢性肾功能不全；就诊前接受维生素D（VitD）治疗者；静脉或口服钙剂者；2周以内曾住院治疗者；采标本前接受血制品者；入住ICU后24小时之内死亡者。共入选44例患者。

2. 方法

所有入选患者入院后当日采集以下资料：血总钙、血磷、乳酸（LAC）、动脉血pH、白蛋白（ALB），并记录性别、年龄、诊断、日照情况。日照情况分为：≥2h或不足2h。

3. 仪器设备

血总钙、血磷、乳酸、白蛋白采用日立7600生化仪测定，方法为离子选择电极间接法。血气分析采用Gempremire 300血气仪测定。

正常值范围：血钙：2.1～2.5mmol/L；LAC：＜2.1mmol/

L；动脉血气分析pH：7.35～7.45；ALB：35～55g/L。

4. 统计分析

使用SPSS 13进行统计学分析，连续性变量采用均数±标准差描述，分类变量采用频数分布进行描述。

二、结果

1. 低钙血症发生率

共入选44例患者，其中血钙＜2.1mmol/L者20例，低钙血症发生率为45.4%；血钙在正常范围内共24例；入选患者中无高钙血症病例。

2. 低钙血症相关因素分析

根据血钙水平将患者分为低钙血症组和正常血钙组，两组患者一般资料及实验室检查结果见表1。两组间性别、年龄、动脉血气pH无差异，低钙血症组血磷、LAC水平高于正常血钙组而ALB水平低于正常血钙组；日照时间＜2h者低钙血症组为45.0%，而正常血钙组仅为11.2%，差异有统计学意义。

3. 基础疾病分布

44例患者中全身性感染18例，发生低钙血症者11例（发生率为61.1%）；其余为心血管疾病、神经系统疾病、创伤及其他疾病（包括急性药物中毒、过敏性休克、肝性脑病、DIC等）分别为5例、8例、5例、8例，低钙发生率分别为40.0%、12.5%、40.0%、50.0%。低钙血症发生率自高到低依次为全身性感染、其他疾病、心血管疾病、创伤和神经系统疾病（表2）。

表1 低钙血症相关因素分析

变量	低钙（n=20）	正常血钙（n=24）	P值
年龄	66.2±14.8	68.0±13.5	＞0.05
性别			
男	11（55.0%）	12（50.0%）	＞0.05
女	9（45.0%）	12（50.0%）	＞0.05
血磷（mmol/L）	1.2±0.4	1.1±0.5	＜0.05
pH	7.3±0.1	7.4±0.2	＞0.05
Lac	4.2±3.4	3.2±3.2	＜0.05
ALB	29.5±5.5	33.0±4.8	＜0.05
日照时间			
＜2h	9（45.0%）	4（11.2%）	＜0.05
≥2h	11（55.0%）	20（88.8%）	＜0.05

表2 基础疾病分布

诊断	低钙（n=20）	正常组（n=24）
全身性感染	11（61.1）	7（38.9）
心血管疾病	2（40.0）	3（60.0）
神经系统疾病	1（12.5）	7（87.5）
创伤	2（40.0）	3（60.0）
其他疾病	4（50.0）	4（50.0）

三、讨论

ICU患者多处于不同程度的应激状态，应激状态常导致细胞内外多种电解质紊乱，如Na^+、K^+、Mg^{2+}、Ca^{2+}等，其中Na^+、K^+等电解质紊乱因为可于短期内导致严重的后果而引起临床高度重视；而低钙血症因临床表现隐匿，在ICU患者中常常被忽视，事实上低钙血症在ICU患者中非常常见，尤其是全身性感染患者中低钙血症发生率更高，严重低钙血症如不及时处理，将出现非常严重的心血管和神经系统并发症[6,8]。临床和动物实验研究均表明，ICU中的低钙血症患者肾衰和院内感染发生率以及接受血制品治疗的比例更大，且与疾病严重程度、ICU住院时间、ICU病死率具有相关性[1,7,9]。进行危重症患者低钙血症发生率调查及相关的危险因素分析对于在临床工作中提高对低钙血症的诊断意识进而采取有效措施进行干预，从而防治危重患者因低钙所致的神经系统或心血管系统的严重并发症具有重要意义。但低钙血症是否可以作为评估疾病严重程度的一种可靠指标以及是否可以作为预后的预测因素仍不明确[5,10]，有待进一步的临床研究。

ICU患者低钙血症的发生机制尚不明确，目前认为与以下因素有关：①细胞因子介导的炎症反应降低机体对甲状旁腺素（PTH）的反应性；②交感神经兴奋、儿茶酚胺水平过高以及器官衰竭可导致PTH分泌障碍或PTH抵抗，并引起细胞内外钙离子的转移；③降钙素原（PCT）或LAC促使钙螯合增加；④VitD缺乏和（或）活化障碍[5,6]。据文献报道，低钙血症的发生率为15%～88%[1-6]，本研究为45.4%，表明ICU患者在应激状态下低钙血症十分常见。

研究中低钙血症组蛋白水平低于正常血钙组，差异具有统计学意义。有人认为，由低蛋白水平导致的血总钙水平下降，不能真实反映体内起生理作用的游离钙的水平，因此建议存在低蛋白血症时应用蛋白校正公式[6]计算出校正后的血钙水平，使用该校正公式一般白蛋白每下降10g/L，血总钙水平下降0.2mmol/L。但Dickerson等[3]的研究表明，ICU患者使用蛋白校正公式计算出的血钙水平常高于患者实际水平，换言之灵敏性较差，认为该校正公式并非由危重症患者推导出来的，因而也不适用于危重症患者[6]。

ICU患者常存在不同原因的缺血缺氧，致LAC生成增加，而LAC增高影响钙的螯合，血总钙水平降低。本研究中低钙血症组LAC水平高于低钙血症组，证实高乳酸血症是低钙血症的危险因素之一，MuEller等[11]报道血游离钙水平与LAC水平呈负相关。

有研究表明，碱中毒时游离钙与钙蛋白结合增加，致游离钙水平下降，pH每增加0.1，血游离钙水平下降0.05mmol/L[12]，对于纠正酸中毒的患者尤其应该考虑蛋白结合力变化对血钙的影响[6]。本实验中低钙血症组动脉血pH与正常血钙组比较无统计学差异，考虑与入选患者中无严重酸碱失衡有关。

体内调节钙磷代谢的最主要激素之一就是PTH，生理状况下PTH通过以下三种途径发挥作用：①PTH与肾远端小管细胞膜上特异性受体结合后，通过G蛋白介导，激活腺苷酸环化酶，生成cAMP，再激活蛋白激酶A(PKA)，进而催化蛋白质与酶的磷酸化，促进对钙的重吸收，使血钙升高。同时，PTH还能促进近端小管对磷的重吸收，使血磷降低。②PTH可使骨细胞膜对钙的通透性增高，使骨中的Ca^{2+}进入细胞，然后钙泵活动增强，将Ca^{2+}促转运至细胞外液中，引起血钙升高。③PTH可激活肾内的1α羟化酶，后者可使25（OH）D3转变成有活性的1,25（OH）$2D_3$。而应激状况下，由于PTH分泌障碍或由于器官功能障碍对PTH相对抵抗，导致血钙降低，血磷升高。本研究中低钙血症组血磷水平高于正常血钙组，

提示PTH可能是危重症患者低钙血症发生的原因之一。

1,25（OH）$_2$D$_3$是体内另外一种调节钙磷代谢的重要激素，而1,25（OH）$_2$D$_3$是由VitD活化而来，途径如下：人体皮肤和脂肪组织中的7-脱氢胆固醇通过阳光（紫外线）照射下经光化学反应，在皮肤中转化成VitD，后者是类固醇的衍生物，是人体所必需的一种营养物质，VitD经肝细胞微粒体内的25-羟化酶作用形成25（OH）D$_3$，后者再经肾脏近曲小管上皮细胞线粒体内的1-α羟化酶羟化后形成VitD的活性形式——1,25（OH）$_2$D$_3$。1,25（OH）$_2$D$_3$与其受体（VDR）结合后，促进肠道和肾脏对钙、磷的吸收和转运，提高血清钙、磷水平。日照时间不足将导致VitD$_3$生成不足而出现低钙血症。本研究证实低钙血症组日照时间明显少于正常血钙组。此外，有研究表明，VitD在免疫调节方面发挥重要作用，VitD缺乏是ICU患者死亡的独立危险因素，因此对于日照不足的ICU患者补充活性VitD是有益的。

本研究中共入选44例患者，其中全身性感染18例、心血管疾病5例，神经系统疾病8例、创伤6例、其他疾病（包括急性药物中毒、过敏性休克、肝性脑病、DIC等）8例。其中，全身性感染患者低钙血症发生率最高为61.1%，然后依次为其他疾病、心血管、创伤和神经系统疾病。研究表明，全身性感染的ICU患者低钙血症与病死率及住院时间有关，动物实验得到了相同的结论。Muller等[11]研究认为，全身性感染患者低钙血症的发生与PCT升高有关。降钙素（CT）是体内调节钙磷代谢的激素之一，其主要作用是降低血钙和血磷，其受体主要分布在肾和骨骼，CT与其受体结合后，经过cAMP-PKA途径和IP3/DG-PKC途径抑制破骨细胞的活动，从而降低血钙。PCT是CT的前体，全身性感染时PCT增加，继而造成低钙血症。

体内血钙几乎全部存在于血浆中，可分为扩散钙和非扩散钙两大类。体内钙分为游离钙和总钙，其中游离钙占总钙的40%～50%，发挥主要的生理作用，因此游离钙测定比总钙更能反应体内钙的真实情况，但目前游离钙测量尚未在所有医院普及，因此本研究中仍选用了总钙水平来定义低钙血症。建议有条件或存在严重低蛋白血症、碱中毒时首选游离钙测定。

参考文献

[1] Zivin JR，Gooley T，Zager RA，et al. Hypocalcemia: A pervasive metabolic abnormality in the critically ill. Am J Kidney Dis，2001，37(4):689-698.
[2] Hastbacka J，Pettila V. Prevalence and predictive value of ionized hypocalcemia among critically ill patients. Acta Anaesthesiol Scand，2003，47(10):1264-1269.
[3] Dickerson RN，Alexander KH，Morgan LM，et al. Accuracy of methods to estimate ionized and "corrected" serum calcium concentrations in critically ill multiple trauma patients receiving specialized nutrition support. JPEN J Parenter Enteral Nutr，2004，28(3):133-141.
[4] Vivien B，Langeron O，Morell E，et al. Early hypocalcemia in severe trauma. Crit Care Med，2005，33(9):1946-1952.
[5] Iqbal M，Rehmani R，Hijazi M，et al. Hypocalcemia in a Saudi intensive care unit. Ann Thorac Med，2008，3(2):57-59.
[6] Dickerson RN. Treatment of hypocalcemia in critical illness--part 1. Nutrition，2007，23(4):358-361.
[7] Holowaychuk MK，Hansen BD，DeFrancesco TC，et al. Ionized Hypocalcemia in Critically ill Dogs. J Vet Intern Med，2009，23(3):509-513.
[8] Dickerson RN，Henry NY，Miller PL，et al. Low serum total calcium concentration as a marker of low serum ionized calcium concentration in critically ill patients receiving specialized nutrition support. Nutr Clin Pract，2007，22(3):323-328.
[9] Carlstedt F，Lind L，Rastad H，et al. Parathyroid hormone and ionized calcium levels are related to the severity of illness and survival in critically ill patients. Eur J Clin Invest，1998，28(11):898-903.
[10] Slomp J，van der Voort PH，Gerritsen RT，er al. Albumin-adjusted calcium is not suitable for diagnosis of hyper-and hypocalcemia in the critically ill. Crit Care Med，2003，31(5):1389-1393.
[11] Muller B，Becker KL，Kranzlin M，et al. Disordered calcium homeostasis of sepsis: association with calcitonin precursors. Eur J Clin Invest，2000，30(9):823-831.
[12] Wang S，McDonnell EH，Sedor FA，et al. pH effects on measurements of ionized calcium and ionized magnesium in blood. Arch Pathol Lab Med，2002，126(8):947-950.

中华医学会第十七次全国医学信息学术会议

时间：2011年10月18日至22日

地点：湖南长沙

中华医学会第十七次全国医学信息学术会议将于2011年10月18日-22日在湖南省长沙市召开，此次会议的主题是“围绕十二五卫生中心工作，促进我国医药卫生信息事业创新发展”。会议期间将重点组织高水平的专题报告和学术交流，重点涵盖医学信息研究与医学科技创新、医学情报调研与信息分析评价、医药卫生体制改革与卫生信息化、图书馆资源建设与利用、医学信息教育与人才培养、知识管理与知识服务、数字医学等方面的新进展。

2011年是国家“十二五”开局之年，科学发展是时代主题。本次会议还将召开分组交流专题研讨会，就医疗卫生信息化与新医改、医药信息研究与医学科技创新、医学文献资源建设与学科服务等热点问题进行专题研讨。欢迎全国从事本领域的科技工作者踊跃投稿，积极报名参加本次学术大会。大会组委会也力争把本次会议的组织工作做得更好。

大会也特别欢迎医学信息学领域的相关企业能够前来参会，展示你们的新产品、新技术，并与会议代表进行交流，就双方感兴趣的问题进行了解和沟通。

本次会议的举办地长沙，位于中国中南部的长江以南地区，是我国的历史文化名城和旅游城市。其周边有着丰富的旅游资源。十月的长沙气候宜人，我们愿与各位同道在此一起度过美好时光，举办又一次成功的学术交流年会。

肖剑辉[1] 杨明施[2]

1.长沙市第一医院 重症医学科 长沙 410013

2.中南大学湘雅三医院 重症医学科湖南 长沙 410013

摘要

目的:通过调查了解湖南省三级医院ICU危重症患者营养支持治疗应用现状，并与2009美国危重病医学会和肠外肠内营养学会制定的“成年危重病患者营养支持治疗与评估指南推荐方案（以下简称2009年CPG）”相对照，为改善湖南省危重症患者营养支持治疗现状提供临床依据。方法:采用分层整群随机抽样法在湖南省内抽取8家三级医院的8个综合ICU参加，用问卷填表收集病例信息，建立数据库。结果：1.参加调查的6个ICU(75%)对EN具体实施有明确的规定;2个ICU (25%)无相关具体流程。2.参加调查的77例ICU患者均存在营养风险并全部实施营养支持治疗，其中应用TEN支持的有42例（55.84%），应用EN联合PN支持的有26例（22.27%），PN支持的有9例（16.88%）。3.早期(入住ICU48h内)开始TEN 36 例(46.75%),TPN21例(27.27%),EN联合PN 15例(19.48%)，早期未接受任何营养支持的5例(6.49%)。应用TEN支持的42例患者入住ICU时平均EN提供能量为目标热卡的51.51%。应用TPN支持的26例患者入住ICU时平均PN提供能量为目标热卡的121.33%。应用TEN支持的42例患者入住ICU时平均EN提供蛋白质为目标蛋白质的35.20%。4.8所医院均对应用EN的患者实施了胃残余量的监测，因为胃残余量被迫中止EN的患者有10例（14.71%），68例应用EN的患者37例（54.41%）将床头抬高30～45度；35例应用PN的患者8例(22.99%)使用谷氨酰胺。结论：我省三级医院ICU危重症患者营养支持治疗已得到广泛认可和重视，但与2009年CPG仍存在较大的差距：EN存在喂养不足和累积能量摄入的缺乏，PN存在使用指证过松现象。医院应通过具体的实施方案规范临床行为。

关键词：营养支持治疗，肠内营养，肠外营养

责任作者及联系方式：杨明施,E-mail:xyyms2004@163.com

湖南省三级医院ICU营养支持治疗现状调查

A Survey of the Current Status of Nutrition Support to Critical Ill Patients in ICU of Tertiary Hospitals in Hunan Province

Jian-hui Xiao[1], Ming-shi Yang[2]

1.Department of Intensive Medicine, the first hospital of Changsha 410013

2.Department of Intensive Medicine the third Xiangya Hospital affiliated to Central South University 410013

Abstract

Objective: This article provides the clinical evident for improving the present state of nutrition support therapy for critical ill patients in Hunan province, by investigating the current application status of nutrition support for critical ill patients in ICU of tertiary hospitals of Hunan province and comparing with the Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patients of 2009 (2009 Guidelines).

Methods: Sectional survey is conducted among eight ICUs of eight tertiary hospitals in Hunan province. Investigation questionnaires are designed to collect patients' information to set up a database .

Results: (1) 6 out of 8(75%) ICUs, involved in the survey, have definite regulation for EN's operation, the other 2 have not relevant process. (2). All of 77 cases involved in the survey have nutrition risk and all of them were treated with nutritional support, including 42 cases (55.84%) for EN delivery, 26 cases (22.27%) for EN combined PN (EN+PN) one and 9 cases (16.88%) for parenteral nutrition (PN) one. (3). 36 cases (46.75%) received early total EN (< 48 hrs), 21 cases (27.27%) for TPN, 15 cases (19.48%) for EN plus PN and 5 cases without any early nutritional support. For 42 patients under TEN, the energy provided by average EN achieves 51.51% of the energy requirement goal during the ICU-stay. For 26 patients under TPN, the average PN reached 121.33%. 42 patients under TEN reached 35.20% of the goal protein requirement on average during the ICU-stay. (4). All 8 hospitals involved in the survey had monitored gastric residual volumes (GRV) for patients under EN, finding that 10 cases were forced to suspend EN because of gastric-intestinal intolerance, 37 cases (54.41%) of 68 patients under EN were maintained the head-of-bed (HOB) to 30-45 degrees, 35 cases of application of PN in 8 patients (22.99%) with glutamine.

Conclusion: Nutrition support to critical ill patients has been widely recognized and emphasized in ICU of tertiary hospitals in Hunan province, but there is still a wide gap between CPG in 2009. Underfeeding and negative cumulated energy balance is found in patients under EN. Besides, there is overused and overfeeding phenomenon of PN. Therefore, Standard and concrete instructions should be implemented in hospital.

Key Words: nutritional support treatment; enteral nutrition(EN); parenteral nutrition(PN)

Corresponding Author：Ming-shi Yang，E-mail: xyyms2004@163.com

一、对象和方法

1. 调查对象

采用分层整群随机抽样法，在湖南省内抽取8家三级医院的8个综合ICU参加，其中包括：湘雅三医院ICU、长沙市一医院ICU、长沙市中心医院ICU、衡阳市南华大学附二医院ICU、邵阳市中心医院ICU、株洲市一医院ICU、岳阳市一医院ICU、常德市一医院ICU；患者纳入标准：1.)时间：2010年06月01日至2010年12月31日期间各医院ICU住院患者。2.)机械通气时间 48 h及以上。3.)并且预计在ICU治疗时间为72 h及以上。4.)年龄：18岁及以上的成年患者。所有接受调查患者或家属均知情并同意。

2. 调查方法

在查阅文献、专家咨询的基础上自制《湖南省营养支持治疗现况调查病例报告表》调查问卷作为研究工具。用问卷

填表收集病例，建立数据库。调查表内容包括以下部分：1.各医院ICU信息调查表：医院级别，ICU床位数以及是否有营养支持治疗方案等。2.患者出入ICU及预后情况调查表：患者性别，年龄，体重，入院诊断，入住ICU原因，APACHEⅡ评分，NRS评分，入住ICU时间，28天预后等。3.营养支持治疗具体实施观察表：营养支持方式及途径，目标热卡与实际供给热卡，床头抬高，胃残余量监测及胃动力药的使用，是否不恰当中止营养支持治疗及原因，辅助治疗等。

3.统计学方法

计量资料服从正态分布的采用均数±标准差（$\bar{x}\pm s$）表示；不服从正态分布的采用中位数和四分位数间距M（P25-P75）进行描述；计数资料用例数（百分数）描述。

二、结果

1.调查医院一般情况

本次调查有湖南省各地区三级医院的8所综合ICU参加，其中6所(75%)为教学医院，2所(25%)为非教学医院。6个ICU(75%)对EN具体实施有明确的规定，包括病人床头抬高、胃残余量监测、中止喂养或转为小肠喂养指征等方面；8个ICU(100.00%)均有计划地主动监测血糖，并应用胰岛素控制血糖。目标血糖均为10mmol/L以下。

2.调查对象基本特征

严格按照入选标准最终将83例ICU患者纳入调查。其中有效调查表为77例，有效率为92.77%。参加本次调查病人情况详见表1。

表1 77例纳入调查病人的基本情况

基本情况	结果
年龄（岁）	60.31±13.77
性别（女/男）	26/51
体重指数	22.61±2.63
入住ICU原因[n（%）]	
内科疾病	37（48.05%）
外科择期手术	11（14.29%）
急诊手术	29（37.66%）
入院诊断[n（%）]	
心脑血管疾病	21（27.27%）
呼吸系统疾病	23（29.87%）
创伤	26（33.77%）
胃肠道疾病	4（5.19%）
其它	3（3.90%）
APACHEⅡ评分（分）	17.86±4.60
呼吸衰竭[n（%）]	48（62.34%）
机械通气时间（天）	7.40±2.88
入住ICU时间（天）	9.47±4.53
住院时间（天）	22.95±9.90
28天病死率[n（%）]	11（14.29%）

3.营养风险分布、营养支持种类及分布

本次调查77例ICU住院患者中营养风险总评分均大于等于3分，即100.00%的患者存在营养风险。77名患者全部实施营养支持，其中应用TEN支持的有42例（55.84%），应用EN联合PN支持的有26例（22.27%），TPN支持的有9例（16.88%）。三种不同营养支持方式占77名患者ICU入住时间的百分比分别为52.59%、32.30%及15.11%。

4.营养支持应用情况

（1）营养支持途径

EN支持(TEN和EN+PN形式)的68例患者中，其中55例(80.88%)经胃喂养，13例(19.12%)经小肠喂养。

（2）营养支持时机

早期(入住ICU48h内)开始TEN36例(46.75%)，TPN21例(27.27%)，EN联合PN15例(19.48%)，早期未接受任何营养支持的5例(6.49%)。

（3）营养支持能量供给（详见表2）

表2 营养支持能量供给

营养支持实际提供热卡分比（%）		目标热卡	占预计目标热卡百
TEN（kcal）			
第1天	546.9±148.1		30.35±8.22
第2天	612.2±234.2	1802.6±237.7	33.98±13.00
第3天	776.7±300.3		43.12±16.67
第7天	1267.2±340.5		70.34±18.90
平均	910.1±394.0		51.51±23.12
TPN（kcal）			
第1天	1806.8±253.7		98.91±13.89
第2天	2061.4±163.0	1826.7±306.8	112.85±8.92
第3天	1972.8±175.2		108.24±12.67
第7天	1946.4±165.3		106.55±9.04
平均	2210.3±241.2		121.33±15.07

（4）EN蛋白质供给及动态评估（详见表3）

表3 营养支持蛋白质供给

EN实际提供蛋白质（g）		目标蛋白质（g）	占目标蛋白质百分比（%）
第1天	24.95±4.24		20.77±3.12
第2天	27.93±6.70		23.25±5.28
第3天	35.43±8.60	120.10±15.85	29.50±7.57
第7天	57.81±9.75		48.13±8.64
平均	41.52±11.28		35.20±9.97

（5）EN的监测及耐受性评估

①胃残余量的监测

参加本次调查的8所ICU均对应用EN的患者实施了胃残余量的监测，其中5所ICU（62.5%）胃残余量的临界值（达到此水平时必须中止EN）为150mL，3所医院（37.5%）胃残余量的临界值为250mL，本次调查因为胃残余量被迫中止EN的患者有10例（14.71%），使7.89%的喂养时间被迫中断。

②胃动力药的应用

本次调查的8所医院ICU有胃残余的65例患者中27例未应用胃动力药（41.54%）。

③床头抬高的应用

本次调查的8所医院ICU 68例应用EN的患者中仅37例（54.41%）床头抬高达30～45度。

（6）谷氨酰胺的应用

本次调查的8所医院ICU应用PN的35例患者8例（22.99%）使用谷氨酰胺辅助治疗。

三、讨论

1.关于危重症患者营养风险分布及营养评估

营养风险这一临床营养的指标是与临床结局相关的，ESPEN指出当住院患者通过营养风险筛查工具NRS 2002发现有营养风险时，应制定营养支持计划。本次调查显示我省77例患者营养总评分均大于等于3分且其营养支持率达到100%，即

普遍存在营养风险并已得到营养支持。2009年CPG认为传统营养评估指标在重症监护中效果不够确切[17,18]。开始营养治疗前，评估应该包括患者体重丢失和入院前的营养摄入情况，疾病的严重程度，合并疾病的状况，以及胃肠道功能。我省三级医院ICU仍倾向于采用传统的蛋白标志物进行营养评估，综合性营养评估对于营养支持治疗时机及选择营养支持方式等均有十分重要的意义。

2. 营养支持种类及分布

2009年CPG推荐对于需要营养支持治疗的重症患者首选EN；循证医学证据表明既往无营养不良并不能接受EN的危重病患者，7日内给予PN相对标准治疗来说不但不能使病人获益，反而使感染等并发症明显增加及死亡率增高[28-39]。对于EN不足7-10天的患者补充PN不但不能改善预后，而且可能会带来不利影响[30,33,35-39]。调查显示TEN有42例（55.84%），EN联合PN有26例（22.27%），TPN的有9例（16.88%）。在应用PN支持的9例患者中有6例并无证据证明其入院时存在蛋白质-热卡缺乏型营养不良；在应用EN联合PN支持的26例患者10例于EN同天即应用PN，余16例也于EN后1-3天应用PN，本次调查显示我省三级医院危重症病人营养支持已得到广泛认可和重视，但总体上存在EN使用比例不高和PN使用存在指征过松的情况；本研究分析其原因，营养学相关的培训教育及营养支持组织机构的欠缺是其重要因素。

3. EN的应用现状及思考

2009年CPG认为对于大多数危重症患者，EN方式优于PN，无论是否存在肠鸣音及有无肛门排气/排便证据，均要求在患者入ICU的第一个24-48小时内早期开始EN。且在开始营养支持时即应确定EN的目标，并应在入ICU的第一周内提供目标热卡的50-65%以上的能量以获得临床益处。另外还应动态评估患者蛋白补充是否充足以及监测EN是否充分以及患者的耐受性。本调查68例EN(TEN和EN+PN形式)患者，其中51例(75.00%)于早期开始实施。在应用TEN支持的42例患者中入住ICU第1、2、3、7天EN提供能量分别为目标热卡的30.25%、33.98%、43.12%、70.34%；入住ICU平均EN提供能量为目标热卡的51.51%。TEN的42例患者入住ICU平均提供蛋白质为目标蛋白质的35.20%。因为胃残余量被迫中止EN的患者有10例（14.71%），使7.89%的喂养时间被迫中断。

本次研究表明我省三级医院ICU已具有要早期开始营养支持这一观念，但许多问题仍需改进，其中主要的问题就是EN喂养不足以及不恰当的中止喂养。研究表明虽然小剂量喂养（10-30mL/h）足以预防肠粘膜萎缩，但并不能达到EN的治疗目标，将EN提供的能量从目标热卡的37-40%提高到59-64%能显著改善患者的临床预后[20,21]。EN喂养不足不仅仅体现在热卡的补充缺乏，在蛋白质的补充缺乏尤其突出，TEN患者入住ICU平均提供蛋白质仅为目标蛋白质的35.20%。2009年CPG推荐应动态评估蛋白补充是否充足，传统的血浆蛋白标志物不作为判断蛋白质供给是否充足的可靠指标，大多数重症患者对蛋白质的需求量高于对能量的需求，因此动态评估蛋白补充十分必要。

我省三级医院ICU不恰当的中止EN表现在实施EN的患者有约15%的患者仅因为胃残余量过多就使7.89%的喂养时间被迫中断。而这种中止应当是可以避免的。我省ICU胃残余量的临界值绝大部分为150mL及以下。而许多研究表明胃残余量与胃排空、肺炎及返流和误吸的发生率并无确切的关系[22,23,24,27]。将胃残余量临界值从50-150mL增加至250-500 mL不会增加返流、误吸或肺炎的风险[24,25,26]。降低胃残余量临界值不能减少患者发生上述并发症的风险，且常导致EN的不恰当中止，或因减少EN的剂量而对预后产生不利影响。虽然胃残余量在250-500mL可能会引起担心并采取相应措施减少误吸的风险，但当缺乏其它不能耐受的征象时，胃残余量不超过500mL不应成为中止肠内营养的理由[24,25,26,27]。

除以上两方面之外，我省三级医院ICU对于改善患者对EN耐受性方面仍有待提高。本调查中，EN支持(TEN和EN+PN形式)患者80.88%经胃喂养,仅19.12%采取经小肠喂养。胃残余患者应用胃动力药不足60%，其中包括最简单的将床头抬高30-45度这一方面，其实施率不足55%，EN喂养不足及不恰当的中止的一个重要因素就是病人的耐受性障碍，提高患者对EN耐受性可以切实有效的保障EN的顺利进行，从而显著改善危重患者预后。我省重症医学同行应在思想上高度重视，相关操作规定也有待全体医护人员的认真执行。

4. PN的应用现状及思考

2009年CPG认为对于所有ICU患者，在营养支持的初始阶段可考虑适度的允许性低热卡PN，以提供能量需求的80%为最初目标。研究表明允许性低热卡方案可使PN发挥最大功效并避免能量摄入过多诱发的胰岛素抵抗，与高热卡PN相比，前者可降低高血糖和感染的发生率，缩短机械通气时间、住院时间和ICU停留时间。本次调查中，TPN支持的26例患者中入住ICU第1、2、3、7天PN提供能量分别为目标热卡的98.91%、112.85%、108.24%、106.55%；入住ICU平均PN提供能量为目标热卡的121.33%。表明我省三级医院ICU患者PN能量供给过足，已超过CPG推荐目标。

2009年CPG推荐对ICU应用PN的重症患者应考虑静脉补充谷氨酰胺。谷氨酰胺的作用机制与其产生全身性抗炎作用、维护肠道完整性、为细胞复制提供原料等方面密切相关。本次调查的8所医院ICU 77例患者50例（64.94%）使用谷氨酰胺辅助治疗，27例（35.06%）未使用谷氨酰胺。分析谷氨酰胺使用比例不高原因，有制剂价格、医保报销比例及相关人员对其重要性的重视程度不够等因素；今后应该更加重视和加强谷氨酰胺的临床应用，从而达到改善重症患者营养治疗效果。

四、结语

综上所述，我省三级医院ICU危重症患者的营养支持治疗已得到广泛认可和重视，但与2009年CPG对比仍存有明显差距及较大改进空间；EN存在喂养不足及不恰当中止胃肠道喂养，喂养不足主要包括能量和蛋白质供给的偏低，PN存在使用指征过松及能量供给过足，PN中添加谷氨酰胺比例普遍较低。危重病人的营养支持治疗复杂且困难，临床实践中应具体分析患者个体情况，从代谢支持及调理等角度出发，选择

恰当的时机和途径,提供适当的营养物质进行合理、有效、安全的营养支持治疗，从而使患者得到最大获益并节约医疗成本。

参考文献

[1] Martindale RG, Maerz LL. Management of perioperative nutrition support[J]. Curr Opin Crit Care, 2006 Aug ,12(4):290-4.

[2] Raguso CA, Dupertuis YM, Pichard C. The role of visceral proteins in the nutritional assessment of intensive care unit patients[J]. Curr Opin Clin Nutr Metab Care, 2003 Mar;6(2):211-6.

[3] Barr J, Hecht M, .Flavin KE, Khorana A, Gould MK. Outcomes in critically ill patients before and after the implementation of an evidence-based nutritional management protocol[J]. Chest, 2004 Apr 125(4):1446-1457.

[4] Ziegler TR, Smith RJ, O' Dwyer ST, Demling RH, Wilmore DW. Increased intestinal permeability associated with infection in burn patients[J]. Arch Surg, 1988 Nov, 123(11):1313-9.

[5] Pinilla JC, Samphire J, Arnold C, Liu L, Thiessen B. Comparison of gastrointestinal tolerance to two enteral feeding protocols in critically ill patients: a prospective, randomized controlled trial[J]. JPEN J Parenter Enteral Nutr, 2001 Mar-Apr;25(2):81-6.

[6] Montejo JC, Minambres E, Bordeje L, et al. Gastric residual volume during enteral nutrition in ICU patients: the REGANE study[J]. Intensive Care Med, 2010 Aug, 36(8):1386-93.

[7] Tarling MM, Toner CC, Withington PS, Baxter MK, Whelpton R, Goldhill DR. A model of gastric emptying using paracetamol absorption in intensive care patients[J]. Intensive Care Med, 1997 Mar, 23(3):256-60.

[8] Landzinski J, Kiser TH, Fish DN, Wischmeyer PE, MacLaren R.Gastric motility function in critically ill patients tolerant vs intolerant to gastric nutrition[J]. JPEN J Parenter Enteral Nutr, 2008 Jan-Feb, 32(1):45-50.

[9] Cohen J, Aharon A, Singer P. The paracetamol absorption test: a useful addition to the enteral nutrition algorithm?[J]. Clin Nutr, 2000 Aug, 19(4):233-6.

[10] McClave SA, Lukan JK, Stefater JA, et al. Poor validity of residual volumes as a marker for risk of aspiration in critically ill patients[J]. Crit Care Med, 2005 Feb, 33(2):324-30.

[11] Woodcock NP, Zeigler D, Palmer MD, Buckley P, Mitchell CJ, Macfie J. Enteral versus parenteral nutrition: a pragmatic study[J]. Nutrition, 2001 Jan, 17(1):1-12.

[12] Braga M, Gianotti L, Gentilini O, Parisi V, Salis C, Di C. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition[J]. Crit Care Med, 2001 Feb, 29(2):242-8.

[13] Pacelli F, Bossola M, Papa V, et al. Enteral vs parenteral nutrition after major abdominal surgery: an even match[J]. Arch Surg, 2001 Aug, 136(8):933-6.

[14] Bozzetti F, Braga M, Gianotti L, Gavazzi C, Mariani L. Postoperative enteral versus parenteral nutrition in malnourished patients with gastrointestinal cancer: a randomised multicentre trial[J]. Lancet, 2001 Nov 3, 358(9292):1487-92.

[15] Olóh A, Pardavi G, Belágyi T, Nagy A, Issekutz A, Mohamed GE.Early nasojejunal feeding in acute pancreatitis is associated with a lower complication rate[J]. Nutrition, 2002 Mar, 18(3):259-62.

[16] Abou-Assi S, Craig K, O' Keefe SJ. Hypocaloric jejunal feeding is better than total parenteral nutrition in acute pancreatitis: results of a randomized comparative study[J]. Am J Gastroenterol, 2002 Sep, 97(9):2255-62.

[17] Gupta R, Patel K, Calder PC, Yaqoob P, Primrose JN, Johnson CD. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II ≥ 6)[J]. Pancreatology, 2003, 3(5):406-13.

[18] Louie BE, Noseworthy T, Hailey D, Gramlich LM, Jacobs P, Warnock GL. Enteral or parenteral nutrition for severe pancreatitis: a randomized controlled trial and health technology assessment[J].Can J Surg, 2005 Aug, 48(4):298-306.

[19] Petrov MS, Kukosh MV, Emelyanov NV. A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition[J].Dig Surg, 2006, 23(5-6):336-44.

[20] Eckerwall GE, Axelsson JB, Andersson RG. Early nasogastric feeding in predicted severe acute pancreatitis: a clinical, randomized study[J]. Ann Surg, 2006 Dec, 244(6):959-65.

[21] Casas M, Mora J, Fort E, et al. Total enteral nutrition vs. total parenteral nutrition in patients with severe acute pancreatitis[J]. Rev Esp Enferm Dig, 2007 May, 99(5): 264-9.

[22] Shirabe K, Matsumata T, Shimada M, et al. A comparison of parenteral hyperalimentation and early enteral feeding regarding systemic immunity after major hepatic resection: the results of a randomized prospective study[J]. Hepatogastroenterology, 1997 Jan-Feb, 44(13):205-9.

中华医学会肿瘤学分会第七届全国中青年肿瘤学术会议

会议日期：2011-11-25至11-27
所在城市：山东省济南市
具体地点：山东大厦
主办单位：中华医学会 中华医学肿瘤学分会
会议网站：http://www.cmacso.org/cn

会议背景：为了加快我国肿瘤学后备人才的培养，增进我国与国际肿瘤同行的学术交流，为中青年肿瘤工作者搭建展示学术才能的平台，由中华医学会、中华医学会肿瘤学分会联合主办的第七届全国肿瘤中青年学术会议将于2011年11月25-27日在山东济南山东大厦召开。会议期间将进行“中华肿瘤明日之星”大型评选活动以及中华医学会肿瘤学分会中青年委员全国遴选大会。本次大会的主题是“二十一世纪肿瘤的转化研究——基础与临床”。

征文要求:

* 征文范围：1）肿瘤的基础研究；2）肿瘤内科；3）肿瘤外科；4）肿瘤放疗、影像、病理、检验及射频等；5）肿瘤护理
* 文章作者年龄不得超过45岁（1966（含）年以后出生）；
* 投稿摘要字数为：800-1000字，摘要以研究目的，研究方法，研究结果，讨论的方式排列顺序。
* 本次投稿采用网上投稿的方式。具体投稿方式请登录大会网站：www.cmacso.org 点击“网上论文提交”按钮，先进行新用户注册征文投稿系统，然后按照提示进行网上论文投稿。

黄静[1] 顾海潮[1] 李德亮[2]
1.云南省中医院麻醉科 650021
2.云南省第一人民医院麻醉科 650021

摘要

根据新医改精神,三年内中央要重点支持2000所左右县级医院的建设 ,这对基层医院无疑是巨大的利好.笔者曾参加过上级卫生主管部门等实施的“万名医师支援农村卫生工程”行动到基层县级中医院麻醉科工作一年，主要任务是参与所在医院麻醉工作，规范和帮助提高麻醉工作质量，为基层人民提供更好的医疗卫生服务,感受到基层医院的确存在医疗工作环境、硬件设施，医疗技术水平、诊疗规范等方面的欠缺，医务工作者是在较艰苦的条件下从事医疗工作，并且存在很大的医疗隐患。通过这一年的实践个人认为该项“工程”的正确性和必要性，同时也呼吁卫生行政部门，重视基层医院的人才培养，加大经费投入和扶持，发展农村医疗卫生事业，进一步解决农村看病难、看病贵的问题。

关键词：万名医师下乡行动；基层医院；麻醉工作；医疗隐患

浅谈基层地区医院麻醉工作现状和隐患

Effect of Dexmedetomidine on Elderly

Jing Huang[1], Hai-chao Gu[1], De-liang Li[2]
1.Department of anesthesiology, traditional Chinese medicine hospital of Yun'nan Province,650021
2.Department of anesthesiology, the first hospital of Yun'nan Province,650021

为帮助扶持农村基层医院医疗技术的发展，笔者作为一省级三甲医院麻醉医生，参加了云南省卫生厅“万名医师支援农村卫生工程”下乡扶贫活动到基层县级中医院麻醉科工作一年，一年工作中共行择期手术375例、急诊手术512例（含抢救性手术124例），包括严重创伤失血性休克、感染性休克、宫外孕破裂大出血、并发严重心律失常、重症呼吸疾患、感染高热、电解质紊乱等急诊手术病人，下面浅谈这一年工作中特别是在抢救性手术麻醉中存在的问题和困惑，为卫生行政部门提供一点重视基层医院医疗质量和基础设施建设的依据。

一、药品短缺和硬件设施不足：由于药品短缺，术中出现一些异常情况没法纠正，如出现严重心律失常而缺少抢救药；医院没有血液储备条件，大失血病人存在用血困难及缺少血浆代用品而延误抢救时机；手术室内必要的麻醉机、监护仪、抢救设施配置不足及过于陈旧，甚至在手术多的情况下只能在无任何监护抢救条件下贸然进行麻醉和手术，一旦出现危险，后患无穷。

二、麻醉工作者不具备基本的麻醉医师学历和资格，人员编制不够，甚至在乡镇卫生院或一些私立医院，为了经济利益都在开展手术，未取得执业医师资质的人在从事麻醉工作。没有经过系统专业培训，欠缺麻醉相关基础知识及业务能力，对突发事件的诊断和处理救治能力较差。

⑴如对硬膜外麻醉效果不佳或无效的病人，无论手术和患者年龄大小，一概用氯胺酮作为补救措施。

⑵虽然熟练椎管内麻醉操作，但对椎管麻醉的适应症不清楚，如凝血功能异常、低血容量、失血或感染性休克病人、服用阿司匹林等病人仍然选择椎管内麻醉。

⑶不掌握全麻插管技术，一些麻醉医生不会气管内插管甚至不知道辅助呼吸，对麻醉及抢救药物的基本药理性质不清，遇到紧急状况无法应对。

⑷麻醉医生人员编制不足：由于麻醉人员的短缺而导致超负荷运转，工作时间的延长、无规律性和疲劳工作，存在一定安全隐患。

三、手术医生操作规范不够，对手术难度、部位的认识不足，对麻醉风险缺乏足够的认识和理解。两科之间沟通不够，术前准备不充分，手术操作不熟练而引起的牵拉刺激、出血、脏器损伤、缺血再灌注损伤等以及手术时间的延长都对麻醉和患者安全带来较大的威胁。

四、病人因素：老年或小儿病员多，大多数病人由于经济贫困或地处偏僻而拖延病情，导致疾病加重、甚至重要器官功能受损等并发症而增加手术和麻醉的风险性

五、医院环境和管理因素

1.医院行政领导对科室建设及重视力度不够，经费的短缺导致医疗环境差、设施简陋、医生收入低等都可能使麻醉科队伍不稳定、人才流失，而增加麻醉风险性。

2.缺乏完善的规章制度和诊疗护理规范，如无术前访视谈话签字书、术后随访记录等，在发生医疗纠纷的情况下无法举证。

3.术前准备方面：由于缺乏仪器设备，对特殊病人如高血压、冠心病、心律失常、严重贫血、甲亢、糖尿病、严重肺疾患、电解质紊乱等手术患者术前一些必要的常规检查和治疗纠正都无法完成。

4.手术室条件：与外界通风、设施简陋，存在空气污染、外界嘈音干扰，不符合国家卫生部门规定的必须在四级以上手术室完成手术。

医疗体制改革是当前社会普遍关注的一个热点话题。目前而言，我国医疗改革尚面临诸多亟待解决的问题,2011年国家卫生部门称今年的医改重点为优先发展县级医院，并选择300个覆盖县域人口较多、基础较好的开展综合改革试点。在我国基层医院担负着全国三分之二人口的医疗卫生服务工作，但是基层医院特别是中医医院及乡镇卫生院的确存在基础设施差、医疗设备陈旧落后、人才流失现象严重，无专业麻醉人员。随着现代诊疗技术水平和仪器设备的不断发展进步，人民生活和健康意识以及医疗法律意识的增强，医疗安全一直是医患双方共同担心和顾虑的问题 ，麻醉是一门界于内、外科交叉的桥梁学科，也属于医疗差错和事故的易发和多发科室之一，麻醉工作直接关系到手术的成败和病人的生命安危。希望上级医疗卫生部门重视基层地区医院特别是基层中医院的经济投入和人才培养。“万名医师支援农村卫生工程”是非常正确和务实的，由各大医院定期委派技术骨干到较基层地区医院帮助支持卫生工作起到肯定的辅助效果，同时在艰苦环境下工作的麻醉者一定要努力提高自身专业素质、牢固树立安全麻醉意识、增强自我保护意识，完善规章制度，特别是要遵守医疗原则，赢得领导的重视和支持，让社会和手术医生认识影响麻醉安全的因素。

《2011年中国医疗器械最具竞争力企业10强》竞争力报告

实力的显示：评选数据监测结果及分析

主　办：上海市生物医学工程学会　医疗信息研究院
主　编：范关荣　中华医学会理事
副主编：于布为　中华医学会麻醉学分会主任委员　　祁　吉　中华医学会放射学分会原主任委员　　康熙雄　中国医院协会临床实验室委员会主任委员
　　王新房　中华医学会超声学会名誉主任委员　　陈克敏　上海医学会放射学分会原主任委员

2010-2011年度中国医疗器械企业竞争力评比体系构成的指标权重和其反映的意义及价值

指标	因素	子因素	指标名称	指标权重	指标性质及主要意义	可反映的其他含义和影响
医疗器械企业竞争力综合指标	直接计量指标（财务数据硬指数）权重为70%	规模子因素	销售收入	26%	规模	市场份额
			净资产	6%	资本实力	融资能力
			净利润	12%	盈利水平	规模
		效率子因素	总资产利润率	11%	资金利用效率	负债的影响，融资能力
			净资产收益率	11%	资本盈利和增值能力	负债的影响
			全员劳动贡献率	5%	员工劳动效率	销售收入及冗员
		增长子因素	近三年销售收入平均增长率	15%	业务增长	市场份额、成长性
			近三年净利润平均增长率	14%	持续盈利能力	成长性
				合计：100%		
	间接计量指标（软指数）权重为30%		技术创新	34%	长期发展潜力和潜在的技术竞争力	技术密集程度和技术优势
			客户满意度	18%	反映客户忠诚度和市场份额的变化	企业长期的盈利能力和员工满意度
			品牌知名度	12%	公司品牌形象	吸引人才竞争中的优势
			企业家及管理水平	11%	整合，分配企业资源的能力	驾驭外部环境和获取外部资源的能力
			企业文化	25%	企业凝聚力和员工对组织的认同感和忠诚度	企业持续发展的能力和组织动员能力
				合计100%		

《2010-2011年度中国医疗器械最具竞争力企业10强》评选活动工作总结

自2008年到2011年，我们已经对中国医疗器械企业竞争力进行了连续三年的监测。在对三年的数据进行深入分析的过程中，我们得到了一系列十分有意义的结果，这些分析结果一方面说明了中国医疗器械企业竞争力变化的情况；另一方面通过这些企业的数据反映了中国医疗器械市场发展的进程与问题。

1．中国医疗器械企业竞争力的稳定性与客观性

由于企业竞争力是企业在长期发展中所积累的能力，因而可以推测：总体而言，中国医疗器械企业竞争力的结果有很强的稳定性；但竞争力是在竞争过程中形成和不断变化的，各年度所监测到的企业竞争力表现也必然会具有相当程度的差异性。我们对三个年度的企业竞争监测结果进行了统计分析，参见下表：

2009-2011年医疗器械企业竞争力监测结果的相关性

	2009年监测结果	2010年监测结果	2011年监测结果
2009年监测结果	-	0.9097	0.7429
2010年监测结果	0.9097	-	0.8038
2001年监测结果	0.7429	0.8038	-

资料来源：医疗信息研究院企业竞争力研究中心提供.

(1)三个年度企业竞争力监测结果确实有很强的相关性，其相关系数均达到0.7以上。

(2)2009年与2010年的相关系数(0.9097)大于2010年与2011年的相关系数(0.8038)，这与中国医疗器械市场化程度不断加深、企业竞争力变化加快的情况相吻合。

(3)2009年与2010年的相关系数（0.9097）大于2009年与2011年的相关系数（0.7429），这表明三个年度竞争力监测数据之间的相关系数确实能反映中国医疗器械企业竞争力的稳定性。我们可以推测中国医疗器械企业竞争力经过两年的变化会大于经过一年的变化，因而随着时间间隔的增大不同年份间相关系数应在不断减少。上述推测被数据所证实。

2．中国医疗器械上市公司与非上市企业竞争力的比较

中国医疗器械市场持续快速发展，但与此同时，近1年来我国资本市场受金融危机影响，总体呈现熊市状态，股价不断下跌。研究中国医疗器械市场资本面的相关人士对上述悖论从各个角度进行了解释。我们主要通过分析中国医疗器械上市公司平均竞争力与非上市公司竞争力近几年变化的情况，以试图对上述悖论进行解释。我们的初步分析表明，在规模经济明显的子行业，如放射子行业和检验子行业上市公司的平均竞争力要高于非上市公司；而在规模经济不明显的子行业，如麻醉与监护子行业上市公司的平均竞

争力要低于非上市公司。这也许可以推论：如果通过资本上市而融得的资金能够支持企业的规模经济优势，则同时可以增强其资金利用效率进而增强企业的总体竞争力。而如果上市融得的资金并没有明显地发挥提高规模经济的作用，则不仅难以提升企业的总体竞争力，反而可能降低资金的使用效率而降低企业的整体竞争力。这样的推论如果可以成立，那么可以表明，我国医疗器械企业上市融资的实际效果是：通过资本市场的资金吸纳作用，支持了上市公司的规模竞争优势，却以相对降低企业的效率竞争力为代价。

3．中国医疗器械企业竞争力分化程度加剧

我们分别计算了2009年与2011年的净资产收益率的变异系数，结果表明，2011年中国医疗器械企业净资产收益率的变异系数（数值为53）远大于2009年中国医疗器械企业净资产收益率的变异系数（数值为39），这说明中国医疗器械企业竞争力的分化程度在加大。这也许是中国医疗器械市场的市场化程度不断提高的表现。

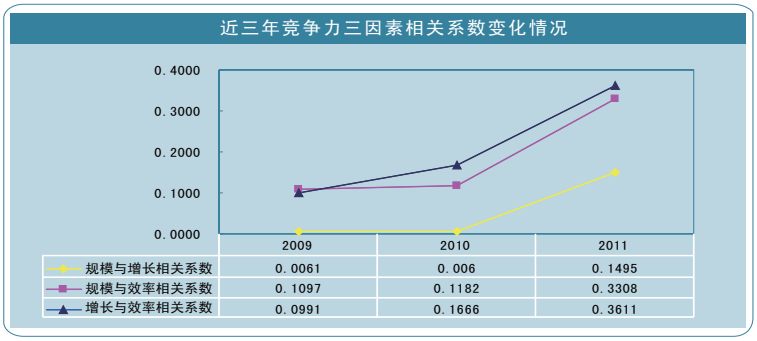
一方面中国医疗器械企业总体竞争力在不断提升，另一方面中国医疗器械企业间竞争力分化也在不断加剧，因此，我们推测，未来的中国医疗器械企业中竞争力最强前几名的企业，竞争力将持续增强。

4．中国医疗器械市场的市场化进程

竞争力监测体系中将竞争力财务数据分为三个子因素，即规模子因素、增长子因素、效率子因素三个指标。规模子因素从绝对量上描述了企业的竞争力，一般来说，企业的规模越大，规模子因素所反映的企业的竞争力会越强。规模子因素包括净利润、销售收入、净资产三个指标。效率子因素从相对量上描述了企业的竞争力，企业的规模增大，效率子因素反映的企业竞争力不一定增强。效率类指标包括净资产收益率、总资产利润率、全员劳动效率三个指标。

规模子因素、增长子因素、效率子因素分别从不同的角度测量了企业的竞争力状况。我们希望对于全部样本而言，三类子因素之间没有相关性，至少要相关性不大，从而能更全面地反映中国医疗器械企业竞争力的全貌。但我们也可以预测，在日渐成熟的中国医疗器械市场，由于市场机制的调节作用，竞争力三个方面又必然会有一定的相关性，特别是效率子因素与增长子因素之间应有较强的相关性，从而表明资源向效率高的企业进行了有效的配置。

从下图中可以看出，总体上三类子因素间的相关性在不断增强，这表明中国医疗器械市场的市场化程度越来越高，已经越来越依据效率原则，依靠市场的力量对生产要素进行配置，因而以上数据说明可以使我们得出结论：中国医疗器械市场的竞争程度已日趋白热化与两极化，强者越强，弱者越弱；规模竞争优势在中国医疗器械市场所占的主导地位越来越明显。



资料来源：医疗信息研究院企业竞争力研究中心提供.

我们2011年企业竞争力报告的研究主题——探讨中国医疗器械成本对企业竞争力的影响。其研究结果显示，目前，大家所较为关注的工资、能源价格的上涨对企业盈利能力影响有限。总体上说，中国医疗器械企业有能力承受较高的工资水平和更高的能源价格所导致的成本上升压力。我们的研究结果还表明，利率市场化后不会过分影响中国医疗器械企业的国际竞争力，相反，为了应对工资上涨所导致的“资本替代劳动” 现象，中国医疗器械企业应尽快加速资本市场化的程度。

在接受上述结论的同时，特别需要指出的是：虽然上述各项因素分别对于企业成本的影响可以控制在医疗器械企业尚可承受的限度内，但如果这些因素集中在同一时间出现，却可能使企业在短期内难以消化。面对成本结构的较大变化，企业需要有一个适应和调整时期，来消化其产生的综合成本上升压力。因而我们认为，尽管从长期看，中国医疗器械企业已经具有了消化成本结构变化的能力，但在当前中国经济出现各种不确定因素和世界经济可能进入严重的衰退期时，短期内如果集中出现推动成本上升的因素，可能会使许多中国医疗器械企业难以承受而陷入经营困境。

此外，回到另一个调研主题——中国医疗器械企业竞争力提升的路径，我们的结论认为最重要的莫过于对主业的专注。与大家分享我们的调研结果，目的只有一个：看看市场已经发生了的事实，分析具竞争力的医疗器械企业如通用，怎么应对外界环境的变化，从理论的高度概括总结出我们的医疗器械企业应该如何去思考，如何在专注主业的基础上付诸实践。

最后，我谨代表《年度中国医疗器械最具竞争力企业10强》评审委员会和组委会全体工作人员感谢业界同仁过去三年给予此项评选活动的支持与关注。我们将在未来一年里一如既往地为行业传递最前沿和最宝贵的信息，为提升中国医疗器械行业竞争力贡献自己的力量！谢谢！

中华医学会理事
医疗信息研究院院长
二零一一年七月

范关荣

一、《2010－2011年度中国医疗器械麻醉与监护领域最具竞争力企业10强》榜单

2010-2011年度中国医疗器械麻醉与监护领域最具竞争力企业10强榜单

公司	排名	直接计量硬指标财务数据加权标准值（权重为70%）									间接计量软指标加权标准值（权重为30%）						竞争力综合指数	竞争力综合得分	数据来源
		销售收入 权重26%	净资产 权重6%	净利润 权重12%	总资产利润率 权重11%	净资产收益率 权重11%	全员劳动贡献率 权重5%	近三年销售收入平均增长率 权重15%	近三年净利润平均增长率 权重14%	直接计量硬指标财务数据加权标准值合计（A）	技术创新 权重34%	客户满意度 权重18%	品牌知名度 权重12%	企业家及管理水平 权重11%	企业文化 权重25%	间接计量软指标加权标准值合计（B）	(A*70%+B*30%)		
通用	1	0.9645	0.1073	0.2997	－0.0943	－0.0046	0.1602	－0.1036	－0.0492	1.2800	0.7699	0.5157	0.6503	0.2776	0.5732	2.7867	1.7320	1000	上市公司年报
德尔格	2	0.9338	－0.0047	0.0605	－0.0841	－0.0661	0.1276	0.0896	0.2504	1.1966	0.6502	0.5921	0.5978	0.2602	0.5887	2.6350	1.6281	992	上市公司年报
飞利浦	3	0.7677	0.0873	0.2297	－0.0114	0.0112	0.1152	－0.0269	－0.0058	1.1670	0.5563	0.5529	0.5717	0.2976	0.6514	2.6201	1.6029	989	上市公司年报
迈瑞	4	0.8555	0.0001	0.0213	0.1389	0.0470	－0.0096	0.0203	0.0140	1.0875	0.4535	0.6182	0.6277	0.2654	0.3607	2.2877	1.4476	978	上市公司年报
理邦	5	0.1192	－0.0215	－0.0387	0.1643	0.1757	－0.2384	0.1500	0.0201	0.3307	0.2266	0.2140	0.2271	0.2059	0.2507	1.1243	0.5687	901	上市公司年报
力康	6	0.1925	－0.0204	－0.0415	0.1150	0.0356	－0.0206	0.0445	0.0122	0.3173	0.2032	0.2025	0.2129	0.2237	0.2651	1.1150	0.5566	897	当地公布的税务资料、行业咨询研究资料、企业自报数据和医院及医疗机构采购招标结果
宝莱特	7	－0.1089	－0.1118	－0.0443	0.1481	0.1624	－0.0189	0.2706	0.1636	0.3166	0.2893	0.1792	0.1687	0.1296	0.1786	1.0067	0.5236	890	当地公布的税务资料、行业咨询研究资料、企业自报数据和医院及医疗机构采购招标结果
上海医疗器械	8	－0.1148	－0.0206	－0.0462	0.1073	0.0493	－0.0219	－0.0728	－0.0323	－0.1520	0.2520	0.2321	0.2282	0.2443	0.2270	1.1738	0.2457	873	母公司上市年报
日本光电	9	－0.1768	－0.0079	－0.0371	0.0026	－0.0183	0.0930	－0.0634	－0.0244	－0.2323	0.4377	0.1383	0.1404	0.1501	0.4433	1.3564	0.2442	872	上市公司年报
蓝韵	10	－0.1781	－0.0206	－0.0457	0.0003	－0.0010	－0.0225	－0.0196	－0.0231	－0.3103	0.3047	0.2403	0.2507	0.1514	0.2547	1.3033	0.1736	860	当地公布的税务资料、行业咨询研究资料、企业自报数据和医院及医疗机构采购招标结果

注1：关于销售收入指标数据，由于所参选企业的销售收入来自其众多产品的销售收入，我们因此所采集的数据是以医疗器械各子领域榜单相关的产品在中国市场的收入作为销售收入。例如：放射领域榜单的销售收入数据采集自各企业其放射产品在中国市场的销售收入。
注2：净利润所采用的数据是该参选企业各子领域相关产品的净利润，如果该公司的年报未体现相关数据，我们将采用该公司整体的利润率按产品贡献比例来推算。
注3：其余的六个评选指标（净资产，总资产利润率，净资产收益率，全员劳动贡献率，近三年销售收入平均增长率，近三年净利润平均增长率）的数据采用将以该参选企业对外公布整体业绩所提供的相关指标为参考标准，不再作细别区分。
注4：净资产收益率有不同的定义方式，为了避免因为上市公司与非上市公司企业所得税税率不同而造成的净利润不可比的问题，我们因此将公式中的分子定义为利润总额而非净利润，计算净资产收益率的公式为：净资产收益率=利润总额/净资产
注5：从监测数据中可以发现，如果企业竞争力主要来源于增长类指标（即近三年销售收入平均增长率&近三年净利润平均增长率），企业竞争力监测指数往往是不稳定的。造成这些企业竞争力不稳定的主要原因是：这些企业原来的销售收入的基数很小，近两年销售增加后会使企业近三年的销售收入平均增长率很高，从而远高于所在行业企业的平均水平。企业可能由于一个指标标准值的异常偏高而使该企业的竞争力基础数据的标准值整体很高。但在第二年或第三年，当该企业的销售收入增长率降到正常的平均水平，而其他指标却没有更高的增长时，该企业的竞争力监测指数就会显著下降。为了避免由于某一个财务指标的异常变动而影响企业竞争力评选结果的客观性，我们进行了一个可行的改进方法，对增长类指标（近三年销售收入平均增长率、近三年净利润平均增长率）的标准值设定上下限[1,-1]，并通过统一的一致性检验，从而可以避免由于某一个增长类指标标准值的异常而对硬指标基础数据标准值产生过大影响。

Ranking of Top 10 competitiveness enterprises in China medical devices industry during 2010-2011

1. Ranking of Top 10 competitiveness enterprises in the anesthesia and monitoring field of China medical devices industry during 2010-2011

Rankings of Top 10 competitiveness enterprises in the anesthesia and monitoring field of China medical devices industry during 2010-2011

Company	Ranking	Standard value weighted of the financial data(70% weight)									Standard value weighted of the survey data (30% weight)						Comprehensive index of competitiveness	Comprehensive score of competitiveness	Source of financial data
		Sales revenues weight 26%	Net assets weight 6%	Net profit weight 12%	Return on total assets weight 11%	Return on net assets weight 11%	Sales revenues contribution per employee weight 5%	The average growth rate of sales revenues for the last three years weight 15%	The average growth rate of net profit for the last three years weight 14%	Total standard value weighted of the financial data (A)	Technology innovation weight 34%	Customer satisfaction weight 18%	Brand awareness weight 12%	Management level of enterprise weight 11%	Corporation culture weight 25%	Total standard value weighted of the survey data (B)	(A*70%+B*30%)		
GE Healthcare	1	0.9645	0.1073	0.2997	－0.0943	－0.0046	0.1602	－0.1036	－0.0492	1.2800	0.7699	0.5157	0.6503	0.2776	0.5732	2.7867	1.7320	1000	Annual report of listed company
Draeger Medical	2	0.9338	－0.0047	0.0605	－0.0841	－0.0661	0.1276	0.0896	0.2504	1.1966	0.6502	0.5921	0.5978	0.2602	0.5887	2.6350	1.6281	992	Annual report of listed company
Philips Healthcare	3	0.7677	0.0873	0.2297	－0.0114	0.0112	0.1152	－0.0269	－0.0058	1.1670	0.5563	0.5529	0.5717	0.2976	0.6514	2.6201	1.6029	989	Annual report of listed company
Mindray	4	0.8555	0.0001	0.0213	0.1389	0.0470	－0.0096	0.0203	0.0140	1.0875	0.4535	0.6182	0.6277	0.2654	0.3607	2.2877	1.4476	978	Annual report of listed company
Edan	5	0.1192	－0.0215	－0.0387	0.1643	0.1757	－0.2384	0.1500	0.0201	0.3307	0.2266	0.2140	0.2271	0.2059	0.2507	1.1243	0.5687	901	Annual report of listed company
Heal Force	6	0.1925	－0.0204	－0.0415	0.1150	0.0356	－0.0206	0.0445	0.0122	0.3173	0.2032	0.2025	0.2129	0.2237	0.2651	1.1150	0.5566	897	Taxation、research & survey information；self-reported figures and hospital's tender results
Biolight	7	－0.1089	－0.1118	－0.0443	0.1481	0.1624	－0.0189	0.2706	0.1636	0.3166	0.2893	0.1792	0.1687	0.1296	0.1786	1.0067	0.5236	890	Taxation、research & survey information；self-reported figures and hospital's tender results
Shanghai Medical Instruments	8	－0.1148	－0.0206	－0.0462	0.1073	0.0493	－0.0219	－0.0728	－0.0323	－0.1520	0.2520	0.2321	0.2282	0.2443	0.2270	1.1738	0.2457	873	Annual report of listed parent company
Nihon Kohden	9	－0.1768	－0.0079	－0.0371	0.0026	－0.0183	0.0930	－0.0634	－0.0244	－0.2323	0.4377	0.1383	0.1404	0.1501	0.4433	1.3564	0.2442	872	Annual report of listed company
Landwind	10	－0.1781	－0.0206	－0.0457	0.0003	－0.0010	－0.0225	－0.0196	－0.0231	－0.3103	0.3047	0.2403	0.2507	0.1514	0.2547	1.3033	0.1736	860	Taxation、research & survey information；self-reported figures and hospital's tender results

Note 1: (About revenues) Because some enterprises have lots of products in different fields, the revenues here refer to one enterprise's sales revenues in China market in special sub-field of medical devices industry. For example: the revenues in the list of the radiology field are the sales revenues of enterprises' radiation products in China market.
Note 2: (About net profit) The indicator refers to the net profit of one enterprise's related products in a special sub-field. If the annual report didn't show the related data, we will calculate it from the total profit rate and products contribution proportion of the enterprise.
Note 3: The other six indicators (net assets, return on total assets, return on net assets, revenues per employee, the average growth rate of revenues for the last three years, and the average growth rate of net profit for the last three years) refer to the related indicators data of overall performance published by the enterprise.
Note 4: The return on net assets has different definitions. In order to avoid the problem of the incomparable value of net income caused by the different income tax rate between listed companies and non-listed companies, we will definite the numerator as the total profit rather than the net profit, the formula for calculating The return on net assets is: The return on net assets = Total profit / Net assets
Note 5: The monitoring data shows that if the competitiveness of enterprises comes mainly from the growth indicators (that is, the average growth rate of revenues for the last three years & the average growth rate of net profit for the last three years), the index of enterprises competitiveness is often unstable. The main reason for this instability is that some enterprises with small original revenues base have rapidly increasing in sales revenues during the past 2 years, which makes the average growth rate of the past 3 years much higher than the industry average level. An extremely high index may cause the enterprises' overall competitiveness standard value of fundamental data improved significantly. But in the future 2 or 3 years, with the growth rate of sales revenues remaining average and other index without rapid increase, the monitoring data will fall. To avoid unfair competition due to this problem, we make some viable improvement by setting the indicator of growth index (the average growth rate of revenues and net profits for the last 3 years)into the limitation of [1,-1]. With the consistency of statistical test, the overdone impact on overall standard value of fundamental data by the abnormal data of growth index can be eliminated.

二、《2010－2011年度中国医疗器械放射领域最具竞争力企业10强》榜单

2010-2011年度中国医疗器械放射领域最具竞争力企业10强榜单

公司	排名	直接计量硬指标财务数据加权标准值（权重为70%）									间接计量软指标加权标准值（权重为30%）						竞争力综合指数 (A*70% +B*30%)	竞争力综合得分	数据来源
		销售收入	净资产	净利润	总资产利润率	净资产收益率	全员劳动贡献率	近三年销售收入平均增长率	近三年净利润平均增长率	直接计量硬指标财务数据加权标准值合计 (A)	技术创新	客户满意度	品牌知名度	企业家及管理水平	企业文化	间接计量软指标加权标准值合计 (B)			
		权重 26%	权重 6%	权重 12%	权重 11%	权重 11%	权重 5%	权重 15%	权重 14%		权重 34%	权重 18%	权重 12%	权重 11%	权重 25%				
西门子	1	0. 8221	0. 2265	0. 5485	0. 0086	0. 1126	0. 0450	-0. 0873	-0. 0170	1. 6590	0. 7672	0. 5989	0. 6170	0. 2658	0. 6144	2. 8633	1. 9992	1000	上市公司年报
通用	2	1. 0334	0. 2971	0. 4758	-0. 0668	0. 0176	0. 0317	-0. 1500	-0. 1053	1. 5335	0. 7695	0. 6336	0. 6524	0. 2771	0. 6264	2. 9590	1. 9611	996	上市公司年报
飞利浦	3	0. 5747	0. 1371	0. 1278	0. 0160	0. 0335	0. 0418	-0. 0048	0. 0253	0. 9514	0. 7740	0. 6285	0. 6470	0. 3019	0. 6446	2. 9960	1. 5647	983	上市公司年报
爱克发	4	-0. 1027	-0. 0058	-0. 0186	-0. 0148	0. 0368	0. 0232	-0. 1500	0. 1400	-0. 0919	0. 5833	0. 4114	0. 3719	0. 3727	0. 3827	2. 1220	0. 7009	922	上市公司年报
东芝	5	0. 1202	-0. 0214	-0. 0288	-0. 0955	-0. 0748	0. 0339	-0. 1060	0. 0324	-0. 1400	0. 7350	0. 5637	0. 5330	0. 2126	0. 5844	2. 6287	0. 6906	920	上市公司年报
锐珂	6	0. 0678	-0. 0061	-0. 0225	-0. 0961	-0. 0756	0. 0304	-0. 1084	0. 0190	-0. 1917	0. 7196	0. 5936	0. 6131	0. 2191	0. 5970	2. 7424	0. 6886	919	上市公司年报
万东	7	0. 0025	-0. 0904	-0. 0425	-0. 0144	-0. 0225	-0. 0137	-0. 0860	0. 1400	-0. 1270	0. 4736	0. 4228	0. 4629	0. 2171	0. 3139	1. 8903	0. 4781	905	上市公司年报
日立	8	-0. 1224	-0. 0172	-0. 0283	-0. 0495	-0. 0639	0. 0315	-0. 1500	-0. 0853	-0. 4851	0. 7455	0. 4434	0. 4172	0. 2827	0. 6306	2. 5194	0. 4163	902	上市公司年报
岛津	9	-0. 1153	-0. 0249	-0. 0278	-0. 0345	-0. 0641	0. 0330	-0. 1500	-0. 1400	-0. 5236	0. 7170	0. 4848	0. 5852	0. 2503	0. 5224	2. 5597	0. 4014	900	上市公司年报
柯尼卡美能达	10	-0. 1158	-0. 0188	-0. 0271	-0. 0654	-0. 0650	0. 0179	-0. 1500	-0. 1400	-0. 5642	0. 6474	0. 4344	0. 4739	0. 1942	0. 4765	2. 2264	0. 2730	887	上市公司年报

注1：关于销售收入指标数据，由于所参选企业的销售收入来自其众多产品的销售收入，我们因此所采集的数据是以医疗器械各子领域榜单相关的产品在中国市场的收入作为销售收入。例如：放射领域榜单的销售收入数据采集自各企业其放射产品在中国市场的销售收入。
注2：净利润所采用的数据是该参选企业各子领域相关产品的净利润，如果该公司的年报未体现相关数据，我们将采用该公司整体的利润率按产品贡献比例来推算。
注3：其余的六个评选指标（净资产，总资产利润率，净资产收益率，全员劳动贡献率，近三年销售收入平均增长率，近三年净利润平均增长率）的数据采用将以该参选企业对外公布整体业绩所提供的相关指标为参考标准，不再作细别区分。
注4：净资产收益率有不同的定义方式，为了避免因为上市公司与非上市公司企业所得税税率不同而造成的净利润不可比的问题，我们因此将公式中的分子定义为利润总额而非净利润，计算净资产收益率的公式为：净资产收益率=利润总额/净资产
注5：从监测数据中可以发现，如果企业竞争力主要来源于增长类指标（即近三年销售收入平均增长率&近三年净利润平均增长率），企业竞争力监测指数往往是不稳定的，造成这些企业竞争力不稳定的主要原因是：这些企业原来的销售收入的基数很小，近两年销售增加后会使企业近三年的销售收入平均增长率很高，从而远高于所在行业企业的平均水平，企业可能由于一个指标标准值的异常偏高而使该企业的竞争力基础数据的标准值整体很高，但在第二年或第三年，当该企业的销售收入增长率降到正常的平均水平，而其他指标却没有更高的增长时，该企业的竞争力监测指数就会显著下降。为了避免由于某一个财务指标的异常变动而影响企业竞争力评选结果的客观性，我们进行了一个可行的改进方法，对增长类指标（近三年销售收入平均增长率、近三年净利润平均增长率）的标准值设定上下限[1,-1]，并通过统一的一致性检验，从而可以避免由于某一个增长类指标标准值的异常而对硬指标基础数据标准值产生过大影响。

2. Ranking of Top 10 competitiveness enterprises in the radiology field of China medical devices industry during 2010-2011

Rankings of Top 10 competitiveness enterprises in the radiology field of China medical devices industry during 2010-2011

Company	Ranking	Standard value weighted of the financial data(70% weight)									Standard value weighted of the survey data (30% weight)						Comprehensive index of competitiveness (A*70%+B*30%)	Comprehensive score of competitiveness	Source of financial data
		Sales revenues	Net assets	Net profit	Return on total assets	Return on net assets	Sales revenues contribution per employee	The average growth rate of sales revenues for the last three years	The average growth rate of net profit for the last three years	Total standard value weighted of the financial data (A)	Technology innovation	Customer satisfaction	Brand awareness	Management level of enterprise	Corporation culture	Total standard value weighted of the survey data (B)			
		weight 26%	weight 6%	weight 12%	weight 11%	weight 11%	weight 5%	weight 15%	weight 14%		weight 34%	weight 18%	weight 12%	weight 11%	weight 25%				
Siemens Healthcare	1	0. 8221	0. 2265	0. 5485	0. 0086	0. 1126	0. 0450	-0. 0873	-0. 0170	1. 6590	0. 7672	0. 5989	0. 6170	0. 2658	0. 6144	2. 8633	1. 9992	1000	Annual report of listed company
GE Healthcare	2	1. 0334	0. 2971	0. 4758	-0. 0668	0. 0176	0. 0317	-0. 1500	-0. 1053	1. 5335	0. 7695	0. 6336	0. 6524	0. 2771	0. 6264	2. 9590	1. 9611	996	Annual report of listed company
Philips Healthcare	3	0. 5747	0. 1371	0. 1278	0. 0160	0. 0335	0. 0418	-0. 0048	0. 0253	0. 9514	0. 7740	0. 6285	0. 6470	0. 3019	0. 6446	2. 9960	1. 5647	983	Annual report of listed company
Agfa Healthcare	4	-0. 1027	-0. 0058	-0. 0186	-0. 0148	0. 0368	0. 0232	-0. 1500	0. 1400	-0. 0919	0. 5833	0. 4114	0. 3719	0. 3727	0. 3827	2. 1220	0. 7009	922	Annual report of listed company
Toshiba Medical	5	0. 1202	-0. 0214	-0. 0288	-0. 0955	-0. 0748	0. 0339	-0. 1060	0. 0324	-0. 1400	0. 7350	0. 5637	0. 5330	0. 2126	0. 5844	2. 6287	0. 6906	920	Annual report of listed company
Carestream Healthcare	6	0. 0678	-0. 0061	-0. 0225	-0. 0961	-0. 0756	0. 0304	-0. 1084	0. 0190	-0. 1917	0. 7196	0. 5936	0. 6131	0. 2191	0. 5970	2. 7424	0. 6886	919	Annual report of listed company
WanDong Medical	7	0. 0025	-0. 0904	-0. 0425	-0. 0144	-0. 0225	-0. 0137	-0. 0860	0. 1400	-0. 1270	0. 4736	0. 4228	0. 4629	0. 2171	0. 3139	1. 8903	0. 4781	905	Annual report of listed company
Hitachi Medical	8	-0. 1224	-0. 0172	-0. 0283	-0. 0495	-0. 0639	0. 0315	-0. 1500	-0. 0853	-0. 4851	0. 7455	0. 4434	0. 4172	0. 2827	0. 6306	2. 5194	0. 4163	902	Annual report of listed company
Shimadzu	9	-0. 1153	-0. 0249	-0. 0278	-0. 0345	-0. 0641	0. 0330	-0. 1500	-0. 1400	-0. 5236	0. 7170	0. 4848	0. 5852	0. 2503	0. 5224	2. 5597	0. 4014	900	Annual report of listed company
Konica Minolta	10	-0. 1158	-0. 0188	-0. 0271	-0. 0654	-0. 0650	0. 0179	-0. 1500	-0. 1400	-0. 5642	0. 6474	0. 4344	0. 4739	0. 1942	0. 4765	2. 2264	0. 2730	887	Annual report of listed company

Note 1: (About revenues) Because some enterprises have lots of products in different fields, the revenues here refer to one enterprise's sales revenues in China market in special sub-field of medical devices industry.
For example: the revenues in the list of the radiology field are the sales revenues of enterprises' radiation products in China market.
Note 2: (About net profit) The indicator refers to the net profit of one enterprise's related products in a special sub-field. If the annual report didn't show the related data, we will calculate it from the total profit rate and products contribution proportion of the enterprise.
Note 3: The other six indicators (net assets, return on total assets, return on net assets, revenues per employee, the average growth rate of revenues for the last three years, and the average growth rate of net profit for the last three years) refer to the related indicators data of overall performance published by the enterprise.
Note 4: The return on net assets has different definitions. In order to avoid the problem of the incomparable value of net income caused by the different income tax rate between listed companies and non-listed companies, we will definite the numerator as the total profit rather than the net profit, the formula for calculating The return on net assets is: The return on net assets = Total profit / Net assets
Note 5: The monitoring data shows that if the competitiveness of enterprises comes mainly from the growth indicators (that is, the average growth rate of revenues for the last three years & the average growth rate of net profit for the last three years), the index of enterprises competitiveness is often unstable. The main reason for this instability is that some enterprises with small original revenues base have rapidly increasing in sales revenues during the past 2 years, which makes the average growth rate of the past 3 years much higher than the industry average level. An extremely high index may cause the enterprises' overall competitiveness standard value of fundamental data improved significantly. But in the future 2 or 3 years, with the growth rate of sales revenues remaining average and other index without rapid increase, the monitoring data will fall. To avoid unfair competition due to this problem, we make some viable improvement by setting the indicator of growth index (the average growth rate of revenues and net profits for the last 3 years)into the limitation of [1,-1]. With the consistency of statistical test, the overdone impact on overall standard value of fundamental data by the abnormal data of growth index can be eliminated.

三、《2010－2011年度中国医疗器械超声领域最具竞争力企业10强》榜单

2010-2011年度中国医疗器械超声领域最具竞争力企业10强榜单

公司	排名	直接计量硬指标财务数据加权标准值（权重为70%）									间接计量软指标加权标准值（权重为30%）						竞争力综合指数	竞争力综合得分	数据来源
		销售收入	净资产	净利润	总资产利润率	净资产收益率	全员劳动贡献率	近三年销售收入平均增长率	近三年净利润平均增长率	直接计量硬指标财务数据加权标准值合计	技术创新	客户满意度	品牌知名度	企业家及管理水平	企业文化	间接计量软指标加权标准值合计			
		权重 26%	权重 6%	权重 12%	权重 11%	权重 11%	权重 5%	权重 15%	权重 14%	(A)	权重 34%	权重 18%	权重 12%	权重 11%	权重 25%	(B)	(A*70% +B*30%)		
飞利浦	1	0. 8017	0. 1439	0. 1285	-0. 0240	0. 0223	0. 1075	-0. 0184	0. 0245	1. 1861	0. 7978	0. 6469	0. 6478	0. 2999	0. 6070	2. 9994	1. 7300	1000	上市公司年报
通用	2	0. 7521	0. 3039	0. 1969	-0. 1069	0. 0064	0. 0833	-0. 0951	0. 0046	1. 1452	0. 7081	0. 6484	0. 6540	0. 2885	0. 6386	2. 9376	1. 6828	996	上市公司年报
西门子	3	0. 5104	0. 2332	0. 1495	-0. 0315	0. 1015	0. 1149	-0. 0447	0. 0181	1. 0514	0. 6333	0. 6298	0. 6244	0. 3036	0. 6532	2. 8443	1. 5892	988	上市公司年报
迈瑞	4	0. 2909	-0. 0033	-0. 0111	0. 1262	0. 0581	-0. 0173	0. 0287	0. 0337	0. 5059	0. 4064	0. 5607	0. 5610	0. 2585	0. 3894	2. 1760	1. 0069	958	上市公司年报
百胜	5	0. 1948	-0. 0179	-0. 0163	0. 0794	0. 0731	0. 0839	-0. 0016	0. 0200	0. 4154	0. 4524	0. 3560	0. 3585	0. 3017	0. 4891	1. 9577	0. 8780	932	上市公司年报
阿洛卡	6	0. 2581	-0. 0157	-0. 0192	0. 0060	0. 0002	0. 1102	-0. 0621	0. 0689	0. 3464	0. 4226	0. 4027	0. 4039	0. 2673	0. 4556	1. 9518	0. 8279	928	上市公司年报
东芝	7	0. 2476	-0. 0146	-0. 0261	-0. 1356	-0. 0860	0. 0885	-0. 0506	0. 0256	0. 0488	0. 4101	0. 3108	0. 3100	0. 2607	0. 6317	1. 9233	0. 6110	914	上市公司年报
麦迪逊	8	0. 0693	-0. 0894	-0. 0202	-0. 0170	-0. 0001	0. 0839	-0. 0279	0. 0164	0. 0150	0. 3468	0. 3269	0. 3281	0. 1915	0. 3795	1. 5728	0. 4928	903	母公司上市年报
蓝韵	9	0. 0608	-0. 0240	-0. 0252	-0. 0126	0. 0101	-0. 0302	-0. 0111	0. 0166	-0. 0156	0. 2413	0. 3224	0. 3449	0. 2734	0. 3242	1. 4841	0. 4343	899	当地公布的税务资料、行业咨询研究资料、企业自报数据和医院及医疗机构采购招标结果统计
日立	10	-0. 0373	-0. 0104	-0. 0250	-0. 0897	-0. 0751	0. 0829	-0. 0817	0. 0076	-0. 2287	0. 4081	0. 3088	0. 3080	0. 2587	0. 6295	1. 9131	0. 4138	896	上市公司年报

注1：关于销售收入指标数据，由于所参选企业的销售收入来自其众多产品的销售收入，我们因此所采集的数据是以医疗器械各子领域榜单相关的产品在中国市场的收入作为销售收入。例如：放射领域榜单的销售收入数据采集自各企业其放射产品在中国市场的销售收入。
注2：净利润所采用的数据是该参选企业各子领域相关产品的净利润，如果该公司的年报未体现相关数据，我们将采用该公司整体的利润率按产品贡献比例来推算。
注3：其余的六个评选指标（净资产、总资产利润率、净资产收益率、全员劳动贡献率、近三年销售收入平均增长率、近三年净利润平均增长率）的数据采用将以该参选企业对外公布整体业绩所提供的相关指标为参考标准，不再作细则区分。
注4：净资产收益率有不同的定义方式，为了避免因为上市公司与非上市公司企业所得税税率不同而造成的净利润不可比的问题，我们因此将公式中的分子定义为利润总额而非净利润，计算净资产收益率的公式为：净资产收益率=利润总额/净资产
注5：从监测数据中可以发现，如果企业竞争力主要来源于增长类指标（即近三年销售收入平均增长率&近三年净利润平均增长率），企业竞争力监测指数往往是不稳定的。造成这些企业竞争力不稳定的主要原因是：这些企业原来的销售收入的基数很小，近两年销售增加后会使企业近三年的销售收入平均增长率很高，从而远高于所在行业企业的平均水平，企业可能由于一个指标标准值的异常偏高而使该企业的竞争力基础数据的标准值整体很高。但在第二年或第三年，当该企业的销售收入增长率降到正常的平均水平，而其他指标却没有更高的增长时，该企业的竞争力监测指数就会显著下降。为了避免由于某一个财务指标的异常变动而影响企业竞争力评选结果的客观性，我们进行了一个可行的改进方法，对增长类指标（近三年销售收入平均增长率、近三年净利润平均增长率）的标准值设定上下限[1,-1]，并通过统一的一致性检验，从而可以避免由于某一个增长类指标标准值的异常而对硬指标基础数据标准值产生过大影响。

3. Ranking of Top 10 competitiveness enterprises in the ultrasound field of China medical devices industry during 2010-2011

Rankings of Top 10 competitiveness enterprises in the ultrasound field of China medical devices industry during 2010-2011

Company	Ranking	Standard value weighted of the financial data(70% weight)									Standard value weighted of the survey data (30% weight)						Comprehensive index of competitiveness	Comprehensive score of competitiveness	Source of financial data
		Sales revenues	Net assets	Net profit	Return on total assets	Return on net assets	Sales revenues contribution per employee	The average growth rate of sales revenues for the last three years	The average growth rate of net profit for the last three years	Total standard value weighted of the financial data	Technology innovation	Customer satisfaction	Brand awareness	Management level of enterprise	Corporation culture	Total standard value weighted of the survey data			
		weight 26%	weight 6%	weight 12%	weight 11%	weight 11%	weight 5%	weight 15%	weight 14%	(A)	weight 34%	weight 18%	weight 12%	weight 11%	weight 25%	(B)	(A*70%+B*30%)		
Philips Healthcare	1	0. 8017	0. 1439	0. 1285	-0. 0240	0. 0223	0. 1075	-0. 0184	0. 0245	1. 1861	0. 7978	0. 6469	0. 6478	0. 2999	0. 6070	2. 9994	1. 7300	1000	Annual report of listed company
GE Healthcare	2	0. 7521	0. 3039	0. 1969	-0. 1069	0. 0064	0. 0833	-0. 0951	0. 0046	1. 1452	0. 7081	0. 6484	0. 6540	0. 2885	0. 6386	2. 9376	1. 6828	996	Annual report of listed company
Siemens Healthcare	3	0. 5104	0. 2332	0. 1495	-0. 0315	0. 1015	0. 1149	-0. 0447	0. 0181	1. 0514	0. 6333	0. 6298	0. 6244	0. 3036	0. 6532	2. 8443	1. 5892	988	Annual report of listed company
Mindray	4	0. 2909	-0. 0033	-0. 0111	0. 1262	0. 0581	-0. 0173	0. 0287	0. 0337	0. 5059	0. 4064	0. 5607	0. 5610	0. 2585	0. 3894	2. 1760	1. 0069	958	Annual report of listed company
Esaote Medical	5	0. 1948	-0. 0179	-0. 0163	0. 0794	0. 0731	0. 0839	-0. 0016	0. 0200	0. 4154	0. 4524	0. 3560	0. 3585	0. 3017	0. 4891	1. 9577	0. 8780	932	Annual report of listed company
Aloka	6	0. 2581	-0. 0157	-0. 0192	0. 0060	0. 0002	0. 1102	-0. 0621	0. 0689	0. 3464	0. 4226	0. 4027	0. 4039	0. 2673	0. 4556	1. 9518	0. 8279	928	Annual report of listed company
Toshiba Medical	7	0. 2476	-0. 0146	-0. 0261	-0. 1356	-0. 0860	0. 0885	-0. 0506	0. 0256	0. 0488	0. 4101	0. 3108	0. 3100	0. 2607	0. 6317	1. 9233	0. 6110	914	Annual report of listed company
Medison	8	0. 0693	-0. 0894	-0. 0202	-0. 0170	-0. 0001	0. 0839	-0. 0279	0. 0164	0. 0150	0. 3468	0. 3269	0. 3281	0. 1915	0. 3795	1. 5728	0. 4928	903	Annual report of listed parent company
Landwind Medical	9	0. 0608	-0. 0240	-0. 0252	-0. 0126	0. 0101	-0. 0302	-0. 0111	0. 0166	-0. 0156	0. 2413	0. 3224	0. 3449	0. 2734	0. 3242	1. 4841	0. 4343	899	Annual report of listed company
Hitachi Medical	10	-0. 0373	-0. 0104	-0. 0250	-0. 0897	-0. 0751	0. 0829	-0. 0817	0. 0076	-0. 2287	0. 4081	0. 3088	0. 3080	0. 2587	0. 6295	1. 9131	0. 4138	896	Taxation、research & survey information、self-reported figures and hospital's tender results

Note 1: (About revenues) Because some enterprises have lots of products in different fields, the revenues here refer to one enterprise's sales revenues in China market in special sub-field of medical devices industry.
For example: the revenues in the list of the radiology field are the sales revenues of enterprises' radiation products in China market.
Note 2: (About net profit) The indicator refers to the net profit of one enterprise's related products in a special sub-field. If the annual report didn't show the related data, we will calculate it from the total profit rate and products contribution proportion of the enterprise.
Note 3: The other six indicators (net assets, return on total assets, return on net assets, revenues per employee, the average growth rate of revenues for the last three years, and the average growth rate of net profit for the last three years) refer to the related indicators data of overall performance published by the enterprise.
Note 4: The return on net assets has different definitions. In order to avoid the problem of the incomparable value of net income caused by the different income tax rate between listed companies and non-listed companies, we will definite the numerator as the total profit rather than the net profit, the formula for calculating The return on net assets is: The return on net assets = Total profit / Net assets
Note 5: The monitoring data shows that if the competitiveness of enterprises comes mainly from the growth indicators (that is, the average growth rate of revenues for the last three years & the average growth rate of net profit for the last three years), the index of enterprises competitiveness is often unstable. The main reason for this instability is that some enterprises with small original revenues base have rapidly increasing in sales revenues during the past 2 years, which makes the average growth rate of the past 3 years much higher than the industry average level. An extremely high index may cause the enterprises' overall competitiveness standard value of fundamental data improved significantly. But in the future 2 or 3 years, with the growth rate of sales revenues remaining average and other index without rapid increase, the monitoring data will fall. To avoid unfair competition due to this problem, we make some viable improvement by setting the indicator of growth index (the average growth rate of revenues and net profits for the last 3 years)into the limitation of [1,-1]. With the consistency of statistical test, the overdone impact on overall standard value of fundamental data by the abnormal data of growth index can be eliminated.

四、《2010－2011年度中国医疗器械检验领域最具竞争力企业10强》榜单

2010-2011年度中国医疗器械检验领域最具竞争力企业10强榜单

公司	排名	直接计量硬指标财务数据加权标准值（权重为70%）									间接计量软指标加权标准值（权重为30%）						竞争力综合指数	竞争力综合得分	数据来源
		销售收入	净资产	净利润	总资产利润率	净资产收益率	全员劳动贡献率	近三年销售收入平均增长率	近三年净利润平均增长率	直接计量硬指标财务数据加权标准值合计	技术创新	客户满意度	品牌知名度	企业家及管理水平	企业文化	间接计量软指标加权标准值合计			
		权重 26%	权重 6%	权重 12%	权重 11%	权重 11%	权重 5%	权重 15%	权重 14%	(A)	权重 34%	权重 18%	权重 12%	权重 11%	权重 25%	(B)	(A*70% +B*30%)		
罗氏	1	0. 5632	0. 2604	0. 2180	0. 0530	0. 1508	0. 0493	-0. 0353	0. 0223	1. 2817	0. 8086	0. 5538	0. 5904	0. 3646	0. 6384	2. 9558	1. 7838	1000	上市公司年报
雅培	2	0. 4883	0. 0011	0. 1617	0. 0190	0. 0695	0. 0552	-0. 0420	0. 0983	0. 8511	0. 7299	0. 4901	0. 4898	0. 3159	0. 7597	2. 7854	1. 4313	979	上市公司年报
希森美康	3	0. 5368	-0. 0076	0. 0181	0. 0090	-0. 0058	0. 0236	-0. 0271	-0. 0468	0. 5002	0. 6502	0. 5825	0. 4526	0. 2911	0. 7326	2. 7090	1. 1628	963	上市公司年报
贝克曼库尔特	4	0. 5020	0. 0033	0. 0178	-0. 0287	-0. 0262	0. 0215	-0. 0131	-0. 0287	0. 4479	0. 7697	0. 4585	0. 4198	0. 2184	0. 7966	2. 6630	1. 1124	960	上市公司年报
西门子	5	0. 1716	0. 2299	0. 0749	-0. 0090	0. 0393	0. 0422	-0. 0277	-0. 0090	0. 5112	0. 6989	0. 3326	0. 3632	0. 2568	0. 6378	2. 2893	1. 0453	954	上市公司年报
日立高新	6	-0. 0172	0. 1515	0. 0066	-0. 0219	-0. 0323	0. 1143	-0. 0178	-0. 0651	0. 1181	0. 6768	0. 3880	0. 3501	0. 1889	0. 4862	2. 0900	0. 7096	936	上市公司年报
强生	7	0. 0555	0. 1605	0. 0821	-0. 0228	-0. 0236	0. 0361	-0. 0351	-0. 1400	0. 1127	0. 5119	0. 3121	0. 2979	0. 2817	0. 6431	2. 0467	0. 6928	935	上市公司年报
迈瑞	8	0. 0973	-0. 0067	-0. 1616	0. 0467	0. 0178	-0. 0098	0. 0457	0. 0749	0. 1043	0. 3934	0. 4055	0. 4273	0. 2786	0. 3936	1. 8984	0. 6425	932	上市公司年报
科华生物	9	0. 0165	-0. 2440	-0. 1574	0. 1318	0. 0993	-0. 0082	0. 1500	0. 0507	0. 0387	0. 3048	0. 3261	0. 3177	0. 2052	0. 2706	1. 4244	0. 4543	919	上市公司年报
迪瑞	10	-0. 0710	-0. 2570	-0. 2079	0. 0343	0. 0155	-0. 0137	0. 0970	0. 0629	-0. 3399	0. 2953	0. 3166	0. 3082	0. 1957	0. 2609	1. 3767	0. 1750	897	参股上市公司年报

注1：关于销售收入指标数据，由于所参选企业的销售收入来自其众多产品的销售收入，我们因此所采集的数据是以医疗器械各子领域榜单相关的产品在中国市场的收入作为销售收入。例如：放射领域榜单的销售收入数据采集自各企业其放射产品在中国市场的销售收入。
注2：净利润所采用的数据是该参选企业各子领域相关产品的净利润，如果该公司的年报未体现相关数据，我们将采用该公司整体的利润率按产品贡献比例来推算。
注3：其余的六个评选指标（净资产，总资产利润率，净资产收益率，全员劳动贡献率，近三年销售收入平均增长率，近三年净利润平均增长率）的数据采用将以该参选企业对外公布整体业绩所提供的相关指标为参考标准，不再作细别区分。
注4：净资产收益率有不同的定义方式，为了避免因为上市公司与非上市公司企业所得税税率不同而造成的净利润不可比的问题，我们因此将公式中的分子定义为利润总额而非净利润，计算净资产收益率的公式为：净资产收益率=利润总额/净资产
注5：从监测数据中可以发现，如果企业竞争力主要来源于增长类指标（即近三年销售收入平均增长率&近三年净利润平均增长率），企业竞争力监测指数往往是不稳定的。造成这些企业竞争力不稳定的主要原因是：这些企业原来的销售收入的基数很小，近两年销售增加后会使企业近三年的销售收入平均增长率很高，从而远高于所在行业企业的平均水平。企业可能由于一个指标标准值的异常偏高而使该企业的竞争力基础数据的标准值整体很高。但在第二年或第三年，当该企业的销售收入增长率降到正常的平均水平，而其他指标却没有更高的增长时，该企业的竞争力监测指数就会显著下降。为了避免由于某一个财务指标的异常变动而影响企业竞争力评选结果的客观性，我们进行了一个可行的改进方法，对增长类指标（近三年销售收入平均增长率、近三年净利润平均增长率）的标准值设定上下限[1,-1]，并通过统一的一致性检验，从而可以避免由于某一个增长类指标标准值的异常而对硬指标基础数据标准值产生过大影响。

4. Ranking of Top 10 competitiveness enterprises in the laboratory medicine field of China medical devices industry during 2010-2011

Rankings of Top 10 competitiveness enterprises in the laboratory medicine field of China medical devices industry during 2010-2011

Company	Ranking	Standard value weighted of the financial data(70% weight)									Standard value weighted of the survey data (30% weight)						Comprehensive index of competitiveness	Comprehensive score of competitiveness	Source of financial data
		Sales revenues	Net assets	Net profit	Return on total assets	Return on net assets	Sales revenues contribution per employee	The average growth rate of sales revenues for the last three years	The average growth rate of net profit for the last three years	Total standard value weighted of the financial data	Technology innovation	Customer satisfaction	Brand awareness	Management level of enterprise	Corporation culture	Total standard value weighted of the survey data			
		weight 26%	weight 6%	weight 12%	weight 11%	weight 11%	weight 5%	weight 15%	weight 14%	(A)	weight 34%	weight 18%	weight 12%	weight 11%	weight 25%	(B)	(A*70%+B*30%)		
Roche Diagnostics	1	0. 5632	0. 2604	0. 2180	0. 0530	0. 1508	0. 0493	-0. 0353	0. 0223	1. 2817	0. 8086	0. 5538	0. 5904	0. 3646	0. 6384	2. 9558	1. 7838	1000	Annual report of listed company
Abbott	2	0. 4883	0. 0011	0. 1617	0. 0190	0. 0695	0. 0552	-0. 0420	0. 0983	0. 8511	0. 7299	0. 4901	0. 4898	0. 3159	0. 7597	2. 7854	1. 4313	979	Annual report of listed company
Sysmex	3	0. 5368	-0. 0076	0. 0181	0. 0090	-0. 0058	0. 0236	-0. 0271	-0. 0468	0. 5002	0. 6502	0. 5825	0. 4526	0. 2911	0. 7326	2. 7090	1. 1628	963	Annual report of listed company
Beckman Coulter	4	0. 5020	0. 0033	0. 0178	-0. 0287	-0. 0262	0. 0215	-0. 0131	-0. 0287	0. 4479	0. 7697	0. 4585	0. 4198	0. 2184	0. 7966	2. 6630	1. 1124	960	Annual report of listed company
Siemens Healthcare	5	0. 1716	0. 2299	0. 0749	-0. 0090	0. 0393	0. 0422	-0. 0277	-0. 0090	0. 5112	0. 6989	0. 3326	0. 3632	0. 2568	0. 6378	2. 2893	1. 0453	954	Annual report of listed company
Hitachi-hitec	6	-0. 0172	0. 1515	0. 0066	-0. 0219	-0. 0323	0. 1143	-0. 0178	-0. 0651	0. 1181	0. 6768	0. 3880	0. 3501	0. 1889	0. 4862	2. 0900	0. 7096	936	Annual report of listed company
Johnson&Johnson Medical	7	0. 0555	0. 1605	0. 0821	-0. 0228	-0. 0236	0. 0361	-0. 0351	-0. 1400	0. 1127	0. 5119	0. 3121	0. 2979	0. 2817	0. 6431	2. 0467	0. 6928	935	Annual report of listed company
Mindray	8	0. 0973	-0. 0067	-0. 1616	0. 0467	0. 0178	-0. 0098	0. 0457	0. 0749	0. 1043	0. 3934	0. 4055	0. 4273	0. 2786	0. 3936	1. 8984	0. 6425	932	Annual report of listed company
Kehua Bio-Engineering	9	0. 0165	-0. 2440	-0. 1574	0. 1318	0. 0993	-0. 0082	0. 1500	0. 0507	0. 0387	0. 3048	0. 3261	0. 3177	0. 2052	0. 2706	1. 4244	0. 4543	919	Annual report of listed company
Dirui	10	-0. 0710	-0. 2570	-0. 2079	0. 0343	0. 0155	-0. 0137	0. 0970	0. 0629	-0. 3399	0. 2953	0. 3166	0. 3082	0. 1957	0. 2609	1. 3767	0. 1750	897	Annual report of listed sharing company

Note 1: (About revenues) Because some enterprises have lots of products in different fields, the revenues here refer to one enterprise's sales revenues in China market in special sub-field of medical devices industry.
For example: the revenues in the list of the radiology field are the sales revenues of enterprises' radiation products in China market.
Note 2: (About net profit) The indicator refers to the net profit of one enterprise's related products in a special sub-field. If the annual report didn't show the related data, we will calculate it from the total profit rate and products contribution proportion of the enterprise.
Note 3: The other six indicators (net assets, return on total assets, return on net assets, revenues per employee, the average growth rate of revenues for the last three years, and the average growth rate of net profit for the last three years) refer to the related indicators data of overall performance published by the enterprise.
Note 4: The return on net assets has different definitions. In order to avoid the problem of the incomparable value of net income caused by the different income tax rate between listed companies and non-listed companies, we will definite the numerator as the total profit rather than the net profit, the formula for calculating The return on net assets is: The return on net assets = Total profit / Net assets
Note 5: The monitoring data shows that if the competitiveness of enterprises comes mainly from the growth indicators (that is, the average growth rate of revenues for the last three years & the average growth rate of net profit for the last three years), the index of enterprises competitiveness is often unstable. The main reason for this instability is that some enterprises with small original revenues base have rapidly increasing in sales revenues during the past 2 years, which makes the average growth rate of the past 3 years much higher than the industry average level. An extremely high index may cause the enterprises' overall competitiveness standard value of fundamental data improved significantly. But in the future 2 or 3 years, with the growth rate of sales revenues remaining average and other index without rapid increase, the monitoring data will fall. To avoid unfair competition due to this problem, we make some viable improvement by setting the indicator of growth index (the average growth rate of revenues and net profits for the last 3 years)into the limitation of [1,-1]. With the consistency of statistical test, the overdone impact on overall standard value of fundamental data by the abnormal data of growth index can be eliminated.

2011年中华医学会全国麻醉学术年会
征 文 通 知（草案）

医学术便函（2010）第0号

各省、自治区、直辖市医学会：

各有关医疗单位：

中华医学会麻醉学分会拟定于2011年9月7—10日在济南召开“2011年中华医学会全国麻醉学术年会”，本次会议是中华医学会一类学术会议，麻醉分会各专业学组年会将同时并会召开，因此是2011年度的重要学术盛会。年会将设各专业学组分会场、专题板块和学术论文报告相结合的形式进行学术交流；现将会议学术论文征文的有关事项通知如下：

一、征文内容及分类：

1. 麻醉学基础研究；
2. 临床麻醉与研究；
3. 疼痛治疗与研究；
4. 重症监测治疗与研究；
5. 麻醉相关新技术、新业务进展；
6. 特殊病例报告；
7. 其它。

二、征文要求：

（一）、年会征文：

1. 凡报送参加年会交流的论文，均提交论文摘要一份（800——1000字以内），并请在稿件左上角按上述征文分类注明论文类别（请自留底稿，恕不退稿）。

2. 格式要求：论文摘要请用Microsoft Word2000或2003编辑，页面设置请用4号字体，A4纸，文稿顺序为题目、单位、邮编、作者姓名、联系电话、摘要内容。

3. 凡已在全国性学术会议上或全国公开发行的刊物上发表过的论文，不予受理。

4. 本次年会仍将进行中青年优秀论文评选，参评条件为1966年9月1日以后出生（投稿时请将身份证复印件扫描成图片格式粘贴在文章的首页）。凡申请参加中青年优秀论文评选的论文，均需提交中、英论文摘要各一份（800--1000字以内）及中文全文一份，论文一律用word文档撰写（请网上投稿）；征文要求同上；并请在稿件右上角

注明“中青年优秀论文评奖”字样。评选设一等奖1名，二等奖3名，三等奖5名（具体参评要求届时见有关会议通知）；获奖者将获得临床科研奖金。

5. 各专业学组征文也按年会要求一并投稿，学科管理学组、疼痛学组、ICU学组、儿科麻醉学组、神经外科麻醉学组、心胸外科麻醉学组、气道管理学组、器官移植麻醉学组、产科麻醉学组及青年委员会，都将在年会期间组织学术活动。

（注：年会还将继续进行2011年度SCI论文奖评选；获奖者将获得优秀论文奖金；具体评选办法请登录年会网址查询）。

三、投稿方式：

1. 网上征文与报名：年会网址：http://www.csaol.cn/；

2. 书面邮寄：“北京东四西大街42号中华医学会麻醉学分会办公室白雪同志收（邮编：100710；投寄的论文请在信封上注明“2011年麻醉年会征文”字样）。联系电话010-85158614，传真：010—85158753；邮箱：csa2011@live.cn）；（请尽量采用网上投稿；以保证投稿和注册的准确性；二种方式只选一种）。

四、截稿日期：

年会：2011年3月31日

五、凡个人邀请外宾来参加全国年会并拟进行学术交流者，请与麻醉学分会办公室白雪同志联系（联系方式同上）。

联系人：白雪　中华医学会麻醉学分会办公室

联系电话：010-85158614；传真：010-85158753；

2011.10.31-11.03

福州海峡国际会展中心

Fuzhou Straight International Conference and Exhibition Center

CMEF为您提供“云”平台

医疗行业

贸易 Trading

学习 Learning

创新 Innovation

Networking 交流

CMEF China International Medical Equipment Fair

ICMD International Component Manufacturing & Design Show

第66届中国国际医疗器械博览会

The 66th China International Medical Equipment Fair

第13届中国国际医疗器械设计与制造技术展览会

The 13th International Component Manufacturing & Design Show

国药励展 Reed Sinopharm Exhibitions

ufi

通过ISO9001质量体系认证

www.CMEF.com.cn

欢迎阅览麻醉与监护论坛电子信息报

www.fam120.com

周刊封面
功能：
为贵公司提供最佳的形象宣传

麻醉与镇痛
功能：
为贵司提供麻醉与镇痛相关的文章报道

协会信息
功能：
为贵司报道各专业行业协会的信息和报道其举办的专业学术活动

企业聚焦
功能：
为贵公司提供最直接的企业文化报道

书籍推荐
功能：
为贵公司提供专业书籍推荐

本期执行主编
功能：
通过贵公司提供的VIP客户，为其制作电子个人专辑，扩大专家在行业内影响力，为贵公司起到直接客服的作用

重症医学
功能：
为贵司提供重症医学相关文章报道

专题报道
功能：
聚焦业内热点，紧跟前沿技术，深入追踪报道

企业精典文章
功能：
麻醉与监护专业领域知名企业所提供的代表企业文化、市场动态等精品文章

行业快讯
功能：
报道业内最新信息

新品发布
功能：
为贵公司新品做详细的产品介绍，使企业logo不断展示，有利于医生更加深入了解产品特性和功能

会议讯息

2011

Information of Notification, Exhibition and Scientific Meeting

展

国内会议信息

第三届（上海）国际减灾与安全博览会暨长三角急救、危重、灾害医学论坛
时　间：2011–10–12至2011–10–14
地　点：上海世博主题馆2号馆
主办单位：上海市医学会急诊与危重病医学分会
　　上海市医疗急救中心
邮　箱：Secretary@yecd2011.com

脊柱相关疾病的手法治疗研修班
时　间：2011–10–21至2011–10–24
地　点：昆明
主办单位：中国针灸推拿协会
联 系 人：王老师
电　话：010–87598342 15300094072
传　真：010–87598348
邮　箱：zjtn2011@163.com

危重病人麻醉管理实践技能培训学习班
时　间：2011–11–5至2011–11–9
地　点：北京
主办单位：首都医科大学宣武医院
联 系 人：刘清海　薛纪秀
电　话：13311177014，15699959630

2011中国养生休闲博览会暨国际养生大会
时　间：2011–11–4 至 2011–11–7
地　点：杭州和平会展中心
主办单位：中国保健养生协会
　　浙江省休闲养生协会
联 系 人：徐先生
电　话：0571–85191164
邮　箱：xchsdp@163.com

2011年河南省医疗器械临床合理使用与安全管理研讨会暨河南省医学工程学术年会
时　间：11月上旬
地　点：郑州
主办单位：河南省医学会
　　河南省人民医院
联 系 人：张晓伟
电　话：0371–65953649　13783507799

深化医疗改革，患者安全目标与病种质量控制研讨会
时　间：2011–10–28 至 2011–11–5
地　点：厦门金宝大酒店银楼
主办单位：中华医学会继续教育部
联 系 人：杨桂芳
电　话：010–88820399
传　真：51798200

第四届全国特色医疗建设专家大会
时　间：2011–11–18
地　点：天津
主办单位：中国医促进会中老年保健专业委员会
联 系 人：张海峰
电　话：010–57019398

第二届国际用药安全高峰论坛
时　间：2011–11–06 至 2011–11–08
地　点：北京
主办单位：中国药学会医院药学专业委员会
联 系 人：王旭 张淑谦
电　话：010–8859 7680

第九届胸腔麻醉亚洲会议（2011 ASCA）
时　间：2011–09–30 至 2011–10–02日
地　点：NTUH International Convention Center，Taipei，Taiwan
主办单位：National Taiwan University
电　话：+886–2–8226–1010
网　址：www.asca2011.org/index.html

2011年中国（国际）应急救援装备展览会暨中国（国际）第9届现代救援医学论坛：突发事件医学救援研讨会
时　间：2011–10–15至2011–10–17
地　点：中国 天津 滨海国际会展中心
联合举办：中国医学救援协会
　　中国灾害防御协会
　　中国医师协会
　　中国武警卫生部
　　中国灾协救援医学会
　　中国急救复苏与灾害医学杂志社
　　国际SOS总部
联 系 人：徐伟
电　话：86–10–83294491
传　真：86–10–83294738
邮　：zgxuwei@163.com

全球华人药学家大会
时　间：2012–07–1
地　点：北京市
主办单位：中国药学会
联 系 人：Mr. Ziye Zhang
电　话：86 10 58699276–822
传　真：86 10 58699272
　：gcpsc@cpa.org.cn
会议网站：http://www.gcpsc–cn.org/

中华医学会肿瘤学分会第七届全国中青年肿瘤学术会议
时　间：2011–11–25至2011–11–27
地　点：山东省 济南市
主办单位：中华医学会
　　中华医学肿瘤学分会
δvvv-bl`brn-nqf.bm

中华医学会第十七次全国医学信息学术会议
时　间：2011–10–18至2011–10–22
地　点：湖南长沙
主办单位：中华医学会
联 系 人：刘文君
电　话：010–85158443

第五届IEEE环境污染与人类健康国际学术会议
时　间：2012–05–17 至 2012–05–20
地　点：上海
联 系 人：胡老师
电　话：13264702230
邮　箱：epph@icbbe.org

国际会议信息

2011年世界药学大会暨FIP第71届年会
时　间：2011–09–03 至 2011–09–08
地　点：印度海德拉巴
联 系 人：葛军华
电　话：010–58699280–823
传　真：010–58699272
邮　箱：gjh6565@163.com

第31届日本临床麻醉学会年会
时　间：2011–11–03 至 2011–11–05
联 系 人：贾丽莉 王岩
电　话：010–81458365 63452416

第一届NUS–NUH 国际护理大会
时　间：2011–11–17 至 2011–11–19
地　点：新加坡
电　话：（65）65163320
传　真：（65）667761735
联系地址：National University of Singapore
网　址：HTTP://MEDICINE.NUS.EDU.SG/NURSING/EVENTS/INC/ABSTRACTS.SHTML

国内展会信息

第3届世界（第21届中国）内镜医师大会暨恩德思世界医疗器械药品博览会
时　间：2011–11–18 至 2011–11–20
地　点：北京“国家会议中心”
主办单位：世界内镜医师协会
　　中华人民共和国科技部国际
联 系 人：张宇
电　话：0731–84327991 15111394545
邮　：yu.zhang@endoscopyassociation.or

第二十届中国国际医用仪器设备展览会暨技术交流会
时　间：2011–11–08 至 2011–11–20
地　点：北京国家会议中心
主办单位：中国卫生部
联 系 人：马冉/南易/张珍桢
电　话：010–88393925/88393927
传　真：010–88393924
邮　箱：info@chinahospeq.com

国际展会信息

2011年美国麻醉师学会(ASA)年会
时　间：2011–10–15 至 2011–10–19
地　点：美国 芝加哥
主办单位：美国麻醉师学会(ASA)

2011年第24届印尼国际医疗器械、医院用品实验室设备及医药展览会
时　间：2011–10–19 至 2011–10–22
地　点：印度尼西亚首都雅加达国际会展中心
主办单位：印度尼西亚医疗行业协会
　　印度尼西亚雅加达医疗行业协会
电　话：0771–2841302

2011年第十五届肯尼亚国际贸易展览会及医疗贸易展览会
时　间：2011–11–26 至 2011–11–28
地　点：肯尼亚·内罗毕
联 系 人：苗小姐
电　话：010–82258800–627
传　真：010–82250600

第二十一届俄罗斯国际医疗展览会
时　间：2011–12–06 至 2011–12–09
地　点：莫斯科国际展览中心
联 系 人：金其露
电　话：021–55315333
传　真：021–51686946
邮　箱：dongsin_jin@msn.com

第37届阿拉伯国际医疗设备展览会（迪拜）Arab Health
时　间：2012–01–23 至 2012–01–26
地　点：阿联酋迪拜国际展览中心
主办单位：IIR公司
联 系 人：姜超
电　话：021–61853513
传　真：021–51714607
邮　箱：expogz@163.com

第15届马来西亚–吉隆坡东南亚医疗器材保健展
时　间：2012–04–17 至 2012–04–19
地　点：马来西亚—吉隆坡
联 系 人：金小姐
电　话：021–55315333
传　真：021–51686946
邮　箱：sales–3@dongsinexpo.com
网　址：www.dongsinexpo.com

稿約

《检验诊断与实验室自动化》

MANUSCRIPT STANDARD

[illegible]

[1] [illegible] 0876 [illegible] 163,65-

[2] Lacouments S, YeoTH,Burrin JM,et al.Fentanyl and β-endophin, ACTH and glucoregulatory hormonal response to surgery.Br J Anaesth,1987,59:713-716.

[3] [illegible] 0883-165,2/5

[4] Tamsen A. Comparison of patient-controlled analgesia with constant infusion and intermittent intramuscular regimes. In: Harmer M, Rose M, Vickens MD, eds. Patient-controlled analgesia .2nd eds. London: Blackwell Scientific,1985. 111-125.

[illegible] lyelectron@yahoo.com.cn; fam@medicalinfo.cc

[illegible]

E-Mali: lyelectron@yahoo.com.cn

famttyy@sina.com

读者服务表

Reader Service

姓名：______________ 性别：□男 □女

生日：____年__月__日 工作单位：______________________

职称：__________________ 部门：______________________

通讯地址：______________ 电话：______________________

邮编：_______________移动电话：______________________

电子邮件：______________ 传真：______________________

毕业院校：

学历：□专科 □本科 □硕士 □博士 □博士后

曾发表文章：□是 □否

（名称：______________ 刊物：______________）

您所在的医院级别：□三甲 □三乙 □二级 □一级

您所在的科室有____人 设ICU： □是 □否

麻醉科主任：______________ ICU主任：______________

电话：______________ 电话：______________

本人欲获赠阅《麻醉与监护论坛》杂志，双月刊，从2011年____月至2011年12月刊，共____套(每期邮寄服务费美金3元或人民币20元，全年美金18元或人民币120元)，总计共______元。

有关缴付邮寄服务费办法请咨询读者服务部或直接登录麻醉与监护论坛网站**www.fam120.com**点击“订阅杂志”版块订阅

电话：021-54830451 00852-35693099

传真：021-54429643 00852-28654177

E-mail：fam@medicalinfo.cc

SUBSCRIPITION FORM for Hong Kong, Macau,Taiwan and Overseas

HK$420(HK$300, plus HK$120 postage) for one year (6 issues, HK$50 per issue) of Forum of Anesthesia and Monitoring from 2011 issue _ to 2011 issue 6.

The subscripition fee, please pay to:

Company Name: Medical Information Limited

Bank Name: The Hong Kong and Shanghai Banking Corporation Limited

Account No.:004-009-378704-001

Rm.2903.29/F., Admiralty Centre Tower 1, No. 18 Harcourt Rd., Hong Kong

Tel:00852-35693099 Fax: 00852-28654177

Dräger

Fabius *plus*
一切如您所愿

值得信赖的品质

Fabius *plus* 符合高品质麻醉的新标准，这是百年通气和麻醉经验的积累。Dräger 与临床专业人员紧密合作，创造出能真正满足您需求的临床治疗解决方案。

创新的功能提升

Fabius *plus* 重要功能的提升，更加坚定了临床使用者的信心

- 精确灵活的通气功能覆盖婴儿到成人的应用范围（容量控制模式可提供最低 20ml 潮气量）
- 高对比度的彩色屏幕，直观的用户操作界面
- 可靠、成本优化的 E-Vent 技术

随需而变

模块化设计使 Fabius *plus* 便于升级

- 根据您的临床需求，可配置 IPPV, PCV, SIMV/PS, 以及手动 / 自主通气模式
- 先进的回路加热系统，低流量组件等升级选项可供选择
- 呼吸系统可置于机器的左侧或右侧，满足不同手术室环境要求
- 作为一个开放的平台，能与 Dräger 的 Infinity 监护系统有机结合，灵活配置麻醉工作站

Dräger. Technology for life®

仙琚®

国药准字 H20093186

ROCURONIUM BROMIDE INJECTION

罗库溴铵注射液

快速诱导插管的非去极化肌松药

（全国医保乙类目录）

携手共创
安全和谐肌松环境

快速
可替代琥珀胆碱用于快速诱导插管的非去极化肌松药

灵活
灵活的剂量模式适用于短、中、长手术的肌松掌握

方便
稳定的水针剂型

安全
无活性和毒性代谢物，稳定的心血管作用，无组胺释放

- **适应症：**全身麻醉辅助用药，用于常规诱导麻醉期间气管插管和术中肌松维持
- **用法用量：**参照说明书，和其他肌松药一样，给药剂量应个体化
- **禁忌症：**既往对罗库溴铵或溴离子有过敏反应者
- **规格：**50mg/5ml

浙江仙琚制药股份有限公司
ZHEJIANG XIANJU PHARMACEUTICAL CO., LTD.

生产地址：浙江省仙居县仙药路1号　邮政编码：317300
客户服务专线：0576-87731178 / 800 857 1797(免费)
网址：http://www.xjpharma.com