Table of Contents
October, 2014

Cardiovascular Anesthesiology

Ambulatory Anesthesiology

Research Report

嚴重阻塞性睡眠呼吸暫停患者在內窺鏡檢查時使用丙泊酚輸注系統的安全性和有效性

(王曉莉 譯，李士通 審校)

Safety and Efficacy of Drug-Induced Sleep Endoscopy Using a Probability Ramp Propofol Infusion System in Patients with Severe Obstructive Sleep Apnea

- Atkins, Joshua H.;
- Mandel, Jeff E.;
- Rosanova, Giulia

Anesthesia & Analgesia. 119(4):805-810, October 2014.

Anesthetic Pharmacology

Research Report

肺切除術期間靜脈注射利多卡因降低豬局部和全身腫瘤壞死因數 α 的表達

(徐歡 譯 陳傑 校)

Intravenous Lidocaine Decreases Tumor Necrosis Factor Alpha Expression Both Locally and Systemically in Pigs Undergoing Lung Resection Surgery

- Garutti, Ignacio;
- Rancan, Lisa;
- Simón, Carlos;
- Cusati, Gabriel;
- Sanchez-Pedrosa, Guillermo;
- Moraga, Francisco;
- Olmedilla, Luis;
- Lopez-Gil, Maria Teresa;
- Vara, Elena

Anesthesia & Analgesia. 119(4):815-828, October 2014.

吸入麻醉後的低通氣可發生再麻醉

(王嘉興譯 薛張綱校)

Hypoventilation After Inhaled Anesthesia Results in Reanesthetization

- Leeson, Stanley;

- Roberson, Russell S.;
- Philip, James H.

Anesthesia & Analgesia. 119(4):829-835, October 2014.

香豆酮的衍生物在不同老鼠實驗模型中的抗過敏與抗炎效應說明蛋白激酶 C 通路的重要性

(王雪譯 李士通審校)

The Antihypersensitive and Antiinflammatory Activities of a Benzofuranone Derivative in Different Experimental Models in Mice: The Importance of the Protein Kinase C Pathway

- de Souza Nunes, Juliana Paula;
- da Silva, Kathryn Ana Bortolini;
- da Silva, Gislaine Francieli;
- Quintão, Nara Lins Meira;
- Corrêa, Rogério;
- Cechinel-Filho, Valdir;
- de Campos-Buzzi, Fátima;
- Niero, Rivaldo

Anesthesia & Analgesia. 119(4):836-846, October 2014.

Technology, Computing, and Simulation

Research Report

評估鎮靜過程中風險的一項新型低氧血症指標

(潘志敏 譯 陳傑 校)

A Novel Index of Hypoxemia for Assessment of Risk During Procedural Sedation

- Niklewski, Paul J.;
- Phero, James C.;
- Martin, James F.;
- Lisco, Steven J.

Anesthesia & Analgesia. 119(4):848-856, October 2014.

Patient Safety

Research Report

根治性前列腺切除術後結局：用芬太尼進行全身麻醉和區域麻醉鎮痛比較：配對佇列研究

(吳赤譯 薛張綱校)

Outcomes After Radical Prostatectomy for Cancer: A Comparison Between General Anesthesia and Epidural Anesthesia with Fentanyl Analgesia: A Matched Cohort Study

- Sprung, Juraj;
- Scavonetto, Federica;
- Yeoh, Tze Yeng;
- Kramer, Jessica M.;
- Karnes, R. Jeffrey;
- Eisenach, John H.;
- Schroeder, Darrell R.;
- Weingarten, Toby N.

Anesthesia & Analgesia. 119(4):859-866, October 2014.

小兒應用硝普鈉進行控制性降壓的預測因素

(王雪 譯，李士通 審校)

Predictors of Arterial Blood Pressure Control During Deliberate Hypotension with Sodium Nitroprusside in Children

- Spielberg, David R.;
- Barrett, Jeffrey S.;
- Hammer, Gregory B.;
- Drover, David R.;
- Reece, Tammy;
- Cohane, Carol A.;
- Schulman, Scott R.

Anesthesia & Analgesia. 119(4):867-874, October 2014.

最佳的鼻咽溫度探頭位置

(殷文 譯 陳傑 校)

Optimal Nasopharyngeal Temperature Probe Placement

- Lee, Jeongwoo;
- Lim, Hyungsun;
- Son, Kyung-geun;
- Ko, Seonghoon

Anesthesia & Analgesia. 119(4):875-879, October 2014.

Critical Care, Trauma, and Resuscitation

Research Report

利用床旁檢測和流式細胞術評估骨髓衰竭病人插入中心靜脈導管前預先輸注血小板的效果和持續時間

(呂越昌譯 薛張綱校)

The Effect and Duration of Prophylactic Platelet Transfusions Before Insertion of a Central Venous Catheter in Patients with Bone Marrow Failure Evaluated with Point-of-Care Methods and Flow Cytometry

- Kander, Thomas;
- Tanaka, Kenichi A.;
- Norström, Eva;
- Persson, Johan;
- Schött, Ulf

Anesthesia & Analgesia. 119(4):882-890, October 2014.

術前使用他汀類藥物不能使高風險患者免受術後發生早期急性呼吸窘迫綜合征的回顧性佇列研究

(王慧娟 譯，李士通 審校)

Preoperative Statin Administration Does Not Protect Against Early Postoperative Acute Respiratory Distress Syndrome: A Retrospective Cohort Study

- Yadav, Hemang;
- Lingineni, Ravi K.;
- Slivinski, Ericka J.;
- Stockler, Katie A.;
- Subramanian, Arun;
- Oderich, Gustavo S.;
- Wigle, Dennis A.;
- Carter, Rickey E.;
- Kor, Daryl J.

Anesthesia & Analgesia. 119(4):891-898, October 2014.

Obstetric Anesthesiology

Research Report

血清孕酮濃度與麻醉鎮痛需求的關係：一個關於接受剖宮產分娩產婦的前瞻性觀察研究

(李慧 譯 陳傑 校)

The Relationship Between Serum Progesterone Concentration and Anesthetic and Analgesic Requirements: A Prospective Observational Study of Parturients Undergoing Cesarean Delivery

- Lee, Jeongwoo;
- Lee, Junho;
- Ko, Seonghoon

Anesthesia & Analgesia. 119(4):901-905, October 2014.

美國大學附屬醫院產科麻醉產後出血預案使用情況的研究

(杜芳譯 薛張綱校)

The Use of Postpartum Hemorrhage Protocols in United States Academic Obstetric Anesthesia Units

- Kacmar, Rachel M.;
- Mhyre, Jill M.;
- Scavone, Barbara M.;
- Fuller, Andrea J.;
- Toledo, Paloma

Anesthesia & Analgesia. 119(4):906-910, October 2014.

麻醉併發症成爲分娩患者的安全指標

(王慧娟 譯，李士通 審校)

Anesthesia Complications as a Childbirth Patient Safety Indicator

- El Haj Ibrahim, Samia;
- Fridman, Moshe;
- Korst, Lisa M.;
- Gregory, Kimberly D.

Anesthesia & Analgesia. 119(4):911-917, October 2014.

Pediatric Anesthesiology

Research Report

在兒科圍術期患者中無創血紅蛋白監測的趨勢和準確性

(林雨軒 譯 陳傑 校)

Trending and Accuracy of Noninvasive Hemoglobin Monitoring in Pediatric Perioperative Patients

- Patino, Mario;
- Schultz, Lindsay;
- Hossain, Monir;
- Moeller, Jennifer;
- Mahmoud, Mohamed;
- Gunter, Joel;
- Kurth, C. Dean

Anesthesia & Analgesia. 119(4):920-925, October 2014.

兒科病人使用高/低新鮮氣體流量以及是否使用熱濕交換器對 **dräger Primus** 麻醉工作站濕度的影響

(江凌慧譯 薛張綱校)

The Humidity in a Dräger Primus Anesthesia Workstation Using Low or High Fresh Gas Flow and With or Without a Heat and Moisture Exchanger in Pediatric Patients

- Bicalho, Gustavo P.;
- Braz, Leandro G.;
- de Jesus, Larissa S. B.;
- Pedigone, Cesar M. C.;
- de Carvalho, Lídia R.;
- Módolo, Norma S. P.;
- Braz, José R. C.

Anesthesia & Analgesia. 119(4):926-931, October 2014.

QT 延長綜合征患兒使用現代麻醉的安全性

(張秋麗 譯，李士通 審校)

The Safety of Modern Anesthesia for Children with Long QT Syndrome

- Whyte, Simon D.;
- Nathan, Aruna;
- Myers, Dorothy;
- Watkins, Scott C.;
- Kannankeril, Prince J.;
- Etheridge, Susan P.;
- Andrade, Jason;
- Collins, Kathryn K.;

- Law, Ian H.;
- Hayes, Jason;
- Sanatani, Shubhayan

Anesthesia & Analgesia. 119(4):932-938, October 2014.

Neuroscience in Anesthesiology and Perioperative Medicine

Research Report

麻醉預處理抑制異氟烷介導的發育中大鼠大腦的細胞凋亡

(王筱婧 譯 陳傑 校)

Anesthetic Preconditioning Inhibits Isoflurane-Mediated Apoptosis in the Developing Rat Brain

- Peng, Jun;
- Drobish, Julie K.;
- Liang, Ge;
- Wu, Zhen;
- Liu, Chunxia;
- Joseph, Donald J.;
- Abdou, Hossam;
- Eckenhoff, Maryellen F.;
- Wei, Huafeng

Anesthesia & Analgesia. 119(4):939-946, October 2014.

血清抗膽鹼能活性與老年患者術後認知功能障礙的關係

(蓋曉冬譯 薛張綱校)

Serum Anticholinergic Activity and Postoperative Cognitive Dysfunction in Elderly Patients

- Rossi, Ariane;
- Burkhart, Christoph;
- Dell-Kuster, Salome;
- Pollock, Bruce G.;
- Strebel, Stephan P.;
- Monsch, Andreas U.;
- Kern, Christian;
- Steiner, Luzius A.

Anesthesia & Analgesia. 119(4):947-955, October 2014.

General Article

Research Report

人體滲透壓和呼吸調節：健康志願受試者輸注高張生理鹽水後機體高氯血代謝性酸中毒的呼吸代償往往是缺失的

(張秋麗 譯，李士通 審校)

Osmolality and Respiratory Regulation in Humans: Respiratory Compensation for Hyperchloremic Metabolic Acidosis Is Absent After Infusion of Hypertonic Saline in Healthy Volunteers

- Moen, Vibeke;
- Brudin, Lars;
- Rundgren, Mats;
- Irestedt, Lars

Anesthesia & Analgesia. 119(4):956-964, October 2014.

Pain Medicine

Research Report

硬膜外給予阿片類藥物行術後鎮痛效果最好且副作用最少：一項隨機對照試驗的 **meta** 分析

(張帆 譯 陳傑 校)

What Epidural Opioid Results in the Best Analgesia Outcomes and Fewest Side Effects After Surgery?: A Meta-Analysis of Randomized Controlled Trials

- Youssef, Nayer;
- Orlov, David;
- Alie, Tristan;
- Chong, Matthew;
- Cheng, Ji;
- Thabane, Lehana;
- Paul, James

Anesthesia & Analgesia. 119(4):965-977, October 2014.

Pain and Analgesic Mechanisms

Research Report

糖原合酶激酶-3β 抑制劑通過調節 AMPA 受體的表達和功能來抑制瑞芬太尼誘導的術後痛覺過敏

(郝光偉譯 薛張綱校)

Glycogen Synthase Kinase-3β Inhibition Prevents Remifentanil-Induced Postoperative Hyperalgesia via Regulating the Expression and Function of AMPA Receptors

- Li, Yi-ze;
- Tang, Xiao-hong;
- Wang, Chun-yan;
- Hu, Nan;
- Xie, Ke-liang;
- Wang, Hai-yun;
- Yu, Yong-hao;
- Wang, Guo-lin

Anesthesia & Analgesia. 119(4):978-987, October 2014.

甘氨酸轉運體抑制劑可減輕癌痛

(陳淩君 譯，李士通 審校)

Relief of Cancer Pain by Glycine Transporter Inhibitors

- Motoyama, Naoyo;
- Morita, Katsuya;
- Shiraishi, Seiji;
- Kitayama, Tomoya;
- Kanematsu, Takashi;
- Uezono, Yasuhito;
- Dohi, Toshihiro

Anesthesia & Analgesia. 119(4):988-995, October 2014.

Regional Anesthesia

Brief Report

全髖關節置換術中局部浸潤鎮痛後羅哌卡因的藥代動力學

(隋永恆 譯 陳傑 校)

Ropivacaine Pharmacokinetics After Local Infiltration Analgesia in Hip Arthroplasty

- Affas, Fatin;

- Eksborg, Staffan;
- Wretenberg, Per;
- Olofsson, Christina;
- Stiller, Carl-Olav

Anesthesia & Analgesia. 119(4):996-999, October 2014.

聚焦：旨在促進心血管手術室品質和安全性的心血管麻醉醫生協會倡議

FOCUS: The Society of Cardiovascular Anesthesiologists' Initiative to Improve Quality and Safety in the Cardiovascular Operating Room

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Anesthesia & Analgesia 2014 119 777–783

爲了尋找一種促進心血管外科手術室(CVOR)的品質和安全性的嚴格科學方法，心血管麻醉醫師協會(SCA)首次於 2005 年提出倡議：心血管手術完美標準化系統。本專案由 SCA 基金贊助，主要目的在於區分危害以及發展基於證據的臨床決策以提高心臟手術的安全性。危害是指任何可能導致潛在的可預防性的不良事件。聚焦策略性計畫具體包括以下三個目標：(1) 確認 CVOR 中存在的危害；(2) 危害分級並發展降低風險的手術；(3) 推廣此類手術。總之，此項倡議，通過各學科人員的配合，包括臨床醫學、人因工程、心理學以及組織社會學等，已經區分和記錄了每天發生在 CVOR 內顯而易見的危害。一些比較常見的可以降低心臟手術安全性和品質的例子包括工作團隊內人員不足，手術室設計缺陷，技術不足以及未能遵守最佳操作。目前有數項計畫致力於更好地理解這些危害以及研究緩解措施。通過倡議，SCA 開啓了科學引導品質和安全性改進之旅。然而，這是一條漫長且充滿艱辛的必然道路。

（俞芳 譯 陳傑 校）

The Society of Cardiovascular Anesthesiologists (SCA) introduced the FOCUS initiative (Flawless Operative Cardiovascular Unified Systems) in 2005 in response to the need for a rigorous scientific approach to improve quality and safety in the cardiovascular operating room (CVOR). The goal of the project, which is supported by the SCA Foundation, is to identify hazards and develop evidence-based protocols to improve cardiac surgery safety. A hazard is anything that has the potential to cause a preventable adverse event. Specifically, the strategic plan of FOCUS includes 3 goals: (1) identifying hazards in the CVOR, (2) prioritizing hazards and developing risk-reduction interventions, and (3) disseminating these interventions. Collectively, the FOCUS initiative, through the work of several groups composed of members from different disciplines such as clinical medicine, human factors engineering, industrial psychology, and organizational sociology, has identified and documented significant hazards occurring daily in our CVORs. Some examples of frequent occurrences that contribute to reduce the safety and quality of care provided to cardiac surgery patients include deficiencies in teamwork, poor OR design, incompatible technologies, and failure to adhere to best practices. Several projects are currently under way that are aimed at better understanding these hazards and developing interventions to mitigate them. The SCA, through the FOCUS initiative, has begun this journey of science-driven improvement in quality and safety. There is a long and arduous road ahead, but one we need to continue to travel.

肺切除術期間靜脈注射利多卡因降低豬局部和全身腫瘤壞死因數 α 的表達

Intravenous Lidocaine Decreases Tumor Necrosis Factor Alpha Expression Both Locally and Systemically in Pigs Undergoing Lung Resection Surgery

Garutti, Ignacio PhD, MD*; Rancan, Lisa DVM†; Simón, Carlos PhD, MD‡; Cusati, Gabriel MD*; Sanchez-Pedrosa, Guillermo MD*; Moraga, Francisco MD*; Olmedilla, Luis PhD, MD*; Lopez-Gil, Maria Teresa PhD, MD*; Vara, Elena PhD, MD†

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背景：肺切除手術與炎症反應相關。單肺通氣（OLV）的使用似乎增加該反應的可能性。已經對不同的預防和治療措施進行了研究以防止 OLV 繼發性肺損傷。利多卡因是常用的局部麻醉藥物，具有抗炎活性。本研究的主要目的是探討在肺切除手術 OLV 期間，靜脈注射利多卡因對肺腫瘤壞死因數（TNF-α）表達的影響。

方法：十八隻豬行左肺尾葉切除術。動物隨機分爲 3 組：對照組，利多卡因組和假手術組。所有動物接受全身麻醉。利多卡因組動物在手術過程中持續靜脈輸注利多卡因（1.5 mg/kg/h）。假手術組動物只行開胸手術。OLV 開始前、結束時、手術結束時和手術後 24h 收集支氣管肺泡灌洗（BAL）液和血漿樣品。術前從左尾葉（基線），以及術後 24h 從縱隔葉和左上葉採集肺活檢標本。樣品速凍並存儲用於檢測以下炎症標誌物水準：白細胞介素（IL）-1β，IL-2，IL-10，TNF-α，核因數 κB，單核細胞趨化蛋白-1，誘導型一氧化氮合酶，內皮型一氧化氮合酶。同時檢測細胞凋亡標誌物（caspase-3，caspase-9，Bad，Bax 和 Bcl-2，）。此外，在 BAL 液和血漿樣品中確定基質金屬蛋白酶與一氧化氮代謝物水準。非參數檢驗用來檢驗統計意義。

結果：OLV 引起肺損傷伴隨 BAL、血漿和肺樣本中 TNF-α 的表達增加。其他炎症（IL-1β，核因數 κB，單核細胞趨化蛋白-1）和凋亡（caspase-3，caspase-9 和 Bax）標記物也增加。靜脈注射利多卡因使同一樣品 TNF-α 水準與對照組相比顯著降低。利多卡因也減少在對照組中觀察到的炎症和細胞凋亡的變化。血流動力學、血氣和氣道壓力在所有組中相似。

結論：本研究結果表明，利多卡因可以通過減輕促炎細胞因數和肺細胞凋亡的表達來預防 OLV 引起的肺損傷。利多卡因可能有助於防止 OLV 肺外科手術引起的肺損傷。

（徐歡 譯 陳傑 校）

BACKGROUND: Lung resection surgery is associated with an inflammatory reaction. The use of 1-lung ventilation (OLV) seems to increase the likelihood of this reaction. Different prophylactic and therapeutic measures have been investigated to prevent lung injury secondary to OLV. Lidocaine, a commonly used local anesthetic drug, has antiinflammatory activity. Our main goal in this study was to investigate the effect of IV lidocaine on tumor necrosis factor 僞 (TNF-僞) lung expression during lung resection surgery with OLV.

METHODS: Eighteen pigs underwent left caudal lobectomy. The animals were divided into 3 groups: control, lidocaine, and sham. All animals received general anesthesia. In addition, animals in the lidocaine group received a continuous IV infusion of lidocaine during surgery (1.5 mg/kg/h). Animals in the sham group only underwent thoracotomy. Samples of bronchoalveolar lavage (BAL) fluid and plasma were collected before initiation of OLV, at the end of OLV, at the end of surgery, and 24 hours after surgery. Lung biopsy specimens were collected from the left caudal lobe (baseline) before surgery and from the mediastinal lobe and the left cranial lobe 24 hours after surgery. Samples were flash-frozen and stored to measure levels of the following inflammatory markers: interleukin (IL) 1 尾, IL-2, IL-10, TNF-僞, nuclear factor 魏 B, monocyte chemoattractant protein-1, inducible nitric oxide synthase, and endothelial nitric oxide synthase. Markers of apoptosis (caspase 3, caspase 9, Bad, Bax, and Bcl-2) were also measured. In addition, levels of metalloproteinases and nitric oxide metabolites were determined in BAL fluid and in plasma samples. A nonparametric test was used to examine statistical significance.

RESULTS: OLV caused lung damage with increased TNF-僞 expression in BAL, plasma, and lung samples. Other inflammatory (IL-1 尾, nuclear factor 魏 B, monocyte chemoattractant protein-1) and apoptosis (caspase 3, caspase 9, and BAX) markers were also increased. With the use of IV lidocaine there was a significant decrease in the levels of TNF-僞 in the same samples compared with the control group. Lidocaine administration also reduced the inflammatory and apoptotic changes observed in the control group. Hemodynamic values, blood gas values, and airway pressure were similar in all groups.

CONCLUSIONS: Our results suggest that lidocaine can prevent OLV-induced lung injury through reduced expression of proinflammatory cytokines and lung apoptosis. Administration of lidocaine may help to prevent lung injury during lung surgery with OLV.

評估鎮靜過程中風險的一項新型低氧血症指標

A Novel Index of Hypoxemia for Assessment of Risk During Procedural Sedation

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Anesthesia & Analgesia 2014 119 875–879

背景：操作鎮靜方法在多項操作中必不可少。鎮靜在安全性方面有優勢，但是並非全無風險。因其罕有發生，故在臨床研究中使用臨床預後來評估風險較爲困難。因此，替代終點常代替臨床結果而用於臨床研究。由於一個臨床醫師通過整合一項生理參數的多個方面來決定潛在風險，替代終點應該採取類似方法。本研究確認並檢測了一種可能用於臨床研究的新型替代終點的可行性，即氧飽和度曲線下面積(AUCDesat)。引入一篇麻醉醫師記錄的患者鎮靜綜述，旨在評價替代終點與麻醉風險理解的關聯性。

方法：本研究爲一項對麻醉醫師感知風險進行評估的析因分析。由 13 位經美國訓練並通過職業認證的麻醉醫師將生理參數進行分級作爲風險指標，然後從 SEDASYS 系統中 3 組完整的鎮靜研究中回顧分析了 204 個病例。回顧分析後，每位麻醉醫師基於過度鎮靜相關後遺症的風險認知對每個病例給予 likert 評分。後者經分析後決定其與去飽和事件的發生/未發生、持續、深度、數量和涉及每個組成的 AUCDesat 的關係。

結果：麻醉醫師們將動脈血氧列爲事後評估風險的最重要因素（平均秩次 4.69/5，P=0.0007 與次高歸因指數—呼吸頻率 比較，N=13）。與 AUCDesat 獨立因素、去氧飽和度二元分析（rs=0.73）、去氧飽和深度（rs=-0.70）、去氧飽和持續時間（rs=0.70）和去氧飽和發生率（rs=0.55）比較，AUCDesat 與 Likert 評分相關性更好（rs=0.85） (4 項比較 rs=0.85，P<0.0001)。

結論：麻醉醫師確認動脈血氧飽和度爲評估鎮靜風險和潛在不良臨床預後的最重要的生理參數。AUCDesat 是一項由去氧飽和度持續時間、發生率和深度整合的複合指標，與 Likert 評分有更好的相關性。AUCDesat 給出的僅是一個數值變數，在臨床鎮靜研究中對不良預後風險評估方面是一個理想的終點指標。需要 AUCDesat 和真實生理預後相關的進一步研究來定義這項終點指標。

（ 潘志敏 譯 陳傑 校）

BACKGROUND: Procedural sedation is essential for many procedures. Sedation has an excellent safety profile; however, it is not without risks. Assessment of risk using clinical outcomes in clinical studies is difficult due to their rare occurrence. Therefore, surrogate end points are frequently used in a clinical study in lieu of clinical outcomes. As a clinician integrates multiple aspects of a physiological variable to determine potential risk, a surrogate end point should consider a similar approach. In this study, we identified and tested the appropriateness of a new surrogate end point that may be used in clinical studies, area under the curve of oxygen

desaturation (AUCDesat). A review of patient sedation records by anesthesiologists was conducted to assess its relationship to the anesthesia professional perception of risk.

METHODS: This study was a post hoc analysis and assessment of perceived risk by anesthesiologists. It consisted of 13 U.S.-trained board-certified anesthesiologists ranking physiological variables as indicators of risk and then reviewing 204 records from 3 completed sedation studies involving the SEDASYS® System. After review, each anesthesiologist assigned a Likert score based on his or her perception of risk for oversedation-related sequelae in each record. These scores were analyzed to determine their relationship to desaturation presence/absence, duration, depth, number of events, and AUCDesat that incorporates each component.

RESULTS: Anesthesiologists ranked arterial oxygenation to be the most important factor in assessing risk post hoc (mean rank of 4.69 of 5, P = 0.0007 compared with next highest ranked factor—respiratory rate, N = 13). AUCDesat was better correlated to the Likert scores (rs = 0.85) when compared with the individual elements of AUCDesat, binary assessment of desaturation (rs = 0.73), desaturation depth (rs = −0.70), desaturation duration (rs = 0.70), and incidence of desaturations (rs = 0.55) (all 4 comparisons versus rs = 0.85, P < 0.0001).

CONCLUSIONS: Anesthesiologists determined arterial oxygenation to be the most important physiological variable in assessing sedation risk and the potential for adverse clinical outcomes. AUCDesat, a composite index that incorporates duration, incidence, and depth of oxygen desaturation, was better correlated to the Likert scores. AUCDesat, given that it is a single numerical variable, is an ideal end point for assessment of risk of adverse clinical outcomes in clinical sedation studies. Future studies using AUCDesat and actual physiological outcomes may be useful in further defining this end point.

最佳的鼻咽溫度探頭位置

Optimal Nasopharyngeal Temperature Probe Placement

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背景：鼻咽部是全麻手術期間最常用來監測體溫的部位，但並不清楚麻醉醫生盲目放置鼻咽溫度探頭的位置是否恰當，本文研究目的爲 1）探究鼻咽粘膜最接近頸內動脈(ICA)的位置，（2）評估麻醉住院醫生和麻醉護士擺放鼻咽溫度探頭的尖端位置。

方法：研究第一階段回顧了 100 名患者的增強軸向 CT 圖像來確定鼻咽粘膜最接近左或右頸內動脈的位置，隨後在矢狀位元圖像上測量此點至鼻孔的距離。研究第二階段用鼻內窺鏡評估由麻醉住院醫生（224 名患者）或麻醉護士（116 名患者）放置的鼻咽溫度探頭位置。位置不佳時將探頭重新定位到最佳的位置，並記錄兩者的溫度差異。

結果：CT 圖像顯示，分別有 60%，38%及 2%的患者，其粘膜最接近頸內動脈的最佳位置在鼻咽部的上部，中部及下部。頸內動脈和上部鼻咽部粘膜的平均距離較與下部之間的要更短（女：9.4 vs 16.8 mm，p<0.001；男：12.4 vs 18.8 mm，p<0.001）。通過下鼻道從鼻孔至鼻咽部上部的平均距離（95%預測區間）女性爲 9.1（8.1-10.2）cm，男性爲 9.7（8.6-10.3）cm。由住院醫師和護士正確地將溫度探頭放置在鼻咽部上部或中部的概率分別爲 43%（95%的可信區間，37%-49%）和 41%（95%的可信區間，36%-50%）。當溫度探頭在鼻腔位置不佳時，測得鼻咽部上部的體溫中位數差異（95%CI）爲 0.2℃（0.15℃—0.25℃）。

結論：鼻咽粘膜最接近頸內動脈的位置爲鼻咽腔上部或中部，鼻孔到鼻咽部上 1/3 的深度大致爲 10cm，醫生盲目地放置鼻咽部溫探頭，其最佳位置的放置率低於 50%。

（殷文 譯 陳傑 校）

BACKGROUND: Although the nasopharynx is a commonly used temperature-monitoring site during general anesthesia, it is unknown whether the position of nasopharyngeal temperature probes placed blindly by anesthesia practitioners is optimal. The purposes of this study were (1) to determine where the nasopharyngeal mucosa is in closest proximity to the internal carotid artery (ICA) and (2) to evaluate the tip position of nasopharyngeal temperature probes that were placed by anesthesiology residents and nurse anesthetists.

METHODS: In the first phase of the study, we reviewed enhanced axial computed tomography images of 100 patients to determine where the nasopharyngeal mucosa was in closest proximity to the left or the right ICA. The distance from this point to the nares was then measured in the sagittal image. In the second phase of the study, nasendoscopy was used to evaluate the positioning of nasopharyngeal temperature probes placed by anesthesiology residents (244 patients) or nurse anesthetists (116 patients). Malpositioned probes were repositioned to an optimal location, and the temperature differences were recorded.

RESULTS: In the computed tomography images, the mucosa in closest proximity to the ICA was in the upper, mid-, and lower nasopharynx in 60%, 38%, and 2% of patients, respectively. The average distances between the ICA and the nasopharyngeal mucosa in the upper portion were significantly shorter than those in the lower portion (female: 9.4 vs 16.8 mm, $P < 0.001$; male: 12.4 vs 18.8 mm, $P < 0.001$). The average distances (95% prediction interval) from the nares to the upper portion of the nasopharynx through the inferior meatus were 9.1 (8.1–10.2) cm in females and 9.7 (8.6–10.8) cm in males. Temperature probes were correctly positioned in the upper or mid-nasopharynx by residents and nurses in 43% (95% confidence interval [CI], 37%–49%) and 41% (95% CI, 36%–50%), respectively. When the probe was inadvertently placed in the nasal cavity, the median (95% CI) temperature difference from the upper nasopharynx was 0.2℃ (0.15℃–0.25℃).

CONCLUSIONS: The closest portion of the nasopharyngeal mucosa to the ICA is within the upper or mid-nasopharynx. The depth from the nares to the upper one-third of the nasopharynx is approximately 10 cm. Less than half of nasopharyngeal temperature probes placed blindly by practitioners were optimally positioned.

血清孕酮濃度與麻醉鎮痛需求的關係：一個關於接受剖宮產分娩產婦的前瞻性觀察研究

The Relationship Between Serum Progesterone Concentration and Anesthetic and Analgesic Requirements: A Prospective Observational Study of Parturients Undergoing Cesarean Delivery

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背景：在臨床實踐中，孕婦相比非妊娠婦女接受全麻時有著更低的麻醉藥物需求。雖然激素變化，如與妊娠相關的孕激素可能影響吸入麻醉藥的最小肺泡濃度，麻醉或鎮痛需求和足月婦女孕激素水準的相關性還未被研究。這項研究試圖確定麻醉或鎮痛需求和母體孕酮血藥濃度的關係。

方法：研究了 100 例孕齡大於 36 周，擇期行全麻下剖腹產的孕婦。採集靜脈血測定孕婦孕激素濃度。使用硫噴妥鈉 4-5 mg/kg 和羅庫溴銨 0.8 mg/kg 行麻醉誘導。麻醉維持期間，以動脈血壓，心率，和腦電雙頻指數爲基礎，吸入 0.5%-2%七氟醚、50%氧化亞氮維持麻醉。記錄生命體征、腦電雙頻指數、呼氣末七氟醚濃度和每小時七氟醚用量。同時記錄術後第 2h、第 24h 和第 48h 疼痛視覺類比評分和累積鎮痛藥物用量。

結果：平均血清孕酮濃度爲 128.2±83 ng/mL。每小時七氟醚用量與血清孕酮濃度與之間存在顯著的負相關（Pearson 相關係數 r＝−0.26；95%置信區間，0.44 到−−0.05，P = 0.01）。累計鎮痛藥物用量在術後第 2 小時（R =−0.20，P = 0.05），第 24 小時（R =−0.25，P = 0.02），和第 48 小時（R =−0.28，P = 0.01）與血清孕酮濃度呈負相關。高孕酮水準婦女（高於中位數值）相對於低孕酮水準婦女（低於中位數值），每小時七氟醚用量（P = 0.02）和術後 48 小時累積鎮痛藥物用量（P = 0.02）更少。

結論: 近足月產婦對麻醉和鎮痛藥物需求降低可能部分取決於血清孕酮濃度。

（李慧 譯 陳傑 校）

BACKGROUND: In clinical practice, pregnant women have lower anesthetic requirements for general anesthesia than nonpregnant women. Although the hormonal changes such as progesterone associated with pregnancy may affect the minimum alveolar concentration of volatile anesthetics, the relationship between the anesthetic or analgesic requirements and progesterone level in full-term women has not been studied. In this study, we attempted to identify relationships between anesthetic or analgesic requirements and maternal serum concentrations of progesterone.

METHODS: We studied 100 parturients >36 weeks' gestation who were scheduled for planned cesarean delivery under general anesthesia. Venous blood was collected to measure the maternal progesterone concentration. Anesthesia was induced with 4 to 5 mg/kg thiopental and 0.8 mg/kg rocuronium. During anesthetic maintenance, sevoflurane 0.5% to 2.0% and nitrous oxide 50% in oxygen were titrated based on arterial blood pressure, heart rate, and bispectral index value. Vital signs, bispectral index, end-tidal sevoflurane concentration, and sevoflurane consumption per hour were recorded. Visual analog scale pain scores and cumulative analgesic consumption were recorded at 2, 24, and 48 hours postoperatively.

RESULTS: The mean serum progesterone concentration was 128.2 ± 83.0 ng/mL. There was a significant negative correlation between sevoflurane consumption per hour and serum progesterone concentration (Pearson correlation r = −0.26; 95% confidence interval, −0.44 to −0.05, P = 0.01). Cumulative analgesic consumption at postoperative hours 2 (r = −0.20, P = 0.05), 24 (r = −0.25, P = 0.02), and 48 (r = −0.28, P = 0.01) were correlated inversely with serum progesterone concentration. Women with high progesterone levels (higher than the median value) had lower sevoflurane consumption per hour (P = 0.02) and 48-hour postoperative cumulative analgesic consumption (P = 0.02) than women with low (below the median value) levels.

CONCLUSIONS: The decreased anesthetic and analgesic requirements of near full-term parturients might partially depend on serum progesterone concentration.

在兒科圍術期患者中無創血紅蛋白監測的趨勢和準確性

Trending and Accuracy of Noninvasive Hemoglobin Monitoring in Pediatric Perioperative Patients

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背景： Rainbow Pulse CO-Oximetry 技術® (Masimo Corporation, Irvine, CA)提供了對動脈血紅蛋白濃度的連續無創監測方法（SpHb）。在接受可能大量失血手術的兒童中，對比由該創新監測儀得到的 SpHb 與普通實驗室得到的血紅蛋白濃度（Hb）來評估該設備的趨勢和準確性。

方法：Hb 濃度分別由 Pulse CO-Oximetry 和傳統血紅蛋白分析儀記錄。使用回歸分析和四象限散點圖來評估 SpHb 和 Hb 測定值的變化趨勢（ΔSpHb 和 ΔHb）。計算 SpHb 的偏

倚、精度和 SpHb 的協議範圍以及與 Hb 對比體內校正 SpHb（SpHb-首次偏倚相對 Hb）的協議範圍。

結果：收集來自於 46 名年齡在 2 個月至 17 歲，血紅蛋白濃度在 16.7g/dL 至 7.9g/dL 之間的患兒形成 158 組 SpHb-Hb 資料對和 105 個變化對（ΔSpHb 和 ΔHb）。爲了評估趨勢，變化（ΔSpHb 和 ΔHb）擬合成曲線後，顯示出這兩者呈正相關（ΔSpHb = 0.022 + 0.76ΔHb），相關係數 r = 0.76，95%CI（置信區間） = 0.57–0.86。相對 Hb 的 SpHb 和體內校正後的 SpHb，其偏倚和精度分別爲 0.4 ± 1.3 g/dL 和 0.1 ± 1.2 g/dL。在校正前後的協議範圍分別爲−2.0 至 3.2 g/dL、−2.4 to 2.2 g/dL（P 值 = 0.04）。平均偏倚百分比（從參考 Hb 濃度）從 4.1% ± 11.9%下降至 0.7% ± 11.3% (P 值 = 0.01)。在研究過程中發現偏差值不隨時間飄移。在測試 SpHb 相關的患兒人口學和生理因素中，只有探頭區域的灌注指數與 SpHb 有微弱的相關。

結論：在正常血紅蛋白和輕度貧血的兒童中，SpHb 的準確性與之前在成人中的報導相似，且除僅與灌注指數有微弱關係，其餘與患兒的人口學和生理狀態無關。在正常血紅蛋白濃度和輕度貧血的兒童中，SpHb 和 Hb 的趨勢呈正相關。但在中重度貧血兒童中仍需更多研究。

（林雨軒 譯 陳傑 校）

BACKGROUND: Rainbow Pulse CO-Oximetry technology® (Masimo Corporation, Irvine, CA) provides continuous and noninvasive measurement of arterial hemoglobin concentration (SpHb). We assessed the trending and accuracy of SpHb by this innovative monitoring compared with Hb concentration obtained with conventional laboratory techniques (Hb) in children undergoing surgical procedures with potential for substantial blood loss.

METHODS: Hb concentrations were recorded from Pulse CO-Oximetry and a conventional hematology analyzer. Regression analysis and 4-quadrant plot were used to evaluate the trending for changes in SpHb and Hb measurements (ΔSpHb and ΔHb). Bias, precision, and limits of agreement of SpHb and of in vivo adjusted SpHb (SpHb − first bias to HB) compared with Hb were calculated.

RESULTS: One hundred fifty-eight SpHb–Hb data pairs and 105 delta pairs (ΔSpHb and ΔHb) from 46 patients aged 2 months to 17 years with Hb ranging from 16.7 to 7.9 g/dL were collected. To evaluate trending, the delta pairs (ΔSpHb and ΔHb) were plotted, which revealed a positive correlation (ΔSpHb = 0.022 + 0.76ΔHb) with correlation coefficient r = 0.76, 95% CI [confidence interval] = 0.57–0.86. The bias and precision of SpHb to Hb and in vivo adjusted SpHb were 0.4 ± 1.3 g/dL and 0.1 ± 1.2 g/dL, respectively; the limits of agreement were −2.0 to 3.2 g/dL before in vivo adjustment and −2.4 to 2.2 g/dL after in vivo adjustment (P value = 0.04). The mean percent bias (from the reference Hb concentration) decreased from 4.1% ± 11.9% to 0.7% ± 11.3% (P value = 0.01). No drift in bias over time was observed during the study procedure. Of patient demographic and physiological factors tested for correlation with the SpHb, only perfusion index at sensor site showed a weak correlation.

CONCLUSIONS: The accuracy of SpHb in children with normal Hb and mild anemia is similar to that previously reported in adults and is independent of patient demographic and physiological states except for a weak correlation with perfusion index. The trending of SpHb and Hb in children with normal Hb and mild anemia showed a positive correlation. Further studies are necessary in children with moderate and severe anemia.

麻醉預處理抑制異氟烷介導的發育中大鼠大腦的細胞凋亡

Anesthetic Preconditioning Inhibits Isoflurane-Mediated Apoptosis in the Developing Rat Brain

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背景：正如之前所做的神經細胞培養試驗所示，本研究假設短時間暴露於異氟烷（ISO）的預處理（PC）會降低長期暴露於異氟烷的新生大鼠的神經性退化。

方法：將 7 日齡的 SD 大鼠隨機分爲 3 組：對照組，1.5% ISO 組及 PC+1.5% ISO 組。對照組暴露於載氣（30%氧氣平衡於氮氣中）中 30min，然後次日再次暴露於載氣中 6 小時；1.5% ISO 組暴露於載氣中 30min，然後次日暴露於 1.5% 異氟烷中 6 小時；PC+1.5% ISO 組暴露於 1.5% ISO 中 30min 進行預處理，然後次日暴露於 1.5% ISO 中 6 小時。在暴露 2 小時後收集血標本和腦組織標本以測定神經退行性生物標誌物，包括 caspase-3、S100β、caspase-12 以及自噬標誌物 Beclin-1.

結果：Western blot 試驗結果表明，與異氟烷預處理組及對照組相比，長時間暴露於異氟烷中能顯著增加 7 日齡大鼠大腦皮層中活化型 caspase-3 的表達。然而，並沒有檢測到其他神經元損傷的標誌物有顯著差異。

結論：異氟烷介導的 7 日齡大鼠腦中活化型 caspase-3 增加，可由短暫麻醉暴露預處理所改善，然而其他神經元損傷的標誌物並沒有檢測到差異。

（王筱婧 譯 陳傑 校）

BACKGROUND: We hypothesized that preconditioning (PC) with a short exposure to isoflurane (ISO) would reduce neurodegeneration induced by prolonged exposure to ISO in neonatal rats, as previously shown in neuronal cell culture.

METHODS: We randomly divided 7-day-old Sprague-Dawley rats into 3 groups: control, 1.5% ISO, and PC + 1.5% ISO. The control group was exposed to carrier gas (30% oxygen balanced in nitrogen) for 30 minutes and then to carrier gas again for 6 hours the following day. The 1.5% ISO group was exposed to carrier gas for 30 minutes and then to 1.5% ISO for 6 hours the following day. The PC + 1.5% ISO group was preconditioned with a 30-minute 1.5% ISO exposure and then exposed to 1.5% ISO for 6 hours the following day. Blood and brain samples were collected 2 hours after the exposures for determination of neurodegenerative biomarkers, including caspase-3, S100, caspase-12, and an autophagy biomarker Beclin-1.

RESULTS: Prolonged exposure to ISO significantly increased cleaved caspase-3 expression in the cerebral cortex of 7-day-old rats compared with the group preconditioned with ISO and the controls using Western blot assays. However, significant differences were not detected for other markers of neuronal injury.

CONCLUSIONS: The ISO-mediated increase in cleaved caspase-3 in the postnatal day 7 rat brain is ameliorated by PC with a brief anesthetic exposure, and differences were not detected in other markers of neuronal injury.

硬膜外給予阿片類藥物行術後鎮痛效果最好且副作用最少：一項隨機對照試驗的 meta 分析

What Epidural Opioid Results in the Best Analgesia Outcomes and Fewest Side Effects After Surgery?: A Meta-Analysis of Randomized Controlled Trials

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背景：硬膜外阿片類藥物被廣泛用於椎管神經阻滯和術後鎮痛。然而,阿片類藥物的鎮痛療效和副作用的個體差異仍有爭議。

方法：此項隨機對照試驗的 meta 分析，比較至少 2 種急性術後連續硬膜外輸注鎮痛方式至少 24 小時以上。個體研究資料使用反向方差法加權。主要結果爲疼痛視覺類比評分量表(VAS)評分。次要結果包括阿片類藥物的副作用，如瘙癢、術後噁心嘔吐(PONV)、鎮靜、低血壓和呼吸抑制。

結果：24 項試驗中有 19 項包含比較以下阿片類藥物中的兩種：嗎啡、芬太尼或舒芬太尼。研究物件共 1513 名。對手術類型進行彙集分析發現在術後任何時候 VAS 疼痛評分並無臨床顯著差異。與芬太尼相比，嗎啡術後 PONV(OR = 1.91，95%可信區間，1.14 - -3.18；P = 0.014)，瘙癢(OR = 1.64，95%可信區間，0.98 - -2.76；P = 0.162)發生率更高。阿片類藥物消耗總量僅在於嗎啡和芬太尼的比較研究中有差異，嗎啡組的患者藥物需要量減少 1.2mg（相當於嗎啡）(95% CI, 0.27–2.18)。除兩個研究外其餘試驗組使用輔助鎮痛劑相似。

結論：根據 VAS 疼痛評分，硬膜外阿片類藥物之間的鎮痛效果是相似的。這些鎮痛藥的相似之處可能反映了同時使用硬膜外局麻藥和阿片類藥物鎮痛的通常方法，根據患者的疼痛狀況確定注入速率。關於副作用方面，儘管這些組之間阿片類藥物消耗總量相似，嗎啡的 PONV 和瘙癢發生率可能比芬太尼更高。

（張帆 譯 陳傑 校）

BACKGROUND: Epidural opioids are widely used for central neuraxial blockade and postoperative analgesia. However, differences in analgesic efficacy and side effect rates among individual opioids remain controversial.

METHODS: We conducted a random-effects meta-analysis of randomized controlled trials that compared at least 2 continuous epidural infusions for acute postoperative analgesia over at least 24 hours. Individual study data were weighted by the inverse-variance method. Visual analog scale (VAS) pain scores were the primary outcome. Secondary outcomes included opioid side effects, such as pruritus, postoperative nausea and vomiting (PONV), sedation, hypotension, and respiratory depression.

RESULTS: Nineteen of the 24 trials included compared 2 of the following opioids: morphine, fentanyl, or sufentanil. The total subjects studied were 1513. Pooled analysis by type of surgery showed no clinically significant differences in VAS pain scores at any time after surgery. There were more PONV (OR = 1.91; 95% CI, 1.14–3.18; P = 0.014) and perhaps pruritus (OR = 1.64; 95% CI, 0.98–2.76; P = 0.162) with morphine compared to fentanyl. Total opioid consumption differed only in the trials comparing morphine and fentanyl, where patients in the morphine group required 1.2 mg (of morphine equivalent) less (95% CI, 0.27–2.18). Use of analgesic adjuncts was similar for all but 2 studies.

CONCLUSIONS: Analgesic outcome, in terms of VAS pain score, was similar between the epidural opioids studied. These similarities in analgesia may reflect the common practices of concurrently using epidural local anesthetics with the opioids and titrating infusion rates according to a patient's pain status. With respect to side effects, the incidence of PONV and possibly pruritus was higher with morphine compared with fentanyl, despite there being similar total opioid consumption between those groups.

全髖關節置換術中局部浸潤鎮痛後羅呱卡因的藥代動力學

Ropivacaine Pharmacokinetics After Local Infiltration Analgesia in Hip Arthroplasty

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本研究納入 15 名擇期行全髖關節置換手術的病人，在其局部浸潤鎮痛後 30 小時期間通過液相質譜法檢測血漿中羅呱卡因的濃度。羅呱卡因血漿濃度的 95%預測範圍的上界值爲 0.032mg/L。有報導顯示當副作用明顯需停止靜脈注射的羅呱卡因動脈血中濃度 0.34-0.85mg/L。在局部浸潤鎮痛的第一個 24 小時，α-1 酸性糖蛋白與未結合羅呱卡因部分沒有相關性。在本研究中未發現全身麻醉毒性的症狀或反應。出現不良反應的 Clopper-Pearson95%置信區間的上限爲 0.218。

（隋永恆 譯 陳傑 校）

In this study, we determined the plasma concentration of ropivacaine by liquid chromatography-mass spectrometry for 30 hours after local infiltration analgesia in 15 patients with elective hip arthroplasty. The 95% upper prediction bound of maximal unbound plasma concentration of ropivacaine was 0.032 mg/L. Side effects sufficient to stop an IV infusion have been reported at arterial concentrations of 0.34 to 0.85 mg/L. Alpha-1-acid glycoprotein did not correlate with the fraction of unbound ropivacaine during the first 24 hours after local infiltration analgesia. No signs or symptoms of systemic local anesthetic toxicity were observed. The Clopper-Pearson 95% upper confidence limit for adverse signs was 0.218.

吸入麻醉後的低通氣可發生再麻醉

Hypoventilation After Inhaled Anesthesia Results in Reanesthetization

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背景：自從吸入麻醉以來，發生低通氣的原因很多。在本研究中，我們研究了吸入麻醉在導致低通氣中發揮的作用以及再麻醉發生的機制。

方法：針對體重爲 70 公斤的模擬人，分別利用地氟醚，七氟醚和異氟醚行吸入麻醉，利用 Gas Man® 電腦類比系統監測麻醉氣體的攝取和排泄。對揮發罐進行設置和調整，從而使得吸入麻醉分佈容積豐富的組織（VRG）包括腦，麻醉深度能夠迅速達到 0.75 MAC（最低肺泡有效濃度），1.0 MAC 和 1.5 MAC，並可保持此麻醉深度 1，2，4，6 小時。在模擬吸入麻醉結束前，將揮發罐刻度調整爲 0，並且新鮮氣體流量設置爲 8L/min。肺泡通氣量（VA）保持爲 4L/min，直到 VRG 達到蘇醒麻醉深度，約爲 0.33 MAC。然後將 VA 調整爲近乎窒息流量 0.1 L/min 和窒息流量 0.0 L/min，並監測 VRG 麻醉深度，若達到 0.5 MAC 或者大於 0.5 MAC，判斷爲重度再麻醉；若 VRG 麻醉深度達到 0.33 MAC 並小於 0.5 MAC，判斷爲輕度再麻醉。此外 VRG 在麻醉深度達到 0.33 MAC 時，研究判何爲最低 VA 從而可防止重度再麻醉的發生。

結果：吸入麻醉 1h 後，所有模擬患者在達到 0.75 MAC 和 1.0 MAC 時均未發生輕度和重度再麻醉。吸入麻醉 4h 到 6h 後，不同麻醉氣體使模擬患者達到 1.0 MAC 和 1.5 MAC，並且在接近窒息和窒息 VA 時均發生重度再麻醉。利用最小肺泡 VA 可防止重度再麻醉發生，比如 6h 的 0.75 MAC 麻醉，VA 可小至 0.5 L/min；6h 的 1.0 MAC 麻醉，VA 可小至 0.5 L/min；6h 的 1.5 MAC 麻醉，VA 可小至 1.2 L/min。對於所有不同類型吸入麻醉的模擬患者，導致再麻醉的來源是肌肉組織，4h 吸入麻醉可達到 0.8 MAC，其中 2h 地氟烷吸入麻醉可達到 0.75 MAC。吸入麻醉 6h 後，脂肪組織麻醉深度小於 0.15 MAC.

結論：吸入麻醉後低通氣可能導致再麻醉。肌肉組織是麻醉和再麻醉氣體的儲存分佈部位，脂肪組織則亦是麻醉氣體的容器並可促使再麻醉的發生。不同麻醉氣體包括地氟醚，七氟醚和異氟醚，吸入麻醉 4h 達到 1.0 MAC 後，如果發生嚴重低通氣，則由於肌肉中麻醉氣體的釋放，導致不同程度的再麻醉。

（王嘉興譯 薛張綱校）

BACKGROUND: During emergence from volatile anesthesia, hypoventilation may result from many causes. In this study, we examined the effect of hypoventilation after initial emergence from volatile anesthesia and the potential for reanesthetization.

METHODS: The uptake and excretion of desflurane (Des), sevoflurane, and isoflurane were studied using the Gas Man® computer simulation program for a 70-kg simulated patient. The vaporizer setting was adjusted so that a VRG (vessel-rich tissue group, including brain) level of 0.75 minimum alveolar concentration (MAC), 1.0 MAC, and 1.5 MAC was rapidly achieved and maintained within tight limits for a 1-, 2-, 4-, and 6-hour period of anesthesia.

At the end of the simulated period of anesthesia, the vaporizer was set to 0 and fresh gas flow was set to 8 L/min. Ventilation (VA) was continued at 4 L/min until the anesthetic level in the VRG reached MAC awake, equal to 0.33 MAC for each drug. Then, the VA was adjusted to 0.1 L/min to simulate near-apnea and 0.0 L/min to simulate true apnea. Severe reanesthetization was said to occur if the VRG level increased to or above 0.5 MAC. Mild reanesthetization was said to occur if VRG increased from its value of 0.33 MAC but did not reach 0.5 MAC. The minimum VA required to avoid severe reanesthetization was studied by trials of decreased VA beginning at the time the VRG reached 0.33 MAC.

RESULTS: After emergence from 1 hour of anesthesia, all simulated patients were protected against mild and severe reanesthetization if anesthesia was at 0.75 or 1.0 MAC. After 4 or 6 hours of anesthesia, severe reanesthetization occurred with all drugs with near or true apnea if anesthesia was at 1.0 or 1.5 MAC. The minimum alveolar VA to protect against severe reanesthetization after 6 hours of anesthesia was no more than 0.5 L/min for all drugs at 0.75 MAC, no more than 0.5 L/min at 1.0 MAC, and no more than 1.2 L/min at 1.5 MAC. In all simulated cases, the source of anesthetic drug that allowed reanesthetization was muscle (MUS), which reached a value of 0.8 MAC within 4 hours with all drugs and reached a value of 0.75 MAC with desflurane after 2 hours. Fat levels of anesthetic remained less than 0.15 MAC for all drugs up to the 6 hours tested.

CONCLUSIONS: Reanesthetization from hypoventilation after inhaled anesthesia is possible. After initial emergence, muscle is a source of anesthetic and predisposes to reanesthetization while fat is a sink for anesthetic and fosters continued emergence. Severe hypoventilation will cause some degree of reanesthetization from anesthetic released from muscle after 4 hours of 1 MAC inhaled anesthesia with desflurane, sevoflurane, or isoflurane.

根治性前列腺切除術後結局：用芬太尼進行全身麻醉和區域麻醉鎮痛比較：配對佇列研究

Outcomes after radical prostatectomy for cancer:a comparison between general anesthesia and epiduralanesthesia with fentanyl analgesia: a matched cohort study

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背景： 腫瘤手術應用區域麻醉能改善腫瘤預後。其中一個可能的機制是靜脈應用阿片類藥物可能引起免疫抑制的減少。我們設計了一項回顧性佇列配對研究，全身麻醉靜脈應用芬太尼，硬膜外麻醉時硬膜外使用芬太尼鎮痛，比較二者根治性前列腺切除術後的長期結

局。由於硬膜外的芬太尼迅速全身重吸收，我們推測 2 組之間長期的腫瘤預後無明顯差異。

方法： 選擇了 486 名 1991 年 1 月 1 日和 1996 年 1 月 31 日之間在硬膜外麻醉下進行前列腺切除術的患者，另有一組患者應用芬太尼靜脈全身麻醉，基於年齡（±5 歲），手術時間（±1 年）和前列腺癌病理學的基線與前者 1:1 配對。對腫瘤的長期預後和全因死亡率進行了比較。採用分層比例風險回歸模型進行統計分析，與行硬膜外麻醉和芬太尼鎮痛的患者相比，僅僅使用芬太尼全身麻醉的患者風險比>1 表示效果更差。

結果：對手術切緣陽性和輔助治療進行調整後，與接受硬膜外麻醉的患者比較，全身麻醉組沒有發現前列腺癌復發風險增加（風險比[HR]=0.79，95％可信區間[CI]爲 0.60-1.04），全身腫瘤進展（HR=0.92，95％CI 爲 0.46-1.84），癌症特異性死亡率（HR=0.53，95％CI 爲 0.18-1.58），總死亡率（HR=1.23，95％CI 爲 0.93-1.63）。

結論： 與靜脈使用阿片類藥物全身麻醉相比較，硬膜外麻醉和芬太尼鎮痛對根治前列腺癌患者的腫瘤預後沒有改善。

（吳赤譯 薛張綱校）

BACKGROUND:The use of regional anesthesia for cancer surgery has been associated with improved oncologic outcomes. One of the proposed mechanisms is a reduction in the use of systemic opioids that may cause immunosuppression. We used a retrospective matched cohort design to compare long-term oncologic outcomes after prostatectomy for cancer performed under general anesthesia with systemic opioids or with epiduralanesthesia with epidural fentanyl analgesia. Since epidural fentanyl is quickly reabsorbed systemically, we hypothesized that there would be no difference in long-term oncological outcomes between the 2 groups.

METHODS:There were 486 men who underwent prostatectomy performed under epidural anesthesia between January 1, 1991, and January 31, 1996. They were 1:1 matched based on age (±5 years), surgical year (±1 year), and baseline prostate cancer pathology to patients who had generalanesthesia with systemic opioids. Long-term cancer outcomes and all-cause mortality were examined. Analyses were performed using stratified proportional hazards regression models, with hazard ratios >1 indicating worse outcome for general anesthesia only compared with epidural. anesthesia and fentanyl analgesia

RESULTS:After adjusting for positive surgical margins and adjuvant therapies, patients in the general anesthesia group were found not to be at increased risk of prostate cancer recurrence (hazard ratio [HR] = 0.79, 95% confidence interval [CI], 0.60-1.04], systemic tumor progression (HR = 0.92, 95% CI, 0.46-1.84), cancer-specific mortality (HR = 0.53, 95% CI, 0.18-1.58), or overall mortality (HR = 1.23, 95% CI 0.93-1.63) when compared with patients who received epidural anesthesia.

CONCLUSIONS:Compared with general anesthesia with systemic opioids, epidural anesthesia and analgesia with fentanyl were not associated with improvement in oncologic outcomes in patients undergoing radical prostatectomy for cancer.

利用床旁檢測和流式細胞術評估骨髓衰竭病人插入中心靜脈導管前預先輸注血小板的效果和持續時間

The Effect and Duration of Prophylactic Platelet Transfusions Before Insertion of a Central Venous Catheter in Patients with Bone Marrow Failure Evaluated with Point-of-Care Methods and Flow Cytometry.

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背景：骨髓衰竭和嚴重血小板減少的病人通常在操作前預先輸注血小板。儘管如此，這樣的輸注在臨床上的效果還沒有確定。我們在行中心靜脈穿刺前預先輸注血小板的骨髓衰竭病人中做了一個前瞻性觀察研究，我們的目的是評估骨髓衰竭致血小板減少的病人行中心靜脈穿刺前預先輸注血小板的效果和持續時間。

方法：39 個血小板計數低於 50 × 10/L 的骨髓衰竭成年病人在預先輸注血小板前依次登記，他們均行鎖骨下中心靜脈穿刺。分別在輸注血小板前、輸注後 1 小時和輸注後 4 小時三個時間點取血液標本。利用常規血液學檢查、轉動栓塞彈力測定法（EXTEM 和 FIBTEM）、多重電極集合度測定法來評估凝血情況，包括磷酸腺苷、膠原蛋白和凝血酶受體激動多肽，同時用流式細胞術檢測 P-選擇素 CD62P 和活化糖蛋白 PAC-1 在血小板的表達。根據對不良反應常用的術語標準把出血併發症分爲五個等級。

結果：此項研究包括 17 位女性和 22 位男性。輸注後 1 小時血小板計數從 24 × 10/L（18-32）增加到 42 × 10/L（31-50），但在輸注後 4 小時並沒有明顯不同（40 × 10/L (29-50)）。血栓彈力測定 EXTEM 得出最大凝血塊強度在輸注後 1 小時從 38mm（32-45）增加到 46mm（41-52），並且在輸注後 4 小時沒有變化。凝血時間在輸注後 1 小時從 58.5 秒（50-78）降至 53 秒（45-61），在輸注後 4 小時（57 秒）也沒有明顯不同。 FIBTEM 得出的輸注後的結果完全沒有變化。所有的多平臺分析結果在輸注後 1 小時明顯增加，在 4 小時沒有變化。流式細胞術分析顯示出不同的結果,卻沒有總體趨勢。

結論：在血小板減少的骨髓衰竭病人中預先輸注血小板可以通過增加血小板的數量而不是增強血小板的功能來改善血液凝集參數。改善的凝血參數和血小板聚集會持續存在輸注後 1-4 小時。

（呂越昌譯 薛張綱校）

BACKGROUND:Patients with bone marrow failure and severe thrombocytopenia are frequently given prophylactic platelet transfusion before interventions. The clinical effects of such transfusions, however, are poorly defined. We performed a prospective observational study on patients with bone marrow failure scheduledfor prophylactic platelet transfusion before the insertion of a central venous catheter. The objectives were to evaluatethe effect and duration of prophylactic platelet transfusions on central venous catheter insertion in thrombocytopenic patients with bone marrow failure.

METHODS:Thirty-nine adult patients with bone marrow failure and platelet counts below 50 × 10/L were consecutively enrolled before prophylacticplatelet transfusion for subclavian central venous catheter insertion. Blood samples were drawn from the patients before platelet transfusion, 1 hour, and 4 hours after completion of the transfusion. The coagulation profile was assessed by conventional hematological tests, thromboelastometry (ROTEM) assays (EXTEM and FIBTEM), multiple electrode aggregometry (Multiplate) assays including adenosine diphosphate, collagen, and thrombin receptor agonist peptide, and by flow cytometry for the platelet expression of P-selectin (CD62P) and activated glycoprotein IIb-IIIa (PAC-1).Bleeding complications were classified with a 5-grade scale, according to the Common Terminology Criteria for Adverse Events.

RESULTS:Seventeen women and 22 men were included in the study. Platelet count was increased from 24 × 10/L (18-32) before to 42 × 10/L (31-50) 1 hour after transfusion ($P < 0.0001$) and was not significantly different 4 hours after transfusion (40 × 10/L (29-50), $P = 0.047$). Maximal clot firmness EXTEM was increased from 38 mm (32-45) before to 46 mm (41-52) 1 hour after transfusion ($P < 0.0001$) and did not change 4 hours after transfusion. Clotting time EXTEM was decreased from 58.5 seconds (50-78) beforehand to 53 seconds (45-61) 1 hour after transfusion ($P = 0.0006$) and was not significantly different 4 hours after transfusion (57 seconds (52-70, $P = 0.025$). FIBTEM results were all unchanged after transfusion. All Multiplate

analyses were significantly increased after 1 hour and were not diminished 4 hours after transfusion. Four grade 1 bleeding episodes occurred, but no grade 2 to 5 bleeding could be detected. Flow cytometry analyses showed mixed results with no overall trend.

CONCLUSIONS:Prophylactic platelet transfusions in thrombocytopenic patients with bone marrow failure improve hemostatic parameters on ROTEM and Multiplate by increasing the number of platelets, and not through enhancement of platelet function. Improved clotting parameters on ROTEM andplatelet aggregation on Multiplate appear to persist between 1 and 4 hours after transfusion.

美國大學附屬醫院產科麻醉產後出血預案使用情況的研究

The use of postpartum hemorrhage protocols in **United States academic obstetric anesthesia units.**

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背景：產後出血（PPH）是導致產婦在住院和分娩中發生嚴重產後併發症，心跳驟停以及死亡的重要原因。計劃性診療已被證實可在多種情況下改善患者預後。National Partnership for Maternal Safety 推薦在美國所有的婦產科機構都應實施 PPH 預案。這項研究旨在確定在美國的大學附屬醫院的產科中，PPH 預案的使用的情況。我們假設大部分（＞80%）的大學附屬醫院的產科麻醉擁有合適的 PPH 預案。

方法：調查由一個專家小組實施。調查的內容包括醫院的特點，PPH 預案的可行性、計畫開展這份預案以及預案包含的內容，包括即將來臨的國家婦產科安全協會關於產後出血的安全倡議。電子調查問卷通過電子郵件發放給美國 104 位大學附屬醫院產科麻醉的負責人。回復的問卷按照 PPH 預案的使用進行適當的分層。單因素分析用來統計描述問卷答覆的特徵，二項分佈用來評價 PPH 預案使用的分佈概率。

結果：問卷的答覆率爲 58%。在回復中，擁有 PPH 預案的單位小於預期假設（P=0.03），回復的單位中，約 67%擁有 PPH 預案（N=40，95%可信區間[CI]: 53%-78%）。在回復問卷的單位中，有 PPH 預案的單位的年分娩量中位數爲 3900，而無 PPH 預案的單位的年分娩量中位數爲 2300，但二者在剖宮產率（P = 0.73）及產後出血發生率（P = 0.69）上沒有差別。回復及未回復問卷單位的年分娩量沒有顯著差別（P = 0.06），提示每年分娩量＞3200 的大學附屬醫院比分娩量較小的醫院更有可能有適當的 PPH 預案（比數比 3.16（95% CI: 1.01-9.90)。研究中，在校正未回復醫院中的分娩量後，所有學術中心的產科麻醉中 67%（95% CI: 55%-77%）擁有合適的 PPH 預案。醫院的規模擴大與 PPH 預案的存在並不相關。95%擁有 PPH 預案的醫院以及 90%沒有 PPH 預案的醫院中都有大量輸血的常規（95% CI of difference: -7% to 7%）。在回復問卷的醫院中，57%擁有產後出血的急救小組，這個比率在有或無 PPH 預案的單位中沒有差別[均差： 4%， 95% CI (-24% to 32%)]。

結論：儘管對國家患者安全品質改進的強調越來越多，在美國，仍然有至少 20%的產科麻醉中心沒有 PPH 預案。分娩量是最重要的預測 PPH 預案是否存在的變數。通過關注小分娩量的單位，可以使國家努力實施在所有大學附屬醫院中廣泛應用 PPH 預案的計畫獲得巨大收益。未來的工作需要在非大學附屬醫院中評估和推行 PPH 預案。

(杜芳譯 薛張綱校)

BACKGROUND: Postpartum hemorrhage (PPH) is the leading cause of severe maternal morbidity, cardiac arrest, and death during the hospitalization for childbirth. Protocol-driven care has been associated with improved outcomes in many settings; the National Partnership for Maternal Safety now recommends that PPH protocols be implemented in every labor and delivery unit in the United States. In this study, we sought to identify the level of PPH protocol availability in academic United States obstetric units. We hypothesized that the majority (>80%) of academic obstetric anesthesia units would have a PPH protocol in place.

METHODS:A survey was developed by an expert panel. Domains included hospital characteristics, availability of PPH protocol or plans to develop such a protocol, and protocol components included in the upcoming National Partnership for Maternal Safety obstetric hemorrhage safety bundle initiative. The electronic survey was emailed to the 104 directors of United States academic obstetric anesthesia units. Responses were stratified by PPH protocol availability as appropriate. Univariate statistics were used to characterize survey responses and the probability distribution for PPH protocol availability was estimated using the binomial distribution.

RESULTS:The survey response rate was 58%. The percentage of responding units with a PPH protocol was lower than hypothesized (P = 0.03); there was a PPH protocol in 67% of responding units (N = 40, 95% confidence interval [CI]: 53%-78%). The median annual delivery volume for responding units with PPH protocol was 3900 vs 2300 for units without PPH protocol (P = 0.002), with no difference in cesarean delivery rate (P = 0.73) or observed PPH rate (P = 0.69). There was no difference in annual delivery volume between responding and nonresponding hospitals (P = 0.06), suggesting that academic centers with delivery volume >3200 births per year are more likely than smaller volume hospitals to have a PPH protocol in place (odds ratio 3.16 (95% CI: 1.01-9.90). Adjusting for delivery volume among nonresponding hospitals, we estimate that 67% (95% CI: 55%-77%) of all academic obstetric anesthesia units had a PPH protocol in place at the time of this survey. Institutional processes for escalation do not correlate with the presence of a PPH protocol. There was a massive transfusion protocol in 95% of units with a PPH protocol and in 90% of units without (95% CI of difference: -7% to 7%). A PPH code team or rapid response team was available in 57% of responding institutions, with no difference between units with or without a PPH protocol [mean difference 4%, 95% CI (-24% to 32%)].

CONCLUSIONS:Despite increasing emphasis on national quality improvement in patient safety, there are no PPH protocols in at least 20% of U.S. academic obstetric anesthesia units. Delivery volume is the most important variable predicting the presence of a PPH protocol. National efforts to ensure universal presence of a PPH protocol in all academic centers will achieve the greatest impact by focusing on small-volume facilities. Future work is needed to evaluate and facilitate PPH implementation in nonacademic obstetric units.

兒科病人使用高/低新鮮氣體流量以及是否使用熱濕交換器對 dräger Primus 麻醉工作站濕度的影響

The humidity in a dräger primus anesthesia workstation using low or high fresh gas flow and with or without aheat and moisture exchanger in pediatric patients.

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背景：全麻下預防乾燥氣體對氣道上皮有害影響的最低絕對濕度被認爲是 20mgH_2O/L。由於兒童分鐘通氣量小，我們假定兒童與成人相比呼吸回路濕度較低。Primus 麻醉工作

站（Dräger Medical, Lübeck, Germany）具有一個內置的加熱器來加熱病人呼出的氣體。熱濕交換器（HME）是一種可以用來進一步加濕和加熱吸入氣體的裝置。爲了評價小兒麻醉時呼吸回路的加濕性能，我們比較了低或高新鮮氣體流量（FGF）以及是否使用熱濕交換器時吸入氣體的溫度和濕度。

方法：根據 Primus 麻醉工作站呼吸回路中的肺通氣方式的不同，將四十名兒童隨機分爲 4 組，分別是低 FGF（1 L/min）HME（Pall BB25FS, Pall Biomedical, East Hills, NY）組、低 FGF 無 HME 組、高 FGF（3 L/min）HME 組、高 FGF 無 HME 組。我們分別在病人連接呼吸回路 10、20、40、60、80 分鐘後測定吸入氣體的溫度和絕對濕度。

結果：研究發現，吸入氣體平均溫度 HME 組（HME1L: 30.3℃ ± 1.1℃; HME3L: 29.3℃ ± 1.2℃）與無 HME 組（1L: 27.0℃ ± 1.2℃; 3L: 27.1℃ ± 1.5℃; P < 0.0001）相比較高。吸入氣體的平均絕對濕度 HME 與無 HME 組相比較高，低流量組與高流量組相比較高（[HME1L: 25 ± 1 mg H_2O/L] > [HME3L: 23 ± 2 mg H_2O/L] > [1L: 17 ± 1 mg H_2O/L] > [3L: 14 ± 1 mg H_2O/L]，P < 0.0001）。

結論：小兒呼吸回路中低或高 FGF 都不能滿足降低呼吸道失水風險的最低濕度水準。使用 HME 可以增加吸入氣體的濕度和溫度，使其更接近生理值。低 FGF 可以提高 HME 的效率從而增加吸入氣體的濕度值。因此，小兒麻醉期間低 FGF 並聯合使用 HME 是保存吸入氣體溫度和濕度的最有效方式。

（江凌慧譯 薛張綱校）

BACKGROUND:An inhaled gas absolute humidity of 20 mg H2O·L is the value most considered as the threshold necessary for preventing the deleterious effects of dry gas on the epithelium of the airways during anesthesia. Because children have small minute ventilation, we hypothesized that the humidification of a circle breathing system is lower in children compared with adults. The Primus anesthesia workstation (Dräger Medical, Lübeck, Germany) has a built-in hotplate to heat the patient's exhaled gases. A heat and moisture exchanger (HME) is a device that can be used to further humidify and heat the inhaled gases during anesthesia. To evaluate the humidifying properties of this circle breathing system during pediatric anesthesia, we compared the temperature and humidity of inhaled gases under low or high fresh gas flow (FGF) conditions and with or without an HME.

METHODS:Forty children were randomly allocated into 4 groups according to the ventilation of their lungs by a circle breathing system in a Dräger Primus anesthesia workstation with low (1 L·min) or high (3 L·min) FGF without an HME (1L and 3L groups) or with an HME (Pall BB25FS, Pall Biomedical, East Hills, NY; HME1L and HME3L groups). The temperature and absolute humidity of inhaled gases were measured at 10, 20, 40, 60, and 80 minutes after connecting the patient to the breathing circuit.

RESULTS:The mean inhaled gas temperature was higher in HME groups (HME1L: 30.3℃ ± 1.1℃; HME3L: 29.3℃ ± 1.2℃) compared with no-HME groups (1L: 27.0℃ ± 1.2℃; 3L: 27.1℃ ± 1.5℃; P < 0.0001). The mean inhaled gas absolute humidity was higher in HME than no-HME groups and higher in low-flow than high-flow groups ([HME1L: 25 ± 1 mg H2O·L] > [HME3L: 23 ± 2 mg H2O·L] > [1L: 17 ± 1 mg H2O·L] > [3L: 14 ± 1 mg H2O·L]; P < 0.0001).

CONCLUSIONS:In a pediatric circle breathing system, the use of neither high nor low FGF provides the minimum humidity level of the inhaled gases thought to reduce the risk of dehydration of airways. Insertion of an HME increases the humidity and temperature of the inhaled gases, bringing them closer to physiological values. The use of a low FGF enhances the HME efficiency and consequently increases the inhaled gas humidity values. Therefore, the association of an HME with low FGF in the breathing circuit is the most efficient way to conserve the heat and the moisture of the inhaled gas during pediatric anesthesia.

血清抗膽鹼能活性與老年患者術後認知功能障礙的關係

Serum Anticholinergic Activity and Postoperative Cognitive Dysfunction in Elderly Patients

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背景：大腦膽鹼能遞質對認知功能具有關鍵性作用，並且假說認爲圍手術期給予抗膽鹼能藥物可引起術後認知功能障礙（POCD）。我們假設圍手術期血清膽鹼能活性（SAA）的升高與老年患者術後認知功能障礙有關。

方法：研究物件是年齡＞65 歲並在標準化全身麻醉（硫噴妥鈉、七氟醚、芬太尼和阿曲庫銨）下行擇期大手術的 79 位患者。使用擴展版的 CERAD-神經心理學評價系列對其術前及術後 7 天的認知功能進行評估。POCD 定義爲在至少兩個測試變數中術後降低＞1Z 得分。在進行認知測試的同時，SAA 也在術前及術後 7 天進行檢測。使用 Hodges-Lehmann 中位差異及它們的 95%可信區間進行組間比較。

結果：在完成這項研究的患者中，46%出現了 POCD。有術後認知功能障礙的患者較沒有術後認知功能障礙的患者稍年老些並且受教育程度相對低。兩組患者的性別、人口統計學校正後的認知功能基線及麻醉時間沒有有意義的差異。兩組患者的術前 SAA 水準（pmol/mL，中位數[四分位差]/中位數差[95%可信區間]，P; 1.14 [0.72, 2.37] vs 1.13 [0.68, 1.68]/0.12 [-0.31, 0.57], P = 0.56）、術後 7 天的 SAA 水準（1.32 [0.68, 2.59] vs 0.97 [0.65, 1.83]/0.25 [-0.26, 0.81], P = 0.37）或者 SAA 的變化（0.08 [-0.50, 0.70] vs -0.02 [-0.53, 0.41]/0.1 [-0.31, 0.52], P = 0.62）均沒有較大差異。SAA 的變化和認知功能的變化沒有顯著的關係（Spearman 秩相關係數術前爲 0.03 [95% CI, -0.21, 0.26]，術後爲-0.002 [95% CI, -0.24, 0.23]）。

結論：本研究中的患者 SAA 基線低並且圍手術期的抗膽鹼能負荷臨床上講較輕微，雖然在某些患者中相關性不能被排除，但是我們的分析認爲 POCD 可能並不是圍手術期抗膽鹼能藥物使用的直接結果，而更傾向於其他機制。

(蓋曉冬譯 薛張綱校)

BACKGROUND: Cerebral cholinergic transmission plays a key role in cognitive function, and anticholinergic drugs administered during the perioperative phase are a hypothetical cause of postoperative cognitive dysfunction (POCD). We hypothesized that a perioperative increase in serum anticholinergic activity (SAA) is associated with POCD in elderly patients.

METHODS: Seventy-nine patients aged >65 years undergoing elective major surgery under standardized general anesthesia (thiopental, sevoflurane, fentanyl, and atracurium) were investigated. Cognitive functions were assessed preoperatively and 7 days postoperatively using the extended version of the CERAD-Neuropsychological Assessment Battery. POCD was defined as a postoperative decline >1 z-score in at least 2 test variables. SAA was measured preoperatively and 7 days postoperatively at the time of cognitive testing. Hodges-Lehmann median differences and their 95% confidence intervals were calculated for between-group comparisons.

RESULTS:Of the patients who completed the study, 46% developed POCD. Patients with POCD were slightly older and less educated than patients without POCD. There were no relevant differences between patients with and without POCD regarding gender, demographically corrected baseline cognitive functions, and duration of anesthesia. There were no large differences between patients with and without POCD regarding SAA preoperatively (pmol/mL, median [interquartile range]/median difference [95% CI], P; 1.14 [0.72, 2.37] vs 1.13 [0.68, 1.68]/0.12 [-0.31, 0.57], P = 0.56), SAA 7 days postoperatively (1.32 [0.68, 2.59] vs 0.97 [0.65, 1.83]/0.25 [-0.26, 0.81], P = 0.37), or changes in SAA (0.08 [-0.50, 0.70] vs -0.02 [-0.53, 0.41]/0.1 [-0.31, 0.52], P = 0.62). There was no significant relationship between changes in SAA and changes in cognitive function (Spearman rank correlation coefficient preoperatively of 0.03 [95% CI, -0.21, 0.26] and postoperatively of -0.002 [95% CI, -0.24, 0.23]).

CONCLUSIONS: In this panel of patients with low baseline SAA and clinically insignificant perioperative anticholinergic burden, although a relationship cannot be excluded in some patients, our analysis suggests that POCD is probably not a substantial consequence of anticholinergic medications administered perioperatively but rather due to other mechanisms.

糖原合酶激酶-3β 抑制劑通過調節 AMPA 受體的表達和功能來抑制瑞芬太尼誘導的術後痛覺過敏

Glycogen Synthase Kinase-3β Inhibition Prevents Remifentanil-Induced Postoperative Hyperalgesia via Regulating the Expression and Function of AMPA Receptors.

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背景：很多研究證實單純應用瑞芬太尼可提高痛覺敏感性。我們之前報導了啓動糖原合酶激酶-3β 可通過調節脊髓背角內 N-甲基-D 天冬氨酸受體的可塑性來促進瑞芬太尼誘導的痛覺過敏。本研究中，我們證實了糖原合酶激酶-3β 抑制劑通過調節脊髓背角內 AMPA 受體的表達和功能來抑制瑞芬太尼誘導的術後痛覺過敏。

方法：首先，我們建立瑞芬太尼誘導的痛覺過敏模型，在開始輸注瑞芬太尼前 1 天、後 2 小時、6 小時、1 天、2 天、3 天、5 天以及 7 天時測定切口模型的機械痛以及熱痛情況。應用 western blot 法測定脊髓背角內 AMPAR 亞單位（Glu-R1 和 Glu-R2）運輸、AMPAR 亞單位磷酸化情況以及糖原合酶激酶-3β 活性。另外，我們應用全細胞膜片鉗記錄法來分析抑制糖原合酶激酶-3β 對脊髓背角內 AMPA 受體誘發電位的影響情況。

結論：瑞芬太尼誘導的術後痛覺過敏的裸鼠脊髓內膜 AMPA 受體亞單位 Glu-R1 上調(275 ± 36.54 [mean ± SD] vs 100 ± 9.53, P = 0.0009)。應用選擇性糖原合酶激酶-3β 抑制劑，如氯化鋰和 TDZD，可改善瑞芬太尼誘導的術後痛覺過敏，並使 AMPA 受體亞單位 Glu-R1 下調(254 ± 23.51 vs 119 ± 14.74, P = 0.0027; 254 ± 23.51 vs 124 ± 9.35, P = 0.0032)。另外，瑞芬太尼孵育可提高背角神經元內 AMPA 受體誘發電位的頻率和波幅(61.09 ± 9.34 pA vs 32.56 ± 6.44 pA, P = 0.0009; 118.32 ± 20.33 ms vs 643.67 ± 43.29 ms, P = 0.0002)，而氯化鋰和 TDZD 均可抑制該效果。瑞芬太尼誘導的術後疼痛可促進 pGluR1 Ser845 和 Rab5 的表達,該效果同樣可被氯化鋰或 TDZD 抑制。

總結：上述結果表明抑制糖原合酶激酶-3β 導致瑞芬太尼誘導的術後痛覺過敏症狀改善是通過下調細胞膜上 AMPA 受體 Glu-R1 的表達以及脊髓背角內 pGluR1 和 Rab5 的表達來實現的。

（郝光偉譯 薛張綱校）

BACKGROUND: Many studies have confirmed that brief remifentanil exposure can enhance pain sensitivity. We previously reported that activation of glycogen synthase kinase-3β (GSK-3β)

contributes to remifentanil-induced hyperalgesia via regulating N-methyl-D-aspartate receptor plasticity in the spinal dorsal horn. In this study, we demonstrated that GSK-3β inhibition prevented remifentanil-induced postoperative hyperalgesia via regulating α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) expression and function in the spinal dorsal horn.

METHODS: Using a rat model of remifentanil-induced incision hyperalgesia, mechanical and thermal pain was tested 1 day before infusion and 2 hours, 6 hours, 1 day, 2 days, 3 days, 5 days, and 7 days after infusion. Western blot analysis was used to detect AMPAR subunit (GluR1 and GluR2) trafficking, AMPAR phosphorylation status, and GSK-3β activity in the spinal dorsal horn. Furthermore, whole-cell patch-clamp recording was used to analyze the effect of GSK-3β inhibition on AMPAR-induced current in the spinal dorsal horn.

RESULTS: Membrane AMPAR subunit GluR1 was upregulated in the spinal cord in remifentanil-induced postoperative hyperalgesia rats (275 ± 36.54 [mean ± SD] vs 100 ± 9.53, P = 0.0009). Selective GSK-3β inhibitors, LiCl and TDZD, treatment ameliorates remifentanil-induced postoperative hyperalgesia, and this was associated with the downregulated GluR1 subunit in the membrane fraction (254 ± 23.51 vs 119 ± 14.74, P = 0.0027; 254 ± 23.51 vs 124 ± 9.35, P = 0.0032). Moreover, remifentanil incubation increased the amplitude and the frequency of AMPAR-induced current in dorsal horn neurons (61.09 ± 9.34 pA vs 32.56 ± 6.44 pA, P = 0.0009; 118.32 ± 20.33 milliseconds vs 643.67 ± 43.29 milliseconds, P = 0.0002), which was prevented with the application of LiCl and TDZD, respectively. Remifentanil-induced postoperative pain induced an increase in pGluR1 Ser845 and Rab5, which was prevented with the application of LiCl and TDZD.

CONCLUSIONS: These results indicate that amelioration of remifentanil-induced postoperative hyperalgesia by GSK-3β inhibition is attributed to downregulated AMPAR GluR1 expression in the membrane fraction and inhibition of AMPAR function via altering pGluR1 and Rab5 expression in the spinal dorsal horn.

血紅蛋白氧載體 HBOC-201 在非心臟手術病人中使用的安全性和有效性的隨機多中心研究

A Safety and Efficacy Evaluation of Hemoglobin-Based Oxygen Carrier HBOC-201 in a Randomized, Multicenter Red Blood Cell Controlled Trial in Noncardiac Surgery Patients

Van Hemelrijck, Jan; Levien, Lewis J.; Veeckman, Luc; Pitman, Arkadiy; Zafirelis, Zafiris; Standl, Thomas

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背景：我們介紹的是 1998-1999 年血紅蛋白氧載體未公開發表的研究結果。

方法：在一個多中心、隨機的、單盲的對比研究中，HBOC-201 對比同種異體的紅細胞灌注，非心臟手術患者接受最多 7 個單位 HBOC-201（n=83）或紅細胞（n=77）。患者可能轉化紅細胞更安全或者其他推論。同種異體紅細胞輸注的有效作用終點被消除和/或減少需要 28 天。

結果：在 HBOC-201 組避免紅細胞輸注的患者比例是 0.427（95%可信區間，0.321-0.533）。HBOC-201 組被試者平均接受 3.2 個單位紅細胞，而對照組爲 4.4 個單位（P=0.004）。29 名（95.2%）HBOC-201 組被試者和 72 名（93.5%）紅細胞組被試者出現不良反應，認爲分別與 59 名（77.1%）和 18 名（23.4）被試者研究性治療有關。HBOC-201 組和紅細胞輸注組 30 天死亡數分別是 5 名（6.0%）和 4 名（5.2%）患者（P=1.00），嚴重不良反應發生率分別是 24（28.9%）和 20（26.0%），而監護室停留時間（對數秩 P=0.15）和出院時間（對數秩 P=0.53）兩組則相近。

結論：直到灌注 7 個單位 HBOC-201 超過 6 天的進程，可使 43%的患者避免的紅細胞的輸注。死亡率和嚴重不良反應發生率沒有顯著差異。HBOC-201 的作用與顯著的過量的非嚴重不良反應有關。

（王曉莉 譯，李士通 審校）

BACKGROUND: We present the results of a previously unpublished hemoglobin-based oxygen carrier (HBOC) study conducted in 1998-1999.

METHODS: In a multicenter, randomized, single-blind, comparative study of HBOC-201 versus allogeneic red blood cell (RBC) transfusions, no-cardiac surgery patients received HBOC-201 to a maximum of 7 units (n = 83) or RBCs (n = 77). Patients could be switched to RBCs for safety or any other reason. The efficacy end points were elimination and/or reduction of allogeneic RBC transfusions for 28 days.

RESULTS: The proportion of patients in the HBOC-201 group that avoided RBC transfusion was 0.427 (95% confidence interval, 0.321-0.533). Subjects in the HBOC-201 group received on average 3.2 units of RBCs versus 4.4 units in the control arm (P = 0.004). Seventy-nine (95.2%) subjects in the HBOC-201 group and 72 (93.5%) in the RBC group experienced adverse events (AEs), judged to be associated with study treatment in 59 (71.1%) and 18 (23.4%) subjects, respectively. Thirty-day mortality, 5 (6.0%) vs 4 (5.2%) patients (P = 1.00), incidence of serious AEs, 24 (28.9%) vs 20 (26.0%) (P = 0.73), or time to intensive care unit (log-rank P = 0.15) or hospital discharge (log-rank P = 0.53) were similar for the HBOC-201 and RBC groups, respectively.

CONCLUSIONS: Up to 7 units of HBOC-201 infused over the course of 6 days resulted in RBC transfusion avoidance in 43% of patients. There were no notable differences in mortality and serious AEs incidence. The use of HBOC-201 was associated with a notable excess of nonserious AEs

嚴重阻塞性睡眠呼吸暫停患者在內窺鏡檢查時使用丙泊酚輸注系統的安全性和有效性

Safety and Efficacy of Drug-Induced Sleep Endoscopy Using a Probability Ramp Propofol Infusion System in Patients with Severe Obstructive Sleep Apnea

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背景：藥物引起的睡眠下內窺鏡檢查使用鎮靜催眠藥誘導中度障礙的睡眠呼吸暫停病人，從而促進阻塞性生理學的組織評估。實現藥物引起的睡眠下內窺鏡檢查使用丙泊酚需要一個劑量策略並且確實可靠地產生阻礙同時將氧飽和度的下降減到最小。

方法：外科醫生在一項舌底的經口機器人切除術前瞻性研究中，登記了 97 名阻塞性睡眠呼吸暫停患者，被多導聯睡眠圖證實持續性氣道正壓通氣失敗。所有的患者都被藥物引起的睡眠下內窺鏡檢查篩查。丙泊酚劑量由 MATLAB（矩陣實驗室）書寫的定制軟體決定，且是預先描寫的。研究在有標準監護儀和復蘇設備的手術室實行。排除表面麻醉，以及除了丙泊酚之外的靜脈藥物。所有患者接受 2 升/分鐘的口部鼻導管輔助給氧。開始丙泊酚鎮靜後，經鼻放置小兒氣管鏡來觀察咽部。鎮靜狀態持續到臨床終點即阻礙發作開始。咽部的觀察需用足夠的時間來獲取妨礙部位的圖像。然後輸注終止。

結果：這一群體具有的特徵是中值體重指數爲 32.1（四分間距[IQR]6.8）kg/m 和呼吸暫停指數爲 48（ICQ32）。所有患者呈現的阻礙在設計變數內。阻礙在 236(±57.9)秒後、預估的效應室濃度在 4.2±1.3mcg/mL 時被觀察到。藥物引起的睡眠下內窺鏡檢查期間飽和度最低中位數顯（91.4%（四分間距 5.1））著地高於標準睡眠研究（81.0%[四分間距 11.2]，P<0.0001）。95%可信區間統計了藥物引起的睡眠下內窺鏡檢查飽和度最低點和體重指數、年齡、呼吸暫停指數，或者執行丙泊酚劑量包括零在內的所有情況。

結論：丙泊酚輸注策略需要限制性的經驗在丙泊酚劑量選擇和只有一個泵定量給藥時在嚴重阻塞性睡眠呼吸暫停患者產生氣道阻礙。臨床阻礙出現比靶控輸注系統的類似過程在相關文獻中的報導更快。類比系統中觀察的氧飽和度下降程度在臨床可接受的範圍內。

（王曉莉 譯，李士通 審校）

BACKGROUND: Drug-induced sleep endoscopy (DISE) uses sedative-hypnotics to induce moderate obstruction in sleep apnea patients, thereby facilitating anatomic assessment of obstructive physiology. Implementation of DISE with propofol requires a dosing strategy that reliably and efficiently produces obstruction while minimizing oxygen desaturation.

METHODS: The surgeon in a prospective study of transoral robotic resection of the tongue base enrolled 97 patients with obstructive sleep apnea confirmed by polysomnography who failed continuous positive airway pressure. All patients were screened by DISE. Propofol dose was determined using custom software written in MATLAB, which has been previously described. Studies were performed in an operating room with standard monitors and resuscitation equipment. No topical anesthesia was used, and no IV drugs other than propofol were used. All patients received 2 L/min supplemental oxygen via a nasal cannula placed in the mouth. After initiation of propofol sedation, a pediatric bronchoscope was positioned via the naris to observe the velopharynx. The sedation sequence was continued until the clinical end point of obstruction onset was noted. Observation of the pharynx was performed for a sufficient period to obtain images of the anatomic site(s) of obstruction. The infusion was then terminated. Statistical analysis was performed with MATLAB (MathWorks, version 2012b). Comparison of saturation nadirs between DISE and subject sleep studies was performed with both the paired and unpaired Student t test.

RESULTS: The subject population was characterized by a median body mass index of 32.1 (interquartile range [IQR] 6.8) kg/m and apnea-hypopnea index of 48 (IQR 32). All patients demonstrated obstruction within the design variables. Obstruction was observed after 236 (±57.9) seconds at an estimated effect-site concentration of 4.2 ± 1.3 mcg/mL. The median saturation nadir during DISE was significantly higher (91.4% (IQR 5.1)) than that during standard sleep studies (81.0% [IQR 11.2], $P < 0.0001$). Ninety-five percent confidence intervals for correlations between DISE saturation nadir and body mass index, age, apnea-hypopnea index, or administered propofol dose included zero in all cases.

CONCLUSIONS: A propofol infusion strategy that requires limited experience with propofol dose selection and only 1 pump dosing change reliably produced airway obstruction in patients with severe sleep apnea. Clinical obstruction was achieved faster than target-controlled infusion-based systems for similar procedures reported in the literature. The observed degree of oxygen desaturation in the model system was within a clinically acceptable range.

香豆酮的衍生物在不同老鼠實驗模型中的抗過敏與抗炎效應說明蛋白激酶 C 通路的重要性

The Antihypersensitive and Antiinflammatory Activities of a Benzofuranone Derivative in Different Experimental Models in Mice: The Importance of the Protein Kinase C Pathway

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背景：BF1 是人工合成的。它的效應是評估機體高敏性和不同藥物導致的水腫模型，結紮部分坐骨神經導致的神經性疼痛。解釋這種作用機理的機制。

方法：試驗中用瑞士老鼠。通過內腳趾注射角叉膠，緩激肽，前列腺素，腎上腺素，脂多糖或者弗氏佐劑或者用神經疼痛模型（von Frey 纖維 0.6g）來誘導高敏反應。通過角叉膠，PGE2，BK 誘導的爪水腫模型引發抗炎反應。PKC 用於佛波醇導致的傷害模型。

結果：BF1 抑制高敏反應和腳底注射角叉膠，BK，PGE2（P<0.001）引起的水腫模型，並且減少弗氏佐劑和腎上腺素（P<0.001）引起的超敏反應是有效的，而不是脂多糖（P<0.257）引起的。BF1 抑制佛波醇誘導的舔的行爲，表明涉及到 PKC 通路。試驗中還觀察到降低結紮部分坐骨神經（P<0.001）導致的超敏反應，抑制嗜中性粒細胞遷移和進入脊髓的白介素-1β 的產生。BF1 治療不會影響運動功能（P=0.0783）,這是其他止痛藥的嚴重副反應。

結論：在急性和慢性疼痛和炎症模型，BF1 有劑量依賴的抗高敏反應和抗炎反應，可能通過 PKC 通路的啓動來。這種容易快速合成的複合物，低成本，低濃度，每天一次的藥物表明可以有望用於未來的臨床研究。

（王雪譯 李士通審校）

BACKGROUND: Benzofuranone (BF1) was synthesized and its effects evaluated on mechanical hypersensitivity and paw edema models induced by different agents and on neuropathic pain induced by partial ligation of the sciatic nerve. An attempt was also made to elucidate the mechanism of action.

METHODS: Swiss mice were used for the tests. Hypersensitivity was induced by intraplantar injection of carrageenan, bradykinin (BK), prostaglandin E2 (PGE2), epinephrine, lipopolysaccharide, or complete Freund adjuvant or by using a neuropathic pain model (evaluated with von Frey filament 0.6 g). The antiinflammatory effects were investigated in a paw edema model induced by carrageenan, PGE2, and BK (measured with a plethysmometer). The involvement of protein kinase C (PKC) was investigated through a nociception model induced by phorbol myristate acetate.

RESULTS: BF1 inhibited the hypersensitivity and paw edema induced by intraplantar injection of carrageen an, BK, and PGE2 ($P < 0.001$), and it was effective in reducing the hypersensitivity evoked by complete Freund adjuvant or epinephrine ($P < 0.001$) but not by lipopolysaccharide ($P = 0.2570$). BF1 inhibited the licking behavior induced by phorbol myristate acetate ($P < 0.001$), suggesting involvement of the PKC pathway. A reduction in hypersensitivity of mice submitted to partial ligation of the sciatic nerve ($P < 0.001$) was observed, with inhibition of neutrophil migration and interleukin-1β production into the spinal cord. BF1 treatment did not interfere with locomotor activity ($P = 0.0783$) and thermal withdrawal threshold ($P = 0.5953$), which are important adverse effects of other analgesics.

CONCLUSIONS: BF1 has dose-dependent antihypersensitive and antiinflammatory effects in both acute and chronic models of pain and inflammation, possibly mediated through interference with the PKC activation pathway. The easy and fast synthesis of this compound, low-cost, low-concentration-requirement, and once-daily-administration drug suggest it as a candidate for future clinical studies.

小兒應用硝普鈉進行控制性降壓的預測因素

Predictors of Arterial Blood Pressure Control During Deliberate Hypotension with Sodium Nitroprusside in Children

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背景：硝普鈉用於特定手術降低動脈血壓。關於硝普鈉控制血壓效果的資料有限。但沒有關於病人和臨床醫生影響動脈血壓的資料。我們評估了行大手術的嬰兒和兒童應用硝普鈉的劑量反應效應以及進行血壓控制的定量評估。

方法：153 例患者在進行控制性降壓的手術操作時注射標記過的硝普鈉。持續輸注硝普鈉，滴定進行控制血壓（MAP 界定爲臨床標準的 10%。）通過動脈導管記錄血壓。用定量統計法統計血壓控制情況。多元法評估病人和方法的效果。

結果：45.4%（SD23.9%；95%可信區間 41.5%-49.18%）的手術時間進行控制血壓。在輸注速率方面，較大的變化與更嚴重的血壓控制有關（少控制 7.99%的血壓速率爲 1ug/kg/min 增加平均滴注量 P=0.0009）。病人基礎血壓與目標血壓很大的差異預示更多的血壓控制（每 mmHg 多控制 0.93%的血壓增加 MAP 的差異性，P=0.0013）。這兩種效果都出現在多元模型中。

結論：硝普鈉降低血壓是有效的。然而，血壓維持目標血壓的時間不到一半的。臨床醫生和病人因素不能預測血壓，雖然確認了 2 種相反的關係。弄清這些關係需要進一步的研究，並且最好應用模型，建議用於小兒控制性降壓時增加劑量。

（王雪 譯，李士通 審校）

BACKGROUND: Sodium nitroprusside (SNP) is used to decrease arterial blood pressure (BP) during certain surgical procedures. There are limited data regarding efficacy of BP control with SNP. There are no data on patient and clinician factors that affect BP control. We evaluated the dose-response relationship of SNP in infants and children undergoing major surgery and performed a quantitative assessment of BP control.

METHODS: One hundred fifty-three subjects at 7 sites received a blinded infusion followed by open-label SNP during operative procedures requiring controlled hypotension. SNP was administered by continuous infusion and titrated to maintain BP control (mean arterial BP [MAP] within ±10% of clinician-defined target). BP was recorded using an arterial catheter. Statistical process control methodology was used to quantify BP control. A multivariable model assessed the effects of patient and procedural factors.

RESULTS: BP was controlled an average 45.4% (SD 23.9%; 95% CI, 41.5%-49.18%) of the time. Larger changes in infusion rate were associated with worse BP control (7.99% less control for 1 μg·kg·min increase in average titration size, P = 0.0009). A larger difference between a patient's baseline and target MAP predicted worse BP control (0.93% worse control per 1-mm Hg increase in MAP difference, P = 0.0013). Both effects persisted in multivariable models.

CONCLUSIONS: SNP was effective in reducing BP. However, BP was within the target range less than half of the time. No clinician or patient factors were predictive of BP control, although 2 inverse relationships were identified. These relationships require additional study and may be best coupled with exposure-response modeling to propose improved dosing strategies when using SNP for controlled hypotension in the pediatric population.

術前使用他汀類藥物不能使高風險患者免受術後發生早期急性呼吸窘迫綜合征的回顧性佇列研究

Preoperative Statin Administration Does Not Protect Against Early Postoperative Acute Respiratory Distress Syndrome: A Retrospective Cohort Study

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背景：他汀類藥物已被證明具有抗炎和免疫調節作用。在本研究中,我們試圖確定存在發生急性呼吸窘迫綜合征(ARDS)風險的手術病人術前他汀類藥物治療能否降低術後 ARDS 的發生率。

方法：我們進行了回顧性佇列評價擇期行高風險胸主動脈血管手術的患者術前他汀類藥物治療與術後早期 ARDS 發生的相關性。對二者相關性的研究我們採用了傾向調整分析方法以控制顯示偏移及混雜因素的影響。

結果：1845 例患者,722 例接受術前他汀類藥物治療。一百二十例患者術後發生了 ARDS。接受了他汀類藥物治療與沒有接受了他汀類藥物治療的患者 ARDS 發生率分別爲 7.2%和 6.1%(OR = 1.20;95%可信區間,0.83 - 1.75;P = 0.330)。無論是分層傾向得分分析(集中 OR 爲 0.93;95%可信區間,0.60 - 1.43)和匹配分析(OR = 0.78;95%可信區間,0.78 - 0.48)都未確定術前他汀類治療與術後 ARDS 發生減少的顯著關聯。通過匹配控制比較發現,所有術後 ARDS 患者死亡率(7.7%比 8.8%,P = 0.51),住院天數(21 天 vs 15 天,P = 0.21),及無需機械通氣天數 (24 天 vs 25 天,P = 0.62)都沒有差別。

結論：行高風險手術的患者,術前他汀類藥物治療沒有顯著降低術後 ARDS。這些結果不支持接受高風險的手術患者術前使用他汀類藥物來預防 ARDS。

（王慧娟 譯，李士通 審校）

BACKGROUND: Statins have been shown to possess antiinflammatory and immunomodulatory effects. In this study, we sought to determine if preoperative statin therapy is associated with a reduced frequency of postoperative acute respiratory distress syndrome (ARDS) in surgical populations at increased risk of developing ARDS.

METHODS: We performed a retrospective cohort evaluation of the association between preoperative statin therapy and early postoperative ARDS in patients undergoing elective high-risk thoracic and aortic vascular surgery. The association between preoperative statin therapy and postoperative ARDS was assessed using propensity-adjusted analyses to control for indication bias and confounding factors.

RESULTS: Of 1845 patients, 722 were receiving preoperative statin therapy. One hundred twenty patients developed postoperative ARDS. Frequencies of ARDS among those receiving statin therapy versus those who were not was 7.2% and 6.1%, respectively (OR = 1.20; 95% CI, 0.83-1.75; P = 0.330). Neither the stratified propensity score analysis (pooled OR 0.93; 95% CI, 0.60-1.43) nor matched analysis (OR = 0.78; 95% CI, 0.48-1.27) identified a statistically significant association between preoperative statin administration and postoperative ARDS. When compared to matched controls, patients who developed postoperative ARDS did not differ in mortality (7.7% vs 8.8%, P = 0.51), hospital length of stay (21 days vs 15 days, P = 0.21), or ventilator-free days (24 days vs 25 days, P = 0.62).

CONCLUSIONS: In patients undergoing high-risk surgery, preoperative statin therapy was not associated with a statistically significant reduction in postoperative ARDS. These results do not support the use of statins as prophylaxis against ARDS in patients undergoing high-risk surgery.

麻醉併發症成爲分娩患者的安全指標

Anesthesia Complications as a Childbirth Patient Safety Indicator

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背景：衛生保健研究與品質機構(AHRQ)建立了多個品質監控和優化的指標集。這是一套患者安全指標(PSIs),其重點是醫院內潛在的可預防的術後、操作和分娩的併發症。本研究旨在確定不同分娩方式的麻醉併發症的患病率，及在醫院使用 AHRQ PSI 評估方法併發症發生率的變化，同時做出一個針對分娩 PSI 的修改方案，此方案的目的是確定麻醉併發症的相關因素。

方法：AHRQ 的一個 PSI—麻醉併發症的品質指標修改爲一個特殊分娩的安全指標。它包含所有分娩方式(陰道分娩和剖腹產手術)及全身麻醉和椎管內麻醉/鎮痛的併發症。我們使用加州醫院出院資料,整理出了非正常住院的發生率,並對年齡、種族、妊娠併發症進行分類統計。

結果：2009 年在加州 254 家醫院總共有 508842 次分娩。每年分娩數小於 200 次的醫院(N = 12)被排除在研究之外。另外 242 醫院，在 AHRQ 標準研究人群中(成人外科病房,其中包括剖腹產手術)麻醉併發症發生率爲 0.13%。特殊分娩的麻醉併發症的發生率爲 0.31%。通過分娩方式的分層研究，我們發現,剖腹產併發症發生率爲 0.49%而陰道分娩爲 0.22%(P < 0.0001)。未經調整的平均值(SD)爲 0.34%(0% - 2.46%)。有 13 家醫院的併發症發生率(包括他們的 95%置信區間)仍在上四分位數，爲異常值,其調整後的發生率爲 0.52%至 2.13%。

結論：分娩相關的麻醉併發症率可能提供一個機會去辨認出併發症發生率低的醫院，這樣的醫院擁有深入系統的方式來提高患者的安全。

（王慧娟 譯，李士通 審校）

BACKGROUND: The Agency for Healthcare Research and Quality (AHRQ) has established multiple sets of indicators for quality monitoring and improvement. One such set is the patient safety indicators (PSIs), which focuses on potentially preventable hospital complications after surgeries, procedures, and childbirth. Our objective in this study was to determine the prevalence of childbirth-related anesthesia complications by method of delivery and to evaluate the variation in complication rates across hospitals using the AHRQ PSI methodology and a modification specific to childbirth with the goal of determining the relevance of tracking anesthesia complications as a potential PSI for childbirth.

METHODS: The technical specifications of the experimental Anesthesia Complication Quality Indicator, one of the PSI defined by AHRQ, were modified to create a childbirth-specific indicator that included all childbirth admissions (vaginal and cesarean deliveries) and complications from general and neuraxial anesthesia/analgesia. Using California hospital discharge data, we calculated hospital-specific rates, adjusting for age, race/ethnicity, and pregnancy complications.

RESULTS:A total of 508,842 deliveries occurred in 254 hospitals in California in 2009. Hospitals with <200 annual deliveries (N = 12) were excluded from analyses. Among 242 hospitals, the rate of anesthesia complications was 0.13% for the standard AHRQ study population (adult surgical admissions, which included cesarean deliveries). The childbirth-specific rate of anesthesia complications was 0.31%. When stratified by method of delivery, complication rates were 0.49% for cesarean delivery and 0.22% for vaginal delivery (P < 0.0001). The unadjusted mean (SD) was 0.34% (0.34%), with range (0%-2.46%). The rates of 13 hospitals (including their 95% confidence limits) remained in the upper quartile as outliers, with adjusted rates from 0.52% to 2.13%.

CONCLUSIONS: Rates of childbirth-related anesthesia complications may provide an opportunity to identify hospitals with extreme rates that may provide insights into systematic ways to improve patient safety.

QT 延長綜合征患兒使用現代麻醉的安全性

The Safety of Modern Anesthesia for Children with Long QT Syndrome

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背景：患有 QT 延長綜合征的患者可能會經歷一系列的臨床症狀，從無症狀、暈厥前期、暈厥、中止心臟驟停到心源性猝死。QT 延長綜合征這一類心律失常往往是由自主神經的變化導致。這些被認爲是高風險的圍手術期心律失常，特別是尖端扭轉型室速（TDP），但這種看法在很大程度上是基於一些有限的關於早於當前麻醉藥品和圍手術期監測標準的文獻。現在我們提出了迄今爲止最大量的關於 QT 延長綜合征幼兒麻醉管理的多中心回顧。

方法：我們進行了一個關於 QT 延長綜合征兒童圍手術期管理的多中心回顧性分析，這些兒童是我們在 2005 年 1 月到 2010 年 1 月之間收集的小於 18 歲並接受全身麻醉的患者。我們分別從 8 個機構的匿名資料庫中收集資料。

結果：103 個 QT 延長綜合征的病人一共經歷了 158 次全身麻醉。患者年齡和體重的中位數分別是 9（3-15）歲及 30.3（15.5-54）千克。81 個人（51%）在與 QT 延長綜合征相關的手術中在全麻時發作（包括心臟起搏器，植入式心臟除顫器），另外 77 個人（49%）是偶然發生的。在手術當天 76%的病人使用 β 受體阻滯劑治療，47%的人接受術前鎮靜治療。19%的病人完全靜脈麻醉，30%的病人完全吸入麻醉，而剩下的 51%的病人接受靜脈吸入複合麻醉。沒有病人使用氟呱利多。這些病人中總共有 5 人發作 QT 延長綜合征，全都是新生兒或嬰兒，且全都是在和 QT 延長綜合征相關的手術中發作，沒有一例是完全因爲麻醉藥物。因此，手術期間 TDF 偶發的發病率（95%可信區間）爲 0/77（0%；0%-5%），而在 QT 延長綜合征相關的手術中的發病率爲 5/81 (6.2%; 2%-14%)。

結論：憑藉優化的圍手術期管理，現代麻醉對於 QT 延長綜合征的患者在高發病率手術中比在沒有對照的可能被建議的病例報告文獻中更安全。我們試驗的建議是圍手術期間 TDF 的風險主要集中在在 QT 延長綜合征首要處理措施失效後需要緊急處理的新生兒和嬰兒身上。

（張秋麗 譯，李士通 審校）

BACKGROUND: Patients with long QT syndrome (LQTS) may experience a clinical spectrum of symptoms, ranging from asymptomatic, through presyncope, syncope, and aborted cardiac arrest, to sudden cardiac death. Arrhythmias in LQTS are often precipitated by autonomic changes. This patient population is believed to be at high risk for perioperative arrhythmia, specifically torsades de pointes (TdP), although this perception is largely based on limited literature that predates current anesthetic drugs and standards of perioperative monitoring. We present the largest multicenter review to date of anesthetic management in children with LQTS.

METHODS: We conducted a multicentered retrospective chart review of perioperative management of children with clinically diagnosed LQTS, aged 18 years or younger, who received general anesthesia (GA) between January 2005 and January 2010. Data from 8 institutions were collated in an anonymized database.

RESULTS: One hundred three patients with LQTS underwent a total of 158 episodes of GA. The median (interquartile range) age and weight of the patients at the time of GA was 9 (3-15) years and 30.3 (15.4-54) kg, respectively. Surgery was LQTS-related in 81 (51%) GA episodes (including pacemaker, implantable cardioverter-defibrillator, and loop recorder insertions and revisions and lead extractions) and incidental in 77 (49%). β-blocker therapy was administered to 76% of patients on the day of surgery and 47% received sedative premedication. Nineteen percent of patients received total IV anesthesia, 30% received total inhaled anesthesia, and the remaining 51% received a combination. No patient received droperidol. There were 5 perioperative episodes of TdP, all in neonates or infants, all in surgery that was LQTS-related,

and none of which was overtly attributable to anesthetic regimen. Thus the incidence (95% confidence interval) of perioperative TdP in incidental versus LQTS-related surgery was 0/77 (0%; 0%-5%) vs 5/81 (6.2%; 2%-14%).

CONCLUSIONS: With optimized perioperative management, modern anesthesia for incidental surgery in patients with LQTS is safer than anecdotal case report literature might suggest. Our series suggests that the risk of perioperative TdP is concentrated in neonates and infants requiring urgent interventions after failed first-line management of LQTS.

人體滲透壓和呼吸調節：健康志願受試者輸注高張生理鹽水後機體高氯血代謝性酸中毒的呼吸代償往往是缺失的

Osmolality and respiratory regulation in humans: respiratory compensation for hyperchloremic metabolic acidosis is absent after infusion of hypertonic saline in healthy volunteers.

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背景：幾個動物實驗說明血漿滲透濃度的改變可能會影響換氣。由血漿滲透濃度增加引起的呼吸抑制往往用來解釋水依賴性體溫調節的抑制作用因爲體液的儲存往往伴隨著體溫的增加。另一方面，妊娠時期呼吸性酸中毒往往和血漿滲透濃度的減少及強離子差有關。我們將研究這個假設，即滲透濃度會影響換氣，因此在所有人機體中血漿滲透壓升高將抑制換氣，而血漿滲透壓降低將刺激機體換氣功能。

方法：我們這項研究的參與者都是健康的男性及女性志願者（ASA I 級），包括 10 個男性志願者（平均年齡 28 歲；年齡範圍 20-40）及 9 個女性志願者（平均年齡 33 歲；年齡範圍 22-43）。所有的女性參與者都處於月經週期的卵泡期及黃體期。高滲透壓主要由靜脈注射 3%的高張生理鹽水誘導產生，而低滲透壓主要是通過飲用自來水產生。收集動脈血樣品來分析電解質、滲透壓及血氣。分別在輸注液體之前及之後行重複呼吸試驗來測定 CO2 的敏感性。

結果：在所有的受試者中高張生理鹽水的輸注都會引起伴有離子差減小的高氯血性代謝性酸中毒。分析這些資料我們發現機體呼吸代償的缺失。基線動脈二氧化碳分壓（PaCO2）平均值（SD）爲 37.8（2.9）mmHg，這仍然保持不變。100 分鐘後 PaCO2 最低爲 37.8 (2.9) mm Hg， P = 0.70，引起 pH 平均從 7.42 (0.02) 降到 7.38 (0.02)，P < 0.001。在液體瀦留期間仍然存在代謝性酸中毒。混合的結果說明飲用水後 80 分鐘 PaCO2 從 38.2mmHg 降至 35.7mmHg，P = 0.002，而 pH 值沒有明顯的改變。pH 7.43 (0.02)- pH 7.42 (0.02), P = 0.14,平均差（可信區間) = pH -0.007 (-0.017 - 0.003).

結論：我們的結果表明滲透壓對換氣功能有影響。在高滲透壓狀態下機體對高氯血性代謝性酸中毒的呼吸代償作用被抑制。液體瀦留會引起血漿滲透壓的降低及代謝性酸中毒，即使離子差的減小和鹽分的儲存比起來是小的，預期的呼吸代償仍然是有的。男性受試者仍然會受刺激產生換氣，因此換氣不受黃體酮水準的影響。我們猜想滲透壓對換氣功能的影響主要是對高滲透壓環境的抑制，這種抑制在低滲透壓時是不存在的。

（張秋麗 譯，李士通 審校）

BACKGROUND: Several animal studies show that changes in plasma osmolality may influence ventilation. Respiratory depression caused by increased plasma osmolality is interpreted as inhibition of water-dependent thermoregulation because conservation of body fluid predominates at the cost of increased core temperature. Respiratory alkalosis, on the other hand, is associated with a decrease in plasma osmolality and strong ion difference (SID) during human pregnancy. We investigated the hypothesis that osmolality would influence ventilation, so that

increased osmolality will decrease ventilation and decreased osmolality will stimulate ventilation in both men and women.

METHODS: Our study participants were healthy volunteers of both sexes (ASA physical status I). Ten men (mean 28 years; range 20-40) and 9 women (mean 33 years; range 22-43) were included. All women participated in both the follicular and luteal phases of the menstrual cycle. Hyperosmolality was induced by IV infusion of hypertonic saline 3%, and hypoosmolality by drinking tap water. Arterial blood samples were collected for analysis of electrolytes, osmolality, and blood gases. Sensitivity to CO2 was determined by rebreathing tests performed before and after the fluid-loading procedures.

RESULTS: Infusion of hypertonic saline caused hyperchloremic metabolic acidosis with decreased SID in all subjects. Analysis of pooled data showed absence of respiratory compensation. Baseline arterial PCO2 (PaCO2) mean (SD) 37.8 (2.9) mm Hg remained unaltered, with lowest PaCO2 37.8 (2.9) mm Hg after 100 minutes, P = 0.70, causing a decrease in pH from mean (SD) 7.42 (0.02) to 7.38 (0.02), P < 0.001. Metabolic acidosis was also observed during water loading. Pooled results show that PaCO2 decreased from 38.2 (3.3) mm Hg at baseline to 35.7 (2.8) mm Hg after 80 minutes of drinking water, P = 0.002, and pH remained unaltered: pH 7.43 (0.02) at baseline to pH 7.42 (0.02), P = 0.14, mean difference (confidence interval) = pH -0.007 (-0.017 to 0.003).

CONCLUSIONS: Our results indicate that osmolality has an influence on ventilation. Respiratory compensation for hyperchloremic metabolic acidosis was suppressed during hyperosmolality. Water loading caused a decrease in plasma osmolality and metabolic acidosis, and although the decrease in SID was smaller compared with salt loading, the expected respiratory compensation was observed. Ventilation was also stimulated in men, therefore independently of progesterone levels. We propose that the influence of osmolality on ventilation consists mainly as depression in conditions of hyperosmolality and that this depression is absent during hypoosmolality.

甘氨酸轉運體抑制劑可減輕癌痛

Relief of Cancer Pain by Glycine Transporter Inhibitors

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背景：近日有研究表明甘氨酸轉運體抑制劑在坐骨神經損傷及糖尿病等有神經病理性疼痛的動物模型中具有鎮痛作用。複雜的生物學機制表明神經性因素在骨腫瘤引起的劇烈疼痛中起一定作用。骨腫瘤改變了阿片類藥物的鎮痛作用，限制其有效性，因此急需找到用於緩解骨癌痛的新藥。

方法：在 C3H/HeN 小鼠股骨遠端髓腔接種溶骨肉瘤細胞 NCTC 2472 建立股骨骨腫瘤小鼠模型。在小鼠股骨腫瘤模型中，我們研究了 GlyT2 抑制劑，ORG 25543 和 ALX 1393,GlyT1 抑制劑，ORG 25935，及在異常疼痛、痛閾值，防禦行爲，和肢體的異常活動等疼痛行爲中通過甘氨酸轉運體 siRNA 下調脊柱甘氨酸轉運蛋白的表達的作用。同時我們也對嗎啡與甘氨酸轉運體抑制劑的聯合作用進行了研究。

結果：GlyT2 抑制劑，ORG 25543 及 ALX 1393,GlyT1 抑制劑、ORG 25935 IV 或口服製劑、下調脊柱甘氨酸轉運蛋白表達可改善接種腫瘤細胞 11 天后骨癌痛小鼠的痛行爲。這種鎮痛效果強大持久。無明顯鎮痛效果的低劑量嗎啡聯合 ORG 25543 可以顯著提高 ORG 25543 的鎮痛效果。小鼠接種腫瘤細胞後第二天，注射 ORG 25543 引起了 3 階段的疼痛反應，最初痛行爲加劇（第 2-4 天），隨後基本消失（5-7 天），接著再次出現。在注射

ORG 25543 一天后鞘內注射士的寧，可短暫的拮抗 ORG 25543 的鎮痛效果。對照組小鼠中，士的寧提高了注射腫瘤細胞四天后的小鼠痛行爲，同時在第 4 到 5 天加劇這一結果。以上證據表明不同機制具有時相依賴性。

結論：甘氨酸轉運蛋白抑制劑聯合或不聯合嗎啡可能是用於治療骨癌痛的新方式，同時也可以進一步研究骨癌痛的發生機制。

（陳凌君 譯，李士通 審校）

BACKGROUND: Recent studies have revealed the antinociceptive effects of glycine transporter (GlyT) inhibitors in neuropathic pain models such as sciatic nerve-injured and diabetic animals. Bone cancer can cause the most severe pain according to complex mechanisms in which a neuropathic element is included. Bone cancer modifies the analgesic action of opioids and limits their effectiveness, and thus novel medicament for bone cancer pain is desired.

METHODS: For the femur bone cancer model, NCTC 2472 tumor cells were injected into the medullary cavity of the distal femur of C3H/HeN mice. Effects of GlyT2 inhibitors, ORG 25543 and ALX 1393, and GlyT1 inhibitors, ORG 25935, and knockdown of the expression of spinal GlyTs protein by GlyTs siRNA on pain-like behaviors, such as allodynia, withdrawal threshold, guarding behavior, and limb-use abnormality, were examined in the femur bone cancer model mice. Effects of morphine in combination with GlyT inhibitor were examined.

RESULTS: GlyT2 inhibitors, ORG 25543 and ALX 1393, and GlyT1 inhibitor ORG 25935 by IV or oral administration or knockdown of the expression of spinal GlyTs protein improved pain-like behaviors at 11 days after tumor transplantation. The pain-relief activity was potent and long lasting. Morphine at a dose with no analgesic activity combined with ORG 25543 further promoted the ORG 25543-induced pain-relief activity. Injection of ORG 25543 on the second day after tumor implantation caused 3 phases of pain responses; pain-like behaviors were initially accelerated (at 2-4 days) and subsequently almost disappeared (5-7 days) and then reappeared. Intrathecal injection of strychnine 1 day after injection of ORG 25543 transiently antagonized the pain-relief activity of ORG 25543. In control mice, strychnine improved pain-like behaviors 4 days after tumor implantation and aggravated the behaviors between 4 and 5 days. The evidence suggests that the different mechanisms are phase-dependently involved.

CONCLUSIONS: GlyT inhibitors with or without morphine may be a new strategy for the treatment of bone cancer pain and lead to further investigations of the mechanisms underlying the development of bone cancer pain.