Cardiovascular Anesthesiology

Research Report

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
(王曉莉 譯，李士通 審校)
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;
- Leven, Lewis J.;
- Veeckman, Luc;
- Pitman, Arkadiy;
- Zafirelis, Zafiris;
- Standl, Thomas


Special Article

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
(俞芳 譯 陳傑 審校)
FOCUS: The Society of Cardiovascular Anesthesiologists’ Initiative to Improve Quality and Safety in the Cardiovascular Operating Room

- Barbeito, Atilio;
- Lau, William Travis;
- Weitzel, Nathaen;
- Abernathy, James H. III;
- Wahr, Joyce;
- Mark, Jonathan B.

Ambulatory Anesthesiology
Research Report

Safety and Efficacy of Drug-Induced Sleep Endoscopy Using a Probability Ramp Propofol Infusion System in Patients with Severe Obstructive Sleep Apnea
  o Atkins, Joshua H.;
  o Mandel, Jeff E.;
  o Rosanova, Giulia

Anesthetic Pharmacology
Research Report

Intravenous Lidocaine Decreases Tumor Necrosis Factor Alpha Expression Both Locally and Systemically in Pigs Undergoing Lung Resection Surgery
  o Garutti, Ignacio;
  o Rancan, Lisa;
  o Simón, Carlos;
  o Cusati, Gabriel;
  o Sanchez-Pedrosa, Guillermo;
  o Moraga, Francisco;
  o Olmedilla, Luis;
  o Lopez-Gil, Maria Teresa;
  o Vara, Elena

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
  o Leeson, Stanley;
Technology, Computing, and Simulation

Research Report

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

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

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.; Kanes, R. Jeffrey; Eisenach, John H.; Schroeder, Darrell R.; Weingarten, Toby N.


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.


Optimal Nasopharyngeal Temperature Probe Placement

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

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


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徵的回顧性佇列研究
(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.


Obstetric Anesthesiology

Research Report
**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


**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 Complications as a Childbirth Patient Safety Indicator**

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


**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


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
溼度的影響

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.


QT 延長綜合徵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.;
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

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
General Article

Research Report

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


Pain Medicine

Research Report

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


Pain and Analgesic Mechanisms
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


Relief of Cancer Pain by Glycine Transporter Inhibitors

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


Regional Anesthesia

Brief Report

Ropivacaine Pharmacokinetics After Local Infiltration Analgesia in Hip Arthroplasty

- Affas, Fatin;
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

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

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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-α (TNF-α) 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-1β, IL-2, IL-10, TNF-α), nuclear factor-κB, 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-α expression in BAL, plasma, and lung samples. Other inflammatory (IL-1β, nuclear factor κB, monocyte chemotactant 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-α 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.

A Novel Index of Hypoxemia for Assessment of Risk During Procedural Sedation
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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 endpoints 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 endpoint 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.

Optimal Nasopharyngeal Temperature Probe Placement

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Anesthesia & Analgesia 2014 119 848–856

背景: 鼻咽部是全麻手术期间最常用来监测体温的部位，但不清楚麻醉医生盲目放置鼻咽温度探头的位置是否恰当。本文研究目的为：1) 探究鼻咽粘膜最接近颅内动脉（ICA）的位置；（2）评估麻醉住院医生和麻醉护士摆放鼻咽温度探头的尖端位置。

方法：研究第一阶段回顾了 100 名患者的增强轴向 CT 图像来确定鼻咽粘膜最接近左或右颅内动脉的位置，随后在矢状位图像中测量此点至鼻孔的距离。研究第二阶段用鼻内窥镜评估由麻醉住院医生（224 名患者）或麻醉护士（116 名患者）放置的鼻咽温度探头位置。位置不佳时将探头重新定位到最佳的位置，并记录两者的温度差异。

结果：CT 图像显示，分别有 60%，38% 及 2% 的患者，其粘膜最接近颅内动脉的最佳位置在鼻咽部的上部，中部及下部。颅内动脉和上部鼻咽部粘膜的平均距离较与下部之间的要更短（女：9.4 vs 16.8 mm，p<0.001；男：12.4 vs 18.8 mm，p<0.001）。通过下鼻道从鼻孔至鼻咽部上部的平均距离（95%预估区间）女性为 9.1（8.1-10.2）cm，男性为 9.7（8.6-10.3）cm。由住院医师和护士正确地将温度探头放置在鼻咽部上部或中部的概率分别为 43%（95%的可信区间，37%-49%）和 41%（95%的可信区间，36%-50%）。当温度探头在鼻腔位置不佳时，测得鼻咽部上部的体温中位数差为 0.2℃（0.15℃—0.25℃）。

结论：鼻咽粘膜最接近颅内动脉的位置为鼻咽腔上部或中部，鼻孔到鼻咽部上 1/3 的深度大致为 10cm，医生盲目地放置鼻咽部温探头，其最佳位置的放置率低于 50%。
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°C (0.15°C–0.25°C).

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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結果：平均血清孕酮濃度為 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

Patino, Mario MD; Schultz, Lindsay BS; Hossain, Monir PhD; Moeller, Jennifer CRNA; Mahmoud, Mohamed MD; Gunter, Joel MD; Kurth, C. Dean MD

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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
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.
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.
**Method:** This randomised controlled trial meta-analysis 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 (equivalent to morphine) 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 to fentanyl, despite there being similar total opioid consumption between those groups.

**Ropivacaine Pharmacokinetics After Local Infiltration Analgesia in Hip Arthroplasty**

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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.

吸人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：針對體重為 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®電脳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，將揮發罐刻度調整為 0，並且新鮮氣體流量設置為 8L/min。肺泡通氣量 (VA) 保持為 4L/min，直到 VRG 達到蘇醒麻醉深度，約為 0.33 MAC。然後將 VA 調整為近乎窒息流量 0.1 L/min 和窒息流量 0.0 L/min，並監測 VRG 麻醉深度，當達到 0.5 MAC 或者大於 0.5 MAC，判斷為重度再麻醉；若 VRG 麻醉深度達到 0.33 MAC 並小於 0.5 MAC，判斷為輕度再麻醉。此外 VRG 在麻醉深度達到 0.33 MAC 時，研究判斷為最低 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 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，吸入麻醉 4h 增加呼吸深度至 0.8 MAC，其中 2h 地氟醚吸入麻醉可達 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.
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 epidural anesthesia with epidural fentanyl analgesia. Since epidural fentanyl is quickly reabsorbed systemically, we hypothesized that there would be no difference in long-term oncologic 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 general anesthesia 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.

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為五個等級。

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結參數。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 scheduled for prophylactic platelet transfusion before the
insertion of a central venous catheter. The objectives were to evaluate the effect and duration of pro-
phylactic 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 prophylactic platelet 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 con-
ventional hematological tests, thromboelastometry (ROTEM) assays (EXTEM and FIBTEM), multi-
ple 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, ac-
cording 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 trans-
fusion (P < 0.0001) and did not change 4 hours after transfusion. Clotting time EXTEM was de-
creased 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 and platelet aggregation on Multiplate appear to persist between 1 and 4 hours after transfusion.

**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，計劃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：問卷的答覆率為 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為 3900，而無 PPH 預案的單位的年分娩量中位數為 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 預案是否存在的重要因素。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 預案的計劃獲得巨大收益。未來的工作需要在非大學附屬醫院中評估和推行 PPH 預案。
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 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.
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。為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為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°C ± 1.1°C; HME3L: 29.3°C ± 1.2°C）與無 HME 組（1L: 27.0°C ± 1.2°C; 3L: 27.1°C ± 1.5°C; 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 H2O/L] > [HME3L: 23 ± 2 mg H2O/L] > [1L: 17 ± 1 mg H2O/L] > [3L: 14 ± 1 mg H2O/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溫度和濕度，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。

（江淩慧譯 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°C ± 1.1°C; HME3L: 29.3°C ± 1.2°C) compared with no-HME groups (1L: 27.0°C ± 1.2°C; 3L: 27.1°C ± 1.5°C; 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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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] vs 1.02 [-0.31, 0.57], P = 0.56), SAA 7 days postoperatively (1.32 [0.68, 2.59] vs 0.97 [0.65, 1.83] vs 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] vs -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.
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 (AMPA receptor) 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

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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）。患者可能需要轉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 組防止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，而對照組為 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。
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.
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.
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 carrageenan, 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.

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.

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.
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.

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

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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.
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 PSIs 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.
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 mult centered 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.

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

Moen V1, Brudin L, Rundgren M, Irestedt L.
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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 hypooosmolality 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 hypooosmolality.

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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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為，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 GlyT2s protein by GlyT2 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 GlyT2s 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.