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聚焦：旨在促进心血管手术室质量和安全性的心血管麻醉医生协会倡议

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

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为了寻找一种促进心血管外科手术室(CVOR)的质量和安全性的严格科学方法，心血管麻醉医师协会(SCA)首次于 2005 年提出倡议：心血管手术完美标准化系统。本项目由 SCA 基金赞助，主要目的在于区分危害以及发展基于证据的临床决策以提高心脏手术的安全性。危害是指任何可能导致潜在的可预防性的不良事件。聚焦策略性计划具体包括以下三个目标：(1) 确认 CVOR 中存在的危害；(2) 危害分级并发展降低风险的手术；(3) 推广此类手术。总之，此项倡议，通过各学科人员的配合，包括临床医学、人因工程、心理学以及组织社会学等，已经区分和记录了每天发生在 CVOR 内显而易见的危害。一些比较常见的可以降低心脏手术安全性和质量的例子包括工作团队内人员不足，手术室设计缺陷，技术不足以及未能遵守最佳操作。目前有数项计划致力于更好地理解这些危害以及研究缓解措施。通过倡议，SCA 开启了科学引导质量和安全性改进之旅。然而，这是一条漫长且充满艰辛的必然道路。

（俞芳 译 陈杰 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.

肺切除术期间静脉注射利多卡因降低猪局部和全身肿瘤坏死因子 α 的表达

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

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背景：肺切除手术与炎症反应相关。单肺通气（OLV）的使用似乎增加该反应的可能性。已经对不同的预防和治疗措施进行了研究以防止 OLV 继发性肺损伤。利多卡因是常用的局部麻醉药物，具有抗炎活性。本研究的主要目的是探讨在肺切除手术 OLV 期间，静脉注射利多卡因对肺肿瘤坏死因子（TNF-α）表达的影响。

方法：十八只猪行左肺尾叶切除术。动物随机分为 3 组：对照组，利多卡因组和假手术组。所有动物接受全身麻醉。利多卡因组动物在手术过程中持续静脉输注利多卡因（1.5 mg/kg/h）。假手术组动物只行开胸手术。OLV 开始前、结束时、手术结束时和手术后 24h 收集支气管肺泡灌洗（BAL）液和血浆样品。术前从左尾叶（基线），以及术后 24h 从纵隔叶和左上叶采集肺活检标本。样品速冻并存储用于检测以下炎症标志物水平：白细胞介素（IL）-1β，IL-2，IL-10，TNF-α，核因子 κB，单核细胞趋化蛋白-1，诱导型一氧化氮合酶，内皮型一氧化氮合酶。同时检测细胞凋亡标志物（caspase-3，caspase-9，Bad，Bax 和 Bcl-2，）。此外，在 BAL 液和血浆样品中确定基质金属蛋白酶与一氧化氮代谢物水平。非参数检验用来检验统计意义。

结果：OLV 引起肺损伤伴随 BAL、血浆和肺样本中 TNF-α 的表达增加。其他炎症（IL-1β，核因子 κB，单核细胞趋化蛋白-1）和凋亡（caspase-3，caspase-9 和 Bax）标记物也增加。静脉注射利多卡因使同一样品 TNF-α 水平与对照组相比显著降低。利多卡因也减少在对照组中观察到的炎症和细胞凋亡的变化。血流动力学、血气和气道压力在所有组中相似。

结论：本研究结果表明，利多卡因可以通过减轻促炎细胞因子和肺细胞凋亡的表达来预防 OLV 引起的肺损伤。利多卡因可能有助于防止 OLV 肺外科手术引起的肺损伤。

（徐欢 译 陈杰 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 伪 (TNF-伪) 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-伪, 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-伪 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-伪 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.

评估镇静过程中风险的一项新型低氧血症指标

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

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背景：操作镇静方法在多项操作中必不可少。镇静在安全性方面有优势，但是并非全无风险。因其罕有发生，故在临床研究中使用临床预后来评估风险较为困难。因此，替代终点常代替临床结果而用于临床研究。由于一个临床医师通过整合一项生理参数的多个方面来决定潜在风险，替代终点应该采取类似方法。本研究确认并检测了一种可能用于临床研究的新型替代终点的可行性，即氧饱和度曲线下面积(AUCDesat)。引入一篇麻醉医师记录的患者镇静综述，旨在评价替代终点与麻醉风险理解的关联性。

方法：本研究为一项对麻醉医师感知风险进行评估的析因分析。由 13 位经美国训练并通过职业认证的麻醉医师将生理参数进行分级作为风险指标，然后从 SEDASYS 系统中 3 组完整的镇静研究中回顾分析了 204 个病例。回顾分析后，每位麻醉医师基于过度镇静相关后遗症的风险认知对每个病例给予 likert 评分。后者经分析后决定其与去饱和事件的发生/未发生、持续、深度、数量和涉及每个组成的 AUCDesat 的关系。

结果：麻醉医师们将动脉血氧列为事后评估风险的最重要因素（平均秩次 4.69/5，P=0.0007 与次高归因指数—呼吸频率 比较，N=13）。与 AUCDesat 独立因素、去氧饱和度二元分析（rs=0.73）、去氧饱和深度（rs=-0.70）、去氧饱和持续时间（rs=0.70）和去氧饱和发生率（rs=0.55）比较，AUCDesat 与 Likert 评分相关性更好（rs=0.85） (4 项比较 rs=0.85，P<0.0001)。

结论：麻醉医师确认动脉血氧饱和度为评估镇静风险和潜在不良临床预后的最重要的生理参数。AUCDesat 是一项由去氧饱和度持续时间、发生率和深度整合的复合指标，与 Likert 评分有更好的相关性。AUCDesat 给出的仅是一个数值变量，在临床镇静研究中对不良预后风险评估方面是一个理想的终点指标。需要 AUCDesat 和真实生理预后相关的进一步研究来定义这项终点指标。

（ 潘志敏 译 陈杰 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.

最佳的鼻咽温度探头位置

Optimal Nasopharyngeal Temperature Probe Placement

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背景：鼻咽部是全麻手术期间最常用来监测体温的部位，但并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颈内动脉(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颈内动脉的位置，随后在矢状位图像上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，其粘膜最接近颈内动脉的最佳位置在鼻咽部的上部，中部及下部。颈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%预测区间）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异（95%CI）为 0.2℃（0.15℃—0.25℃）。

结论：鼻咽粘膜最接近颈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%。

（殷文 译 陈杰 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.

血清孕酮浓度与麻醉镇痛需求的关系：一个关于接受剖宫产分娩产妇的前瞻性观察研究

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：在临床实践中，孕妇相比非妊娠妇女接受全麻时有着更低的麻醉药物需求。虽然激素变化，如与妊娠相关的孕激素可能影响吸入麻醉药的最小肺泡浓度，麻醉或镇痛需求和足月妇女孕激素水平的相关性还未被研究。这项研究试图确定麻醉或镇痛需求和母体孕酮血药浓度的关系。

方法：研究了 100 例孕龄大于 36 周，择期行全麻下剖腹产的孕妇。采集静脉血测定孕妇孕激素浓度。使用硫喷妥钠 4-5 mg/kg 和罗库溴铵 0.8 mg/kg 行麻醉诱导。麻醉维持期间，以动脉血压，心率，和脑电双频指数为基础，吸入 0.5%-2%七氟醚、50%氧化亚氮维持麻醉。记录生命体征、脑电双频指数、呼气末七氟醚浓度和每小时七氟醚用量。同时记录术后第 2h、第 24h 和第 48h 疼痛视觉模拟评分和累积镇痛药物用量。

结果：平均血清孕酮浓度为 128.2±83 ng/mL。每小时七氟醚用量与血清孕酮浓度与之间存在显著的负相关（Pearson 相关系数 r＝−0.26；95%置信区间，0.44 到−−0.05，P = 0.01）。累计镇痛药物用量在术后第 2 小时（R =−0.20，P = 0.05），第 24 小时（R =−0.25，P = 0.02），和第 48 小时（R =−0.28，P = 0.01）与血清孕酮浓度呈负相关。高孕酮水平妇女（高于中位数值）相对于低孕酮水平妇女（低于中位数值），每小时七氟醚用量（P = 0.02）和术后 48 小时累积镇痛药物用量（P = 0.02）更少。

结论: 近足月产妇对麻醉和镇痛药物需求降低可能部分取决于血清孕酮浓度。

（李慧 译 陈杰 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.

在儿科围术期患者中无创血红蛋白监测的趋势和准确性

Trending and Accuracy of Noninvasive Hemoglobin Monitoring in Pediatric Perioperative Patients

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背景： Rainbow Pulse CO-Oximetry 技术® (Masimo Corporation, Irvine, CA)提供了对动脉血红蛋白浓度的连续无创监测方法（SpHb）。在接受可能大量失血手术的儿童中，对比由该创新监测仪得到的 SpHb 与普通实验室得到的血红蛋白浓度（Hb）来评估该设备的趋势和准确性。

方法：Hb 浓度分别由 Pulse CO-Oximetry 和传统血红蛋白分析仪记录。使用回归分析和四象限散点图来评估 SpHb 和 Hb 测定值的变化趋势（ΔSpHb 和 ΔHb）。计算 SpHb 的偏

倚、精度和 SpHb 的协议范围以及与 Hb 对比体内校正 SpHb（SpHb-首次偏倚相对 Hb）的协议范围。

结果：收集来自于 46 名年龄在 2 个月至 17 岁，血红蛋白浓度在 16.7g/dL 至 7.9g/dL 之间的患儿形成 158 组 SpHb-Hb 数据对和 105 个变化对（ΔSpHb 和 ΔHb）。为了评估趋势，变化（ΔSpHb 和 ΔHb）拟合成曲线后，显示出这两者呈正相关（ΔSpHb = 0.022 + 0.76ΔHb），相关系数 r = 0.76，95%CI（置信区间） = 0.57–0.86。相对 Hb 的 SpHb 和体内校正后的 SpHb，其偏倚和精度分别为 0.4 ± 1.3 g/dL 和 0.1 ± 1.2 g/dL。在校正前后的协议范围分别为−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（从参考 Hb 浓度）从 4.1% ± 11.9%下降至 0.7% ± 11.3% (P 值 = 0.01)。在研究过程中发现偏差值不随时间飘移。在测试 SpHb 相关的患儿人口学和生理因素中，只有探头区域的灌注指数与 SpHb 有微弱的相关。

结论：在正常血红蛋白和轻度贫血的儿童中，SpHb 的准确性与之前在成人中的报道相似，且除仅与灌注指数有微弱关系，其余与患儿的人口学和生理状态无关。在正常血红蛋白浓度和轻度贫血的儿童中，SpHb 和 Hb 的趋势呈正相关。但在中重度贫血儿童中仍需更多研究。

（林雨轩 译 陈杰 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.

麻醉预处理抑制异氟烷介导的发育中大鼠大脑的细胞凋亡

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

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背景：正如之前所做的神经细胞培养试验所示，本研究假设短时间暴露于异氟烷（ISO）的预处理（PC）会降低长期暴露于异氟烷的新生大鼠的神经性退化。

方法：将 7 日龄的 SD 大鼠随机分为 3 组：对照组，1.5% ISO 组及 PC+1.5% ISO 组。对照组暴露于载气（30%氧气平衡于氮气中）中 30min，然后次日再次暴露于载气中 6 小时；1.5% ISO 组暴露于载气中 30min，然后次日暴露于 1.5% 异氟烷中 6 小时；PC+1.5% ISO 组暴露于 1.5% ISO 中 30min 进行预处理，然后次日暴露于 1.5% ISO 中 6 小时。在暴露 2 小时后收集血标本和脑组织标本以测定神经退行性生物标志物，包括 caspase-3、S100β、caspase-12 以及自噬标志物 Beclin-1.

结果：Western blot 试验结果表明，与异氟烷预处理组及对照组相比，长时间暴露于异氟烷中能显著增加 7 日龄大鼠大脑皮层中活化型 caspase-3 的表达。然而，并没有检测到其他神经元损伤的标志物有显著差异。

结论：异氟烷介导的 7 日龄大鼠脑中活化型 caspase-3 增加，可由短暂麻醉暴露预处理所改善，然而其他神经元损伤的标志物并没有检测到差异。

（王筱婧 译 陈杰 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.

硬膜外给予阿片类药物行术后镇痛效果最好且副作用最少：一项随机对照试验的 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：硬膜外阿片类药物被广泛用于椎管神经阻滞和术后镇痛。然而,阿片类药物的镇痛疗效和副作用的个体差异仍有争议。

方法：此项随机对照试验的 meta 分析，比较至少 2 种急性术后连续硬膜外输注镇痛方式至少 24 小时以上。个体研究数据使用反向方差法加权。主要结果为疼痛视觉模拟评分量表(VAS)评分。次要结果包括阿片类药物的副作用，如瘙痒、术后恶心呕吐(PONV)、镇静、低血压和呼吸抑制。

结果：24 项试验中有 19 项包含比较以下阿片类药物中的两种：吗啡、芬太尼或舒芬太尼。研究对象共 1513 名。对手术类型进行汇集分析发现在术后任何时候 VAS 疼痛评分并无临床显著差异。与芬太尼相比，吗啡术后 PONV(OR = 1.91，95%可信区间，1.14 - -3.18；P = 0.014)，瘙痒(OR = 1.64，95%可信区间，0.98 - -2.76；P = 0.162)发生率更高。阿片类药物消耗总量仅在于吗啡和芬太尼的比较研究中有差异，吗啡组的患者药物需要量减少 1.2mg（相当于吗啡）(95% CI, 0.27–2.18)。除两个研究外其余试验组使用辅助镇痛剂相似。

结论：根据 VAS 疼痛评分，硬膜外阿片类药物之间的镇痛效果是相似的。这些镇痛药的相似之处可能反映了同时使用硬膜外局麻药和阿片类药物镇痛的通常方法，根据患者的疼痛状况确定注入速率。关于副作用方面，尽管这些组之间阿片类药物消耗总量相似，吗啡的 PONV 和瘙痒发生率可能比芬太尼更高。

（张帆 译 陈杰 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.

全髋关节置换术中局部浸润镇痛后罗哌卡因的药代动力学

Ropivacaine Pharmacokinetics After Local Infiltration Analgesia in Hip Arthroplasty

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本研究纳入 15 名择期行全髋关节置换手术的病人，在其局部浸润镇痛后 30 小时期间通过液相质谱法检测血浆中罗哌卡因的浓度。罗哌卡因血浆浓度的 95%预测范围的上界值为 0.032mg/L。有报道显示当副作用明显需停止静脉注射的罗哌卡因动脉血中浓度 0.34-0.85mg/L。在局部浸润镇痛的第一个 24 小时，α-1 酸性糖蛋白与未结合罗哌卡因部分没有相关性。在本研究中未发现全身麻醉毒性的症状或反应。出现不良反应的 Clopper-Pearson95%置信区间的上限为 0.218。

（隋永恒 译 陈杰 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.

吸入麻醉后的低通气可发生再麻醉

Hypoventilation After Inhaled Anesthesia Results in Reanesthetization

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背景：自从吸入麻醉以来，发生低通气的原因很多。在本研究中，我们研究了吸入麻醉在导致低通气中发挥的作用以及再麻醉发生的机制。

方法：针对体重为 70 公斤的模拟人，分别利用地氟醚，七氟醚和异氟醚行吸入麻醉，利用 Gas Man® 计算机模拟系统监测麻醉气体的摄取和排泄。对挥发罐进行设置和调整，从而使得吸入麻醉分布容积丰富的组织（VRG）包括脑，麻醉深度能够迅速达到 0.75 MAC（最低肺泡有效浓度），1.0 MAC 和 1.5 MAC，并可保持此麻醉深度 1，2，4，6 小时。在模拟吸入麻醉结束前，将挥发罐刻度调整为 0，并且新鲜气体流量设置为 8L/min。肺泡通气量（VA）保持为 4L/min，直到 VRG 达到苏醒麻醉深度，约为 0.33 MAC。然后将 VA 调整为近乎窒息流量 0.1 L/min 和窒息流量 0.0 L/min，并监测 VRG 麻醉深度，若达到 0.5 MAC 或者大于 0.5 MAC，判断为重度再麻醉；若 VRG 麻醉深度达到 0.33 MAC 并小于 0.5 MAC，判断为轻度再麻醉。此外 VRG 在麻醉深度达到 0.33 MAC 时，研究判何为最低 VA 从而可防止重度再麻醉的发生。

结果：吸入麻醉 1h 后，所有模拟患者在达到 0.75 MAC 和 1.0 MAC 时均未发生轻度和重度再麻醉。吸入麻醉 4h 到 6h 后，不同麻醉气体使模拟患者达到 1.0 MAC 和 1.5 MAC，并且在接近窒息和窒息 VA 时均发生重度再麻醉。利用最小肺泡 VA 可防止重度再麻醉发生，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。对于所有不同类型吸入麻醉的模拟患者，导致再麻醉的来源是肌肉组织，4h 吸入麻醉可达到 0.8 MAC，其中 2h 地氟烷吸入麻醉可达到 0.75 MAC。吸入麻醉 6h 后，脂肪组织麻醉深度小于 0.15 MAC.

结论：吸入麻醉后低通气可能导致再麻醉。肌肉组织是麻醉和再麻醉气体的储存分布部位，脂肪组织则亦是麻醉气体的容器并可促使再麻醉的发生。不同麻醉气体包括地氟醚，七氟醚和异氟醚，吸入麻醉 4h 达到 1.0 MAC 后，如果发生严重低通气，则由于肌肉中麻醉气体的释放，导致不同程度的再麻醉。

（王嘉兴译 薛张纲校）

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.

根治性前列腺切除术后结局：用芬太尼进行全身麻醉和区域麻醉镇痛比较：配对队列研究

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： 肿瘤手术应用区域麻醉能改善肿瘤预后。其中一个可能的机制是静脉应用阿片类药物可能引起免疫抑制的减少。我们设计了一项回顾性队列配对研究，全身麻醉静脉应用芬太尼，硬膜外麻醉时硬膜外使用芬太尼镇痛，比较二者根治性前列腺切除术后的长期结

局。由于硬膜外的芬太尼迅速全身重吸收，我们推测 2 组之间长期的肿瘤预后无明显差异。

方法： 选择了 486 名 1991 年 1 月 1 日和 1996 年 1 月 31 日之间在硬膜外麻醉下进行前列腺切除术的患者，另有一组患者应用芬太尼静脉全身麻醉，基于年龄（±5 岁），手术时间（±1 年）和前列腺癌病理学的基线与前者 1:1 配对。对肿瘤的长期预后和全因死亡率进行了比较。采用分层比例风险回归模型进行统计分析，与行硬膜外麻醉和芬太尼镇痛的患者相比，仅仅使用芬太尼全身麻醉的患者风险比>1 表示效果更差。

结果：对手术切缘阳性和辅助治疗进行调整后，与接受硬膜外麻醉的患者比较，全身麻醉组没有发现前列腺癌复发风险增加（风险比[HR]=0.79，95％可信区间[CI]为 0.60-1.04），全身肿瘤进展（HR=0.92，95％CI 为 0.46-1.84），癌症特异性死亡率（HR=0.53，95％CI 为 0.18-1.58），总死亡率（HR=1.23，95％CI 为 0.93-1.63）。

结论： 与静脉使用阿片类药物全身麻醉相比较，硬膜外麻醉和芬太尼镇痛对根治前列腺癌患者的肿瘤预后没有改善。

（吴赤译 薛张纲校）

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.

利用床旁检测和流式细胞术评估骨髓衰竭病人插入中心静脉导管前预先输注血小板的效果和持续时间

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：骨髓衰竭和严重血小板减少的病人通常在操作前预先输注血小板。尽管如此，这样的输注在临床上的效果还没有确定。我们在行中心静脉穿刺前预先输注血小板的骨髓衰竭病人中做了一个前瞻性观察研究，我们的目的是评估骨髓衰竭致血小板减少的病人行中心静脉穿刺前预先输注血小板的效果和持续时间。

方法：39 个血小板计数低于 50 × 10/L 的骨髓衰竭成年病人在预先输注血小板前依次登记，他们均行锁骨下中心静脉穿刺。分别在输注血小板前、输注后 1 小时和输注后 4 小时三个时间点取血液标本。利用常规血液学检查、转动栓塞弹力测定法（EXTEM 和 FIBTEM）、多重电极集合度测定法来评估凝血情况，包括磷酸腺苷、胶原蛋白和凝血酶受体激动多肽，同时用流式细胞术检测 P-选择素 CD62P 和活化糖蛋白 PAC-1 在血小板的表达。根据对不良反应常用的术语标准把出血并发症分为五个等级。

结果：此项研究包括 17 位女性和 22 位男性。输注后 1 小时血小板计数从 24 × 10/L（18-32）增加到 42 × 10/L（31-50），但在输注后 4 小时并没有明显不同（40 × 10/L (29-50)）。血栓弹力测定 EXTEM 得出最大凝血块强度在输注后 1 小时从 38mm（32-45）增加到 46mm（41-52），并且在输注后 4 小时没有变化。凝血时间在输注后 1 小时从 58.5 秒（50-78）降至 53 秒（45-61），在输注后 4 小时（57 秒）也没有明显不同。 FIBTEM 得出的输注后的结果完全没有变化。所有的多平台分析结果在输注后 1 小时明显增加，在 4 小时没有变化。流式细胞术分析显示出不同的结果,却没有总体趋势。

结论：在血小板减少的骨髓衰竭病人中预先输注血小板可以通过增加血小板的数量而不是增强血小板的功能来改善血液凝集参数。改善的凝血参数和血小板聚集会持续存在输注后 1-4 小时。

（吕越昌译 薛张纲校）

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.

美国大学附属医院产科麻醉产后出血预案使用情况的研究

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

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背景：产后出血（PPH）是导致产妇在住院和分娩中发生严重产后并发症，心跳骤停以及死亡的重要原因。计划性诊疗已被证实可在多种情况下改善患者预后。National Partnership for Maternal Safety 推荐在美国所有的妇产科机构都应实施 PPH 预案。这项研究旨在确定在美国的大学附属医院的产科中，PPH 预案的使用的情况。我们假设大部分（＞80%）的大学附属医院的产科麻醉拥有合适的 PPH 预案。

方法：调查由一个专家小组实施。调查的内容包括医院的特点，PPH 预案的可行性、计划开展这份预案以及预案包含的内容，包括即将来临的国家妇产科安全协会关于产后出血的安全倡议。电子调查问卷通过电子邮件发放给美国 104 位大学附属医院产科麻醉的负责人。回复的问卷按照 PPH 预案的使用进行适当的分层。单因素分析用来统计描述问卷答复的特征，二项分布用来评价 PPH 预案使用的分布概率。

结果：问卷的答复率为 58%。在回复中，拥有 PPH 预案的单位小于预期假设（P=0.03），回复的单位中，约 67%拥有 PPH 预案（N=40，95%可信区间[CI]: 53%-78%）。在回复问卷的单位中，有 PPH 预案的单位的年分娩量中位数为 3900，而无 PPH 预案的单位的年分娩量中位数为 2300，但二者在剖宫产率（P = 0.73）及产后出血发生率（P = 0.69）上没有差别。回复及未回复问卷单位的年分娩量没有显著差别（P = 0.06），提示每年分娩量＞3200 的大学附属医院比分娩量较小的医院更有可能有适当的 PPH 预案（比数比 3.16（95% CI: 1.01-9.90)。研究中，在校正未回复医院中的分娩量后，所有学术中心的产科麻醉中 67%（95% CI: 55%-77%）拥有合适的 PPH 预案。医院的规模扩大与 PPH 预案的存在并不相关。95%拥有 PPH 预案的医院以及 90%没有 PPH 预案的医院中都有大量输血的常规（95% CI of difference: -7% to 7%）。在回复问卷的医院中，57%拥有产后出血的急救小组，这个比率在有或无 PPH 预案的单位中没有差别[均差： 4%， 95% CI (-24% to 32%)]。

结论：尽管对国家患者安全质量改进的强调越来越多，在美国，仍然有至少 20%的产科麻醉中心没有 PPH 预案。分娩量是最重要的预测 PPH 预案是否存在的变量。通过关注小分娩量的单位，可以使国家努力实施在所有大学附属医院中广泛应用 PPH 预案的计划获得巨大收益。未来的工作需要在非大学附属医院中评估和推行 PPH 预案。

(杜芳译 薛张纲校)

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.

儿科病人使用高/低新鲜气体流量以及是否使用热湿交换器对 dräger Primus 麻醉工作站湿度的影响

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：全麻下预防干燥气体对气道上皮有害影响的最低绝对湿度被认为是 20mgH_2O/L。由于儿童分钟通气量小，我们假定儿童与成人相比呼吸回路湿度较低。Primus 麻醉工作

站（Dräger Medical, Lübeck, Germany）具有一个内置的加热器来加热病人呼出的气体。热湿交换器（HME）是一种可以用来进一步加湿和加热吸入气体的装置。为了评价小儿麻醉时呼吸回路的加湿性能，我们比较了低或高新鲜气体流量（FGF）以及是否使用热湿交换器时吸入气体的温度和湿度。

方法：根据 Primus 麻醉工作站呼吸回路中的肺通气方式的不同，将四十名儿童随机分为 4 组，分别是低 FGF（1 L/min）HME（Pall BB25FS, Pall Biomedical, East Hills, NY）组、低 FGF 无 HME 组、高 FGF（3 L/min）HME 组、高 FGF 无 HME 组。我们分别在病人连接呼吸回路 10、20、40、60、80 分钟后测定吸入气体的温度和绝对湿度。

结果：研究发现，吸入气体平均温度 HME 组（HME1L: 30.3℃ ± 1.1℃; HME3L: 29.3℃ ± 1.2℃）与无 HME 组（1L: 27.0℃ ± 1.2℃; 3L: 27.1℃ ± 1.5℃; P < 0.0001）相比较高。吸入气体的平均绝对湿度 HME 与无 HME 组相比较高，低流量组与高流量组相比较高（[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）。

结论：小儿呼吸回路中低或高 FGF 都不能满足降低呼吸道失水风险的最低湿度水平。使用 HME 可以增加吸入气体的湿度和温度，使其更接近生理值。低 FGF 可以提高 HME 的效率从而增加吸入气体的湿度值。因此，小儿麻醉期间低 FGF 并联合使用 HME 是保存吸入气体温度和湿度的最有效方式。

（江凌慧译 薛张纲校）

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.

血清抗胆碱能活性与老年患者术后认知功能障碍的关系

Serum Anticholinergic Activity and Postoperative Cognitive Dysfunction in Elderly Patients

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背景：大脑胆碱能递质对认知功能具有关键性作用，并且假说认为围手术期给予抗胆碱能药物可引起术后认知功能障碍（POCD）。我们假设围手术期血清胆碱能活性（SAA）的升高与老年患者术后认知功能障碍有关。

方法：研究对象是年龄＞65 岁并在标准化全身麻醉（硫喷妥钠、七氟醚、芬太尼和阿曲库铵）下行择期大手术的 79 位患者。使用扩展版的 CERAD-神经心理学评价系列对其术前及术后 7 天的认知功能进行评估。POCD 定义为在至少两个测试变量中术后降低＞1Z 得分。在进行认知测试的同时，SAA 也在术前及术后 7 天进行检测。使用 Hodges-Lehmann 中位差异及它们的 95%可信区间进行组间比较。

结果：在完成这项研究的患者中，46%出现了 POCD。有术后认知功能障碍的患者较没有术后认知功能障碍的患者稍年老些并且受教育程度相对低。两组患者的性别、人口统计学校正后的认知功能基线及麻醉时间没有有意义的差异。两组患者的术前 SAA 水平（pmol/mL，中位数[四分位差]/中位数差[95%可信区间]，P; 1.14 [0.72, 2.37] vs 1.13 [0.68, 1.68]/0.12 [-0.31, 0.57], P = 0.56）、术后 7 天的 SAA 水平（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 的变化（0.08 [-0.50, 0.70] vs -0.02 [-0.53, 0.41]/0.1 [-0.31, 0.52], P = 0.62）均没有较大差异。SAA 的变化和认知功能的变化没有显著的关系（Spearman 秩相关系数术前为 0.03 [95% CI, -0.21, 0.26]，术后为-0.002 [95% CI, -0.24, 0.23]）。

结论：本研究中的患者 SAA 基线低并且围手术期的抗胆碱能负荷临床上讲较轻微，虽然在某些患者中相关性不能被排除，但是我们的分析认为 POCD 可能并不是围手术期抗胆碱能药物使用的直接结果，而更倾向于其他机制。

(盖晓冬译 薛张纲校)

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 抑制剂通过调节 AMPA 受体的表达和功能来抑制瑞芬太尼诱导的术后痛觉过敏

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：很多研究证实单纯应用瑞芬太尼可提高痛觉敏感性。我们之前报道了激活糖原合酶激酶-3β 可通过调节脊髓背角内 N-甲基-D 天冬氨酸受体的可塑性来促进瑞芬太尼诱导的痛觉过敏。本研究中，我们证实了糖原合酶激酶-3β 抑制剂通过调节脊髓背角内 AMPA 受体的表达和功能来抑制瑞芬太尼诱导的术后痛觉过敏。

方法：首先，我们建立瑞芬太尼诱导的痛觉过敏模型，在开始输注瑞芬太尼前 1 天、后 2 小时、6 小时、1 天、2 天、3 天、5 天以及 7 天时测定切口模型的机械痛以及热痛情况。应用 western blot 法测定脊髓背角内 AMPAR 亚单位（Glu-R1 和 Glu-R2）运输、AMPAR 亚单位磷酸化情况以及糖原合酶激酶-3β 活性。另外，我们应用全细胞膜片钳记录法来分析抑制糖原合酶激酶-3β 对脊髓背角内 AMPA 受体诱发电位的影响情况。

结论：瑞芬太尼诱导的术后痛觉过敏的裸鼠脊髓内膜 AMPA 受体亚单位 Glu-R1 上调(275 ± 36.54 [mean ± SD] vs 100 ± 9.53, P = 0.0009)。应用选择性糖原合酶激酶-3β 抑制剂，如氯化锂和 TDZD，可改善瑞芬太尼诱导的术后痛觉过敏，并使 AMPA 受体亚单位 Glu-R1 下调(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经元内 AMPA 受体诱发电位的频率和波幅(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)，而氯化锂和 TDZD 均可抑制该效果。瑞芬太尼诱导的术后疼痛可促进 pGluR1 Ser845 和 Rab5 的表达,该效果同样可被氯化锂或 TDZD 抑制。

总结：上述结果表明抑制糖原合酶激酶-3β 导致瑞芬太尼诱导的术后痛觉过敏症状改善是通过下调细胞膜上 AMPA 受体 Glu-R1 的表达以及脊髓背角内 pGluR1 和 Rab5 的表达来实现的。

（郝光伟译 薛张纲校）

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.

血红蛋白氧载体 HBOC-201 在非心脏手术病人中使用的安全性和有效性的随机多中心研究

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：我们介绍的是 1998-1999 年血红蛋白氧载体未公开发表的研究结果。

方法：在一个多中心、随机的、单盲的对比研究中，HBOC-201 对比同种异体的红细胞灌注，非心脏手术患者接受最多 7 个单位 HBOC-201（n=83）或红细胞（n=77）。患者可能转化红细胞更安全或者其他推论。同种异体红细胞输注的有效作用终点被消除和/或减少需要 28 天。

结果：在 HBOC-201 组避免红细胞输注的患者比例是 0.427（95%可信区间，0.321-0.533）。HBOC-201 组被试者平均接受 3.2 个单位红细胞，而对照组为 4.4 个单位（P=0.004）。29 名（95.2%）HBOC-201 组被试者和 72 名（93.5%）红细胞组被试者出现不良反应，认为分别与 59 名（77.1%）和 18 名（23.4）被试者研究性治疗有关。HBOC-201 组和红细胞输注组 30 天死亡数分别是 5 名（6.0%）和 4 名（5.2%）患者（P=1.00），严重不良反应发生率分别是 24（28.9%）和 20（26.0%），而监护室停留时间（对数秩 P=0.15）和出院时间（对数秩 P=0.53）两组则相近。

结论：直到灌注 7 个单位 HBOC-201 超过 6 天的进程，可使 43%的患者避免的红细胞的输注。死亡率和严重不良反应发生率没有显著差异。HBOC-201 的作用与显著的过量的非严重不良反应有关。

（王晓莉 译，李士通 审校）

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

严重阻塞性睡眠呼吸暂停患者在内窥镜检查时使用丙泊酚输注系统的安全性和有效性

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：药物引起的睡眠下内窥镜检查使用镇静催眠药诱导中度障碍的睡眠呼吸暂停病人，从而促进阻塞性生理学的组织评估。实现药物引起的睡眠下内窥镜检查使用丙泊酚需要一个剂量策略并且确实可靠地产生阻碍同时将氧饱和度的下降减到最小。

方法：外科医生在一项舌底的经口机器人切除术前瞻性研究中，登记了 97 名阻塞性睡眠呼吸暂停患者，被多导联睡眠图证实持续性气道正压通气失败。所有的患者都被药物引起的睡眠下内窥镜检查筛查。丙泊酚剂量由 MATLAB（矩阵实验室）书写的定制软件决定，且是预先描写的。研究在有标准监护仪和复苏设备的手术室实行。排除表面麻醉，以及除了丙泊酚之外的静脉药物。所有患者接受 2 升/分钟的口部鼻导管辅助给氧。开始丙泊酚镇静后，经鼻放置小儿气管镜来观察咽部。镇静状态持续到临床终点即阻碍发作开始。咽部的观察需用足够的时间来获取妨碍部位的图像。然后输注终止。

结果：这一群体具有的特征是中值体重指数为 32.1（四分间距[IQR]6.8）kg/m 和呼吸暂停指数为 48（ICQ32）。所有患者呈现的阻碍在设计变量内。阻碍在 236(±57.9)秒后、预估的效应室浓度在 4.2±1.3mcg/mL 时被观察到。药物引起的睡眠下内窥镜检查期间饱和度最低中位数显（91.4%（四分间距 5.1））著地高于标准睡眠研究（81.0%[四分间距 11.2]，P<0.0001）。95%可信区间统计了药物引起的睡眠下内窥镜检查饱和度最低点和体重指数、年龄、呼吸暂停指数，或者执行丙泊酚剂量包括零在内的所有情况。

结论：丙泊酚输注策略需要限制性的经验在丙泊酚剂量选择和只有一个泵定量给药时在严重阻塞性睡眠呼吸暂停患者产生气道阻碍。临床阻碍出现比靶控输注系统的类似过程在相关文献中的报道更快。模拟系统中观察的氧饱和度下降程度在临床可接受的范围内。

（王晓莉 译，李士通 审校）

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实验模型中的抗过敏与抗炎效应说明蛋白激酶 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。它的效应是评估机体高敏性和不同药物导致的水肿模型，结扎部分坐骨神经导致的神经性疼痛。解释这种作用机理的机制。

方法：试验中用瑞士老鼠。通过内脚趾注射角叉胶，缓激肽，前列腺素，肾上腺素，脂多糖或者弗氏佐剂或者用神经疼痛模型（von Frey 纤维 0.6g）来诱导高敏反应。通过角叉胶，PGE2，BK 诱导的爪水肿模型引发抗炎反应。PKC 用于佛波醇导致的伤害模型。

结果：BF1 抑制高敏反应和脚底注射角叉胶，BK，PGE2（P<0.001）引起的水肿模型，并且减少弗氏佐剂和肾上腺素（P<0.001）引起的超敏反应是有效的，而不是脂多糖（P<0.257）引起的。BF1 抑制佛波醇诱导的舔的行为，表明涉及到 PKC 通路。试验中还观察到降低结扎部分坐骨神经（P<0.001）导致的超敏反应，抑制嗜中性粒细胞迁移和进入脊髓的白介素-1β 的产生。BF1 治疗不会影响运动功能（P=0.0783）,这是其他止痛药的严重副反应。

结论：在急性和慢性疼痛和炎症模型，BF1 有剂量依赖的抗高敏反应和抗炎反应，可能通过 PKC 通路的激活来。这种容易快速合成的复合物，低成本，低浓度，每天一次的药物表明可以有望用于未来的临床研究。

（王雪译 李士通审校）

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.

小儿应用硝普钠进行控制性降压的预测因素

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

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背景：硝普钠用于特定手术降低动脉血压。关于硝普钠控制血压效果的数据有限。但没有关于病人和临床医生影响动脉血压的数据。我们评估了行大手术的婴儿和儿童应用硝普钠的剂量反应效应以及进行血压控制的定量评估。

方法：153 例患者在进行控制性降压的手术操作时注射标记过的硝普钠。持续输注硝普钠，滴定进行控制血压（MAP 界定为临床标准的 10%。）通过动脉导管记录血压。用定量统计法统计血压控制情况。多元法评估病人和方法的效果。

结果：45.4%（SD23.9%；95%可信区间 41.5%-49.18%）的手术时间进行控制血压。在输注速率方面，较大的变化与更严重的血压控制有关（少控制 7.99%的血压速率为 1ug/kg/min 增加平均滴注量 P=0.0009）。病人基础血压与目标血压很大的差异预示更多的血压控制（每 mmHg 多控制 0.93%的血压增加 MAP 的差异性，P=0.0013）。这两种效果都出现在多元模型中。

结论：硝普钠降低血压是有效的。然而，血压维持目标血压的时间不到一半的。临床医生和病人因素不能预测血压，虽然确认了 2 种相反的关系。弄清这些关系需要进一步的研究，并且最好应用模型，建议用于小儿控制性降压时增加剂量。

（王雪 译，李士通 审校）

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.

术前使用他汀类药物不能使高风险患者免受术后发生早期急性呼吸窘迫综合征的回顾性队列研究

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

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背景：他汀类药物已被证明具有抗炎和免疫调节作用。在本研究中,我们试图确定存在发生急性呼吸窘迫综合征(ARDS)风险的手术病人术前他汀类药物治疗能否降低术后 ARDS 的发生率。

方法：我们进行了回顾性队列评价择期行高风险胸主动脉血管手术的患者术前他汀类药物治疗与术后早期 ARDS 发生的相关性。对二者相关性的研究我们采用了倾向调整分析方法以控制显示偏移及混杂因素的影响。

结果：1845 例患者,722 例接受术前他汀类药物治疗。一百二十例患者术后发生了 ARDS。接受了他汀类药物治疗与没有接受了他汀类药物治疗的患者 ARDS 发生率分别为 7.2%和 6.1%(OR = 1.20;95%可信区间,0.83 - 1.75;P = 0.330)。无论是分层倾向得分分析(集中 OR 为 0.93;95%可信区间,0.60 - 1.43)和匹配分析(OR = 0.78;95%可信区间,0.78 - 0.48)都未确定术前他汀类治疗与术后 ARDS 发生减少的显著关联。通过匹配控制比较发现,所有术后 ARDS 患者死亡率(7.7%比 8.8%,P = 0.51),住院天数(21 天 vs 15 天,P = 0.21),及无需机械通气天数 (24 天 vs 25 天,P = 0.62)都没有差别。

结论：行高风险手术的患者,术前他汀类药物治疗没有显著降低术后 ARDS。这些结果不支持接受高风险的手术患者术前使用他汀类药物来预防 ARDS。

（王慧娟 译，李士通 审校）

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.

麻醉并发症成为分娩患者的安全指标

Anesthesia Complications as a Childbirth Patient Safety Indicator

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背景：卫生保健研究与质量机构(AHRQ)建立了多个质量监控和优化的指标集。这是一套患者安全指标(PSIs),其重点是医院内潜在的可预防的术后、操作和分娩的并发症。本研究旨在确定不同分娩方式的麻醉并发症的患病率，及在医院使用 AHRQ PSI 评估方法并发症发生率的变化，同时做出一个针对分娩 PSI 的修改方案，此方案的目的是确定麻醉并发症的相关因素。

方法：AHRQ 的一个 PSI—麻醉并发症的质量指标修改为一个特殊分娩的安全指标。它包含所有分娩方式(阴道分娩和剖腹产手术)及全身麻醉和椎管内麻醉/镇痛的并发症。我们使用加州医院出院数据,整理出了非正常住院的发生率,并对年龄、种族、妊娠并发症进行分类统计。

结果：2009 年在加州 254 家医院总共有 508842 次分娩。每年分娩数小于 200 次的医院(N = 12)被排除在研究之外。另外 242 医院，在 AHRQ 标准研究人群中(成人外科病房,其中包括剖腹产手术)麻醉并发症发生率为 0.13%。特殊分娩的麻醉并发症的发生率为 0.31%。通过分娩方式的分层研究，我们发现,剖腹产并发症发生率为 0.49%而阴道分娩为 0.22%(P < 0.0001)。未经调整的平均值(SD)为 0.34%(0% - 2.46%)。有 13 家医院的并发症发生率(包括他们的 95%置信区间)仍在上四分位数，为异常值,其调整后的发生率为 0.52%至 2.13%。

结论：分娩相关的麻醉并发症率可能提供一个机会去辨认出并发症发生率低的医院，这样的医院拥有深入系统的方式来提高患者的安全。

（王慧娟 译，李士通 审校）

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 延长综合征患儿使用现代麻醉的安全性

The Safety of Modern Anesthesia for Children with Long QT Syndrome

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背景：患有 QT 延长综合征的患者可能会经历一系列的临床症状，从无症状、晕厥前期、晕厥、中止心脏骤停到心源性猝死。QT 延长综合征这一类心律失常往往是由自主神经的变化导致。这些被认为是高风险的围手术期心律失常，特别是尖端扭转型室速（TDP），但这种看法在很大程度上是基于一些有限的关于早于当前麻醉药品和围手术期监测标准的文献。现在我们提出了迄今为止最大量的关于 QT 延长综合征幼儿麻醉管理的多中心回顾。

方法：我们进行了一个关于 QT 延长综合征儿童围手术期管理的多中心回顾性分析，这些儿童是我们在 2005 年 1 月到 2010 年 1 月之间收集的小于 18 岁并接受全身麻醉的患者。我们分别从 8 个机构的匿名数据库中收集数据。

结果：103 个 QT 延长综合征的病人一共经历了 158 次全身麻醉。患者年龄和体重的中位数分别是 9（3-15）岁及 30.3（15.5-54）千克。81 个人（51%）在与 QT 延长综合征相关的手术中在全麻时发作（包括心脏起搏器，植入式心脏除颤器），另外 77 个人（49%）是偶然发生的。在手术当天 76%的病人使用 β 受体阻滞剂治疗，47%的人接受术前镇静治疗。19%的病人完全静脉麻醉，30%的病人完全吸入麻醉，而剩下的 51%的病人接受静脉吸入复合麻醉。没有病人使用氟哌利多。这些病人中总共有 5 人发作 QT 延长综合征，全都是新生儿或婴儿，且全都是在和 QT 延长综合征相关的手术中发作，没有一例是完全因为麻醉药物。因此，手术期间 TDF 偶发的发病率（95%可信区间）为 0/77（0%；0%-5%），而在 QT 延长综合征相关的手术中的发病率为 5/81 (6.2%; 2%-14%)。

结论：凭借优化的围手术期管理，现代麻醉对于 QT 延长综合征的患者在高发病率手术中比在没有对照的可能被建议的病例报告文献中更安全。我们试验的建议是围手术期间 TDF 的风险主要集中在在 QT 延长综合征首要处理措施失效后需要紧急处理的新生儿和婴儿身上。

（张秋丽 译，李士通 审校）

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.

人体渗透压和呼吸调节：健康志愿受试者输注高张生理盐水后机体高氯血代谢性酸中毒的呼吸代偿往往是缺失的

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

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

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背景：几个动物实验说明血浆渗透浓度的改变可能会影响换气。由血浆渗透浓度增加引起的呼吸抑制往往用来解释水依赖性体温调节的抑制作用因为体液的储存往往伴随着体温的增加。另一方面，妊娠时期呼吸性酸中毒往往和血浆渗透浓度的减少及强离子差有关。我们将研究这个假设，即渗透浓度会影响换气，因此在所有人机体中血浆渗透压升高将抑制换气，而血浆渗透压降低将刺激机体换气功能。

方法：我们这项研究的参与者都是健康的男性及女性志愿者（ASA I 级），包括 10 个男性志愿者（平均年龄 28 岁；年龄范围 20-40）及 9 个女性志愿者（平均年龄 33 岁；年龄范围 22-43）。所有的女性参与者都处于月经周期的卵泡期及黄体期。高渗透压主要由静脉注射 3%的高张生理盐水诱导产生，而低渗透压主要是通过饮用自来水产生。收集动脉血样品来分析电解质、渗透压及血气。分别在输注液体之前及之后行重复呼吸试验来测定 CO2 的敏感性。

结果：在所有的受试者中高张生理盐水的输注都会引起伴有离子差减小的高氯血性代谢性酸中毒。分析这些数据我们发现机体呼吸代偿的缺失。基线动脉二氧化碳分压（PaCO2）平均值（SD）为 37.8（2.9）mmHg，这仍然保持不变。100 分钟后 PaCO2 最低为 37.8 (2.9) mm Hg， P = 0.70，引起 pH 平均从 7.42 (0.02) 降到 7.38 (0.02)，P < 0.001。在液体潴留期间仍然存在代谢性酸中毒。混合的结果说明饮用水后 80 分钟 PaCO2 从 38.2mmHg 降至 35.7mmHg，P = 0.002，而 pH 值没有明显的改变。pH 7.43 (0.02)- pH 7.42 (0.02), P = 0.14,平均差（可信区间) = pH -0.007 (-0.017 - 0.003).

结论：我们的结果表明渗透压对换气功能有影响。在高渗透压状态下机体对高氯血性代谢性酸中毒的呼吸代偿作用被抑制。液体潴留会引起血浆渗透压的降低及代谢性酸中毒，即使离子差的减小和盐分的储存比起来是小的，预期的呼吸代偿仍然是有的。男性受试者仍然会受刺激产生换气，因此换气不受黄体酮水平的影响。我们猜想渗透压对换气功能的影响主要是对高渗透压环境的抑制，这种抑制在低渗透压时是不存在的。

（张秋丽 译，李士通 审校）

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.

甘氨酸转运体抑制剂可减轻癌痛

Relief of Cancer Pain by Glycine Transporter Inhibitors

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背景：近日有研究表明甘氨酸转运体抑制剂在坐骨神经损伤及糖尿病等有神经病理性疼痛的动物模型中具有镇痛作用。复杂的生物学机制表明神经性因素在骨肿瘤引起的剧烈疼痛中起一定作用。骨肿瘤改变了阿片类药物的镇痛作用，限制其有效性，因此急需找到用于缓解骨癌痛的新药。

方法：在 C3H/HeN 小鼠股骨远端髓腔接种溶骨肉瘤细胞 NCTC 2472 建立股骨骨肿瘤小鼠模型。在小鼠股骨肿瘤模型中，我们研究了 GlyT2 抑制剂，ORG 25543 和 ALX 1393,GlyT1 抑制剂，ORG 25935，及在异常疼痛、痛阈值，防御行为，和肢体的异常活动等疼痛行为中通过甘氨酸转运体 siRNA 下调脊柱甘氨酸转运蛋白的表达的作用。同时我们也对吗啡与甘氨酸转运体抑制剂的联合作用进行了研究。

结果：GlyT2 抑制剂，ORG 25543 及 ALX 1393,GlyT1 抑制剂、ORG 25935 IV 或口服制剂、下调脊柱甘氨酸转运蛋白表达可改善接种肿瘤细胞 11 天后骨癌痛小鼠的痛行为。这种镇痛效果强大持久。无明显镇痛效果的低剂量吗啡联合 ORG 25543 可以显著提高 ORG 25543 的镇痛效果。小鼠接种肿瘤细胞后第二天，注射 ORG 25543 引起了 3 阶段的疼痛反应，最初痛行为加剧（第 2-4 天），随后基本消失（5-7 天），接着再次出现。在注射

ORG 25543 一天后鞘内注射士的宁，可短暂的拮抗 ORG 25543 的镇痛效果。对照组小鼠中，士的宁提高了注射肿瘤细胞四天后的小鼠痛行为，同时在第 4 到 5 天加剧这一结果。以上证据表明不同机制具有时相依赖性。

结论：甘氨酸转运蛋白抑制剂联合或不联合吗啡可能是用于治疗骨癌痛的新方式，同时也可以进一步研究骨癌痛的发生机制。

（陈凌君 译，李士通 审校）

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.