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大鼠暴露在超重環境下 **14** 天增加丙泊酚的作用

Hypergravity Exposure for 14 Days Increases the Effects of Propofol in Rats

Iwata, Chihiro MD*; Abe, Chikara DDS, PhD*; Nakamura, Mitsuhiro PhD†; Morita, Hironobu MD, PhD*

Anesthesia & Analgesia 2014 118 125–131

背景：有人認爲太空探索的重力環境改變了麻醉藥的效果，然而並沒有相關證據發表過。在這篇研究中，我們試圖提供直接證據表明 14 天暴露在超重環境中增加了麻醉效果並且驗證了可能的原因。

方法：在 3g 環境下飼養 Sprague-Dawley 大鼠 14 天。在進行試驗那天，將大鼠從 3g 環境取出，在 1g 環境下休息 1 至 2 小時，然後靜脈輸注丙泊酚（20mg/kg，輸注時間 5 分鐘）。對照組的大鼠被持續飼養在 1g 環境下。通過測量誘發腦電圖爆發抑制所耗費時間、動脈血壓最低點和受到傷害性電刺激後出現翻正反應的耗時來比較飼養在 1g 和 3g 環境下的大鼠之間的丙泊酚效果。也檢測了丙泊酚血漿濃度的時相。在有前庭病變的大鼠身上也進行了試驗以驗證前庭系統是否影響了觀察結果。所有參數都用平均數±標準差表示。

結果：在 3g 環境下飼養的大鼠比 1g 環境下飼養的大鼠，誘發出腦電圖爆發抑制平均時間更早（195.7 ± 15.1 秒比 267.3 ± 29.4 秒, P = 0.00037），平均動脈血壓的最低點更低（75.0 ± 15.5 mmHg 比 100.6 ± 9.1 mm Hg, P = 0.019），出現翻正反應的平均時間更晚（39.0 ± 8.4 分鐘比 22.0 ± 3.1 分鐘, P < 0.0001）。然而，對比 1g 環境下持續飼養的假處理組大鼠，飼養在 3g 環境下的前庭病變大鼠中誘發出腦電圖爆發抑制的平均時間、平均動脈血壓最低點和出現翻正反應的平均耗時並沒有改變（分別爲 275 ± 29.4 秒、108.7 ± 14.6 mmHg 和 20.8 ± 2.8 分鐘, P 分別= 0.95、0.73 和 0.98）。丙泊酚血漿濃度的時相評定沒有組間差異。

結論：該實驗結果爲暴露在超重環境下 14 天增加丙泊酚的效果提供了依據。它提示了該結果並不是丙泊酚血漿濃度差異造成的，而是由前庭系統介導的敏感性增加造成的。

（盛嘉君 譯， 馬皓琳、李士通 審校）

BACKGROUND: It is thought that the gravitational environment of space exploration alters the effects of anesthetics; however, no evidence has as yet been reported. In the present study, we sought to provide direct evidence showing that hypergravity exposure for 14 days increases anesthetic effects and to examine the possible causes.

METHODS: Sprague-Dawley rats were raised in a 3g environment for 14 days. On the day of the experiment, rats were brought out of 3g and rested at 1g for 1 to 2 hours before IV propofol infusion (20 mg/kg, for 5 minutes). Control rats were continuously raised in a 1g environment. The effects of propofol were compared between rats raised in 1g and 3g environment by measuring time taken to induce the burst suppression in an electroencephalogram, nadir of arterial blood pressure, and time taken for the appearance of the righting response to noxious electrical stimulations. The time course of plasma propofol concentrations was also examined. Experiments were also conducted on rats with vestibular lesions to examine whether the vestibular system participated in the observed results. All values were expressed as mean ± SD.

RESULTS: In rats raised in 3g environment, the mean time to induce burst suppression in the electroencephalogram was earlier (195.7 ± 15.1 seconds, P = 0.00037), the nadir of mean arterial blood pressure was lower (75.0 ± 15.5 mm Hg, P = 0.019), and mean time for the righting response to appear was later (39.0 ± 8.4 minutes, P < 0.0001) than in rats raised in 1g environment (267.3 ± 29.4 seconds, 100.6 ± 9.1 mm Hg, and 22.0 ± 3.1 minutes, respectively). However, mean time to induce burst suppression and for the righting response to appear did not change in rats with vestibular lesions raised in 3g environment (275 ± 29.4 seconds, 108.7 ± 14.6 mm Hg, and 20.8 ± 2.8 minutes, P = 0.95, 0.73, and 0.98 vs sham-treated rats continuously

raised in a 1g environment, respectively). There was no difference between groups in the time course assessment of plasma propofol concentrations.

CONCLUSION: The results provide evidence that hypergravity exposure for 14 days increases the effects of propofol. It is suggested that the results were not caused by differences in plasma propofol concentrations but by increased sensitivity, which was mediated via the vestibular system.

腰硬聯合麻醉和單次腰麻技術用於病態肥胖患者剖宮產手術的麻醉開始時間：一項隨機對照比較研究

A Randomized Controlled Comparison Between Combined Spinal-Epidural and Single-Shot Spinal Techniques in Morbidly Obese Parturients Undergoing Cesarean Delivery: Time for Initiation of Anesthesia

Ross, Vernon H. MD; Dean, Laura S. MD; Thomas, John A. MD; Harris, Lynne C. BSN; Pan, Peter H. MSEE, MD

Anesthesia & Analgesia 2014 118 168–172

背景：雖然已有學者認爲腰硬聯合麻醉（CSE）比單次腰麻（SSS）更適用于病態肥胖患者，但對該類患者的蛛網膜下腔麻醉的最佳方法至今尚無定論。在本項隨機對照研究中，我們比較了 SSS 和 CSE 兩種技術用於擇期行剖宮產手術的病態肥胖患者蛛網膜下腔麻醉開始所需的時間。

方法：擬行擇期剖宮產手術的病態肥胖患者隨機接受通過 SSS 或 CSE 技術實施的蛛網膜下腔麻醉。坐位脊椎穿刺過程由一名有經驗的住院醫師在 10 分鐘內完成，如果穿刺失敗，則改由產科主治麻醉醫師進行操作。主要觀察指標是從引導針刺入（SSS 組）或硬膜外針刺入（CSE 組）到鞘內注射藥物完畢的時間（操作時間）。

結果：共有 44 名患者納入並完成本研究，3 名因違反協議而被剔除。剩餘的患者中，SSS 組 21 人，CSE 組 20 人。兩組人口統計變數和體重指數的均數（標準差）（SSS 組爲 48.7 ± 7.6 kg/m2，CSE 組爲 49.9 ± 8.6 kg/m2）無差異。SSS 組和 CSE 組操作時間的中位數[四分位距]分別爲 210 [116–692]和 180 [75–450]秒(P = 0.36)，差異的 95%可信區間(CI)爲−80 到+180 秒。第一位操作者在 10 分鐘內完成操作的比例，SSS 組爲 71%，CSE 組爲 95%(P = 0.09)，差異的 95%CI 爲−2% 到+45%。SSS 組成功完成操作過程所需的嘗試次數更多(P = 0.007)，差異的 95%CI 爲+1 到+6。

結論：我們的結果提示，由有經驗的住院醫師操作的 CSE 技術比 SSS 技術用於病態肥胖患者蛛網膜下腔麻醉所需時間更短，操作嘗試次數更少。

（陳彬彬 譯， 馬皓琳、李士通 審校）

BACKGROUND: There is no current consensus on the optimal technique for subarachnoid anesthesia in morbidly obese parturients even though some providers prefer the combined spinal-epidural (CSE) over single-shot spinal (SSS) technique. In this randomized controlled study, we compared the time required for initiation of subarachnoid anesthesia between SSS and CSE techniques in morbidly obese parturients undergoing elective cesarean delivery.

METHODS: Morbidly obese parturients presenting for elective cesarean delivery were randomized to receive subarachnoid anesthesia performed either with a SSS or a CSE technique. The spinal procedure in the sitting position was attempted by an experienced resident for up to 10 minutes, and if unsuccessful, the attending obstetric anesthesiologist assumed control of the procedure. The primary outcome was the time it took from the insertion of the introducer needle

(SSS group) or insertion of the epidural needle (CSE group) to the end of intrathecal injection of drugs (procedure time).

RESULTS: Forty-four patients were enrolled and completed the study. Three were excluded due to protocol violations. Of the remaining, 21 patients were in the SSS group and 20 in the CSE group. Demographic variables and mean (SD) body mass index (48.7 ± 7.6 kg/m2 for SSS; 49.9 ± 8.6 kg/m2 for CSE) were not different between groups. The median [interquartile range] for procedure time was 210 [116–692] seconds and 180 [75–450] seconds for SSS and CSE groups, respectively (P = 0.36), while the 95% confidence interval (CI) of the difference was −80 to +180 seconds. The first operator completed the procedure in <10 minutes in 71% of subjects in the SSS group and 95% of those in the CSE group (P = 0.09) and the 95% CI of the difference was −2% to +45%. There were more attempts to successful completion of the procedure in the SSS group (P = 0.007) with its 95% CI of the difference being +1 to +6.

CONCLUSION: Our results suggest that the CSE technique is noninferior to the SS technique in morbidly obese parturients for time of initiation of subarachnoid anesthesia and may be accomplished with fewer attempts than the SSS technique with experienced residents.

對美國學術型麻醉學教職員發表量的考察

Examination of Publications from Academic Anesthesiology Faculty in the United States

Hurley, Robert W. MD, PhD*; Zhao, Kevin MD†; Tighe, Patrick J. MD, MS*; Ko, Phebe S. MD*; Pronovost, Peter J. MD, PhD*; Wu, Christopher L. MD*

Anesthesia & Analgesia 2014 118 192–199

背景：美國麻醉學術協會的領導者發起了一項對麻醉科學歷情況的考察，同時也考察了美國國立衛生研究院對美國麻醉醫師的基金資助及出版刊物的品質。然而，與學術型麻醉醫師（被醫學院校定義爲學術型）相關的出版物的發表量及人群特徵仍未知。我們通過對美國醫學院校協會的 2006 年-2008 年的一個兩年的資料庫的調研，瞭解相關的出版量及人群特徵。

方法：檢索 Pubmed 出版物資料庫中的每個教職員，並將他們的個人資訊，包括工作單位、性別、學歷、學位、工作性質(半日制或全職)、任命狀態(集體或個人)、部門地位、專業認證狀態及研究生培訓情況記錄進一個新的資料庫。

結果：來自任職于 108 項美國麻醉學術專案的 6143 名教職員在 2006 到 2008 年共發表了 8521 篇稿件。37%的教職員發表了稿件，而整體的平均發表率則爲 0。至少有 1 篇發表文獻的教員在高級職稱（教授比講師的比值比（OR）=6.4；可信區間（CI），4.57–8.49；P < 0.0001）、男性(OR 1.3； CI，0.14–1.47； P < 0.0001)、擁有一個優遇的任用狀態(OR 2.1；CI，1.25–3.52；P = 0.0048)、缺少碩士生培養及專業認證(OR（MD 比 MD w/培訓+認證）=1.3；CI，1.11–1.60；P = 0.0020)的教員中佔有更高比例。只有一個 MD 學位的教員比有 MD/PhD 或 PhD 的教員發表率低（分別是：OR 0.45； CI，0.32–0.65； P < 0.0001； OR 0.27； CI， 0.20–0.37； P < 0.0001）。在至少發表一篇文獻的組內，全職教授發表量比講師多 3.8 倍(CI, 2.99–4.88； P < 0.0001)，缺少研究生培訓的教員比培訓並且認證過的教員發表量要多 1.4 倍 (CI, 1.16–1.78；P = 0.0009)。PhD 學位 (P = 0.006)、男性 (P = 0.013)及優遇的麻醉任用(P = 0.037) 同樣有更高的發表率。

結論：醫學院校相關麻醉醫師在這個時期的整體發表率較低。以上資料建立起了美國學術型麻醉醫師爲了將來的競爭發起的“呼籲行動”學術活動的基線。增加結構化住院醫師和專業培訓醫師研究教育項目的利用將同招募更多的 MD/PhD 和 PhD 學位的科學家致力於此領域一起，有助於共同提高麻醉學術部門的出版生產力。

（王贇 譯 馬皓琳 李士通 校）

BACKGROUND: Leaders in academic anesthesiology in the United States have called for an examination of the state of scholarship within anesthesiology departments. National Institutes of Health funding and publication quality of subsets of U.S anesthesiologists have been examined; however, the publication output of and the demographic characteristics that are associated with academic anesthesiologists, defined as faculty associated with a medical college, are unknown. A database from the American Association of Medical Colleges containing demographic information of all academic anesthesiologists in the United States was used to examine the publication output and demographic characteristics of anesthesiology faculty during a 2-year period from 2006 to 2008.

METHOD: All the publications found in the PubMed database for each faculty member were retrieved and included in a database containing their demographics including institution, gender, academic degree, academic rank, nature of appointment (part versus full-time), status of appointment (joint versus primary), departmental division, subspecialty certification status, and additional graduate medical education training.

RESULTS: Six thousand one hundred forty-three faculty who held positions at the 108 U.S. academic anesthesiology programs published 8521 manuscripts between 2006 and 2008. Thirty-seven percent of faculty published a manuscript, and the overall median publication rate was 0. The proportion of faculty with at least 1 publication was larger among faculty with higher rank (Odds Ratio [OR] for professors versus instructors = 6.4; confidence interval [CI], 4.57–8.49; P < 0.0001), male gender (OR 1.3; CI, 0.14–1.47; P < 0.0001), possessing a courtesy appointment status (OR 2.1; CI, 1.25–3.52; P = 0.0048) and lacking postgraduate training and subspecialty certification (OR for MD versus MD w/training + certification 1.3; CI, 1.11–1.60; P = 0.0020). Those faculty with an MD had lower probablility of publishing when compared with MD/PhD or PhD faculty (OR 0.45; CI, 0.32–0.65; P < 0.0001; OR 0.27; CI, 0.20–0.37; P < 0.0001, respectively). Within the group of faculty who published at least 1 paper, full professor faculty had 3.8 times more publications than instructors (CI, 2.99–4.88; P < 0.0001), and those who lacked postgraduate training had 1.4 times more publications than those who were trained and certified (CI, 1.16–1.78; P = 0.0009). PhD degree (P = 0.006), male gender (P = 0.013), and courtesy anesthesia appointment (P = 0.037) also were associated with higher publication rates.

CONCLUSIONS: The overall publication rate of anesthesiologists associated with medical schools was low in this time period. These data establish the pre-“call to action” baseline of scholarly activity by U.S. academic anesthesiologists for future comparisons. Increased use of structured resident and fellow research education programs as well as recruiting more MD/PhD and PhD scientists to the field may help to improve the publication productivity of academic anesthesiology departments.

腰椎手術失敗與椎管內狹窄的硬膜外粘連松解:與預後相關的因素

Epidural Lysis of Adhesions for Failed Back Surgery and Spinal Stenosis: Factors Associated with Treatment Outcome

Hsu, Eugene MD, MBA*; Atanelov, Levan MD†; Plunkett, Anthony R. MD‡; Chai, Nu MD§; Chen, Yian BS ‖ ; Cohen, Steven P. MD¶

Anesthesia & Analgesia 2014 118 215–224

背景:腰椎手術失敗綜合征是一個具有挑戰性的問題。硬膜外粘連松解是被主張用於腰椎手術失敗綜合征的治療措施之一。關於硬膜外粘連松解用於腰椎手術失敗綜合征的研究結果有好有壞，但都因沒有找出與結果相關的因素而受到限制。

方法:我們對 2004 年至 2007 年 115 例接受硬膜外粘連松解的患者進行了多中心、回顧性的研究。其中 104 例爲腰椎手術失敗綜合征，11 例爲椎管內狹窄。從病歷中提取了 27 項人口統計學、臨床和手術變數，研究其與預後的相關性。預後定義爲≥50%的疼痛緩解持續≥1 個月。進行單變數分析，隨後進行多因素 logistic 回歸分析。

結果:總體而言，48.7%的患者（95%可信區間爲 39.3%–58.1%）達到了良好的預後。單因素分析中，達良好預後的人群包括年長的（平均年齡 64.1 歲，95%可信區間爲 59.7–68.6，對比 57.2 歲，95%可信區間爲 53.0–61.4，P=0.02），而較高的疼痛評分基礎數值與不良預後有關（平均 6.7 年，95%可信區間爲 6.0-7.3 對比 7.5 年，95%可信區間爲 6.9-8.0，P = 0.07）。使用透明質酸酶並沒有在單因素分析中與預後呈現相關性（比值比 1.2， 95%可信區間爲 0.6–2.5，P = 0.65）。在多變數分析中，年齡≥81 歲(比值比 7.8，95%可信區間 1.4–53.7), 疼痛評分基礎值≤9 (比值比 4.4，95%可信區間 1.4-16.3, P = 0.02), 以及具有或正在尋求殘疾或勞工賠償的患者(比值比 4.4，95%可信區間 1.1-19.5, P = 0.04) 顯著地更可能經歷積極的預後。

結論:考慮到我們不太高的成功率，根據統計學和臨床因素來選擇進行硬膜外粘連松解手術的患者可有助於更好挑選治療的候選人。手術操作性因素例如透明質酸酶增加了風險和成本，並沒有改善預後。因此將其作爲標準療法前還需要進一步的研究。

（邢怡安 譯 馬皓琳 李士通 校）

BACKGROUND: Failed back surgery syndrome (FBSS) is a challenging problem. One treatment advocated to treat FBSS is epidural lysis of adhesions (LOA). The results of studies examining LOA for FBSS have been mixed, but are limited because no study has ever sought to identify factors associated with outcomes.

METHODS: We performed this multicenter, retrospective study in 115 patients who underwent LOA for FBSS (n = 104) or spinal stenosis (n = 11) between 2004 and 2007. Twenty-seven demographic, clinical, and procedural variables were extracted from medical records and correlated with the outcome, defined as ≥50% pain relief lasting ≥1 month. Univariable analysis was performed, followed by multivariable logistic regression.

RESULTS: Overall, 48.7% (95% confidence interval [CI], 39.3%–58.1%) of patients experienced a positive outcome. In univariable analysis, those who had a positive outcome were older (mean age 64.1 years; 95% CI, 59.7–68.6 vs 57.2; 95% CI, 53.0–61.4 years; P = 0.02), while higher baseline numerical rating scale pain scores were associated with a negative outcome (mean 6.7 years; 95% CI, 6.0–7.3 vs 7.5; 95% CI, 6.9–8.0; P = 0.07). Use of hyaluronidase did not correlate with outcomes in univariable analysis (odds ratio [OR], 1.2; 95% CI, 0.6–2.5; P = 0.65). In multivariable analysis, age ≥81 years (OR, 7.8; 95% CI, 1.4–53.7), baseline numerical rating scale score ≤9 (OR, 4.4; 95% CI, 1.4-16.3, P = 0.02), and patients on or seeking disability or worker's compensation (OR, 4.4; 95% CI, 1.1-19.5, P = 0.04) were significantly more likely to experience a positive outcome.

CONCLUSIONS: Considering our modest success rate, selecting patients for epidural LOA based on demographic and clinical factors may help better select treatment candidates. Procedural factors such as the use of hyaluronidase that increase risks and costs did not improve outcomes, so further research is needed before these become standard practice.

局麻藥誘導人乳腺腫瘤細胞凋亡

Local Anesthetics Induce Apoptosis In Human Breast Tumor Cells.

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Anesthesia & Analgesia 2014 118 116–124

背景：以前的研究已經表明，局麻藥可誘導某些細胞凋亡。在這項研究中，我們研究了局麻藥對人乳腺腫瘤細胞誘導凋亡的作用。

方法：我們選取了人乳腺癌（MCF -7）細胞株和乳腺上皮細胞（ MCF- 10A）細胞株，用利多卡因和/或布比卡因進行處理，評估了細胞活力， DNA 片段化和膜聯蛋白 V 免疫螢光染色。用 Western blot 分析研究對凋亡相關蛋白表達的影響。同時這項研究結果擴展到體內異種移植模型。

結果：經利多卡因和布比卡因處理後的乳腺腫瘤細胞通過誘導細胞凋亡抑制了細胞活力。MCF-7 細胞株比 MCF- 10A 細胞株更加突出。局麻藥誘導了 caspase 7 ，8，9 和聚 ADP-核糖聚合酶的裂解。caspase 抑制劑有效封閉了局麻藥誘導的 caspase 7 和聚 ADP-核糖聚合酶的裂解物。此外，在 MCF-7 細胞株的異種移植模型中，局麻藥誘導後裂解的 caspase 7 表達更高，並增加了原位末端標記法染色的去氧核苷酸轉移酶。

結論：利多卡因和布比卡因在臨床相關濃度可誘導乳腺腫瘤細胞的凋亡。我們的研究結果揭示了局部麻醉藥先前未確認的益處，並需進一步研究在乳腺癌術中其抑癌作用。

（陳實玉 譯 薛張綱校）

BACKGROUND: Previous studies have shown that local anesthetics may induce apoptosis in some cell types. In this study, we investigated the apoptotic effects of local anesthetics in human breast tumor cells.

METHODS: Human breast cancer (MCF-7) and mammary epithelial (MCF-10A) cell lines were treated with lidocaine and/or bupivacaine. Cell viability, DNA fragmentation, and annexin V immunofluorescence staining were assessed. The effects on apoptosis-related protein expression were investigated by Western blot analysis. The findings were extended to studies in an in vivo xenograft model.

RESULTS: Treatment of breast tumor cells with lidocaine and bupivacaine resulted in inhibition of cell viability via induction of apoptosis. The effects were more prominent in MCF-7 cells than in MCF-10A cells. Treatment with local anesthetics induced caspase 7, 8, 9, and poly ADP-ribose polymerase cleavage. The cleavage of caspase 7 and poly ADP-ribose polymerase induced by local anesthetics were effectively blocked by caspase inhibitors. Furthermore, treatment of MCF-7 xenografts with local anesthetics resulted in higher expression of cleaved caspase 7 and an increase in terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) staining.

CONCLUSION: Lidocaine and bupivacaine induce apoptosis of breast tumor cells at clinically relevant concentrations. Our results reveal previously unrecognized beneficial actions of local anesthetics and call for further studies to assess the oncologic advantages of their use during breast cancer surgery.

系統性回顧：笑氣在分娩鎮痛中的應用

Nitrous Oxide for the Management of Labor Pain: A Systematic Review

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Anesthesia & Analgesia 2014 118 153–167

背景：我們系統性地回顧了笑氣對於分娩鎮痛的療效，對笑氣應用于產婦分娩鎮痛時的滿意度及其副作用的等進行了分析。

方法：我們檢索了 MEDLINE,EMBASE,護理累積指數，CINAHL 等資料庫中的英文文獻。研究的物件包括經歷陰道分娩的產婦、暴露于笑氣的參與分娩過程的及新生兒護理的醫護人員。

結果：我們分析了一共 58 篇發表文獻，代表了 59 個不同研究人群，2 組研究品質高，11 組較合理，46 組品質不高。笑氣吸入麻醉對於減少疼痛的效果較硬膜外麻醉差，關於這方面的文章品質大都比較差。這些參差不齊的結果被用來評估婦女對於她們分娩經歷的滿意度，而且分娩疼痛管理導致這項綜合研究較難實現。很多文獻報導的對於母親的負面效應例如噁心，嘔吐，頭暈和昏睡都影響了笑氣的接受範圍。使用笑氣鎮痛出生的新生兒，相較於其他方式鎮痛或未上麻醉的新生兒的 apgar 評分並無明顯差異。 對於職業危害以及職業暴露的證據是有限的。

結論：對於笑氣應用於分娩鎮痛的文獻報導較少，且良莠不齊。涵蓋鎮痛效應，滿意度，還有不利影響這些方面的研究還需繼續。

（蔣鑫梅譯 薛張綱校）

METHODS: We searched the MEDLINE, EMBASE, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases for articles published in English. The study population included pregnant women in labor intending a vaginal birth, birth attendees or health care providers who may be exposed to nitrous oxide during labor, and the fetus/neonate.

BACKGROUND: We systematically reviewed evidence addressing the effectiveness of nitrous oxidefor the management of labor pain, the influence of nitrous oxide on women's satisfaction with their birth experience and labor pain management, and adverse effects associated with nitrous oxide for labor pain management.

RESULTS: We identified a total of 58 publications, representing 59 distinct study populations: 2 studies were of good quality, 11 fair, and 46 poor. Inhalation of nitrous oxide provided less effective pain relief than epidural analgesia, but the quality of studies was predominately poor. The heterogeneous outcomes used to assess women's satisfaction with their birth experience and labor pain management made synthesis of studies difficult. Most maternal adverse effects reported in the literature were unpleasant side effects that affect tolerability, such as nausea, vomiting, dizziness, and drowsiness. Apgar scores in newborns whose mothers used nitrous oxide were not significantly different from those of newborns whose mothers used other labor pain management methods or no analgesia. Evidence about occupational harms and exposure was limited.

CONCLUSIONS: The literature addressing nitrous oxide for the management of labor pain includes few studies of good or fair quality. Further research is needed across all of the areas examined: effectiveness, satisfaction, and adverse effects.

腦電活動遵循 Benford 法則

Brain Electrical Activity Obeys Benford's Law

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Anesthesia & Analgesia 2014 118 183–191

背景：監測和自動線上分析腦電活動經常用於診斷腦部疾病和評估手術中麻醉深度。然而錯誤的診斷會給病人帶來例如術中知曉等災難性後果。這主要是由信號分析過程中不規則所導致。這裡我們主要探討 Benford 法則是否可用於檢測神經生物信號有意或無意的調製。該法則認爲許多資料庫的首批數位資料，例如原子量和河流長度，都是對數分佈且不均等的。我們特意檢測了在使用或不使用麻醉藥物的情況下，來自病人代表全腦生物電活動的記錄信號，以及器官型切片代表單純皮質活動的信號是否遵循 Benford 法則。

方法： 在使用七氟醚前後分別描記來自病以及局部皮質電位。資料資料中第一批數位分佈與 Benford 分佈進行對比。

結果：所有資料顯示 Benford 樣分佈。然而在離體及人體實驗採集的生物電信號，均顯示不同麻醉深度條件下，分佈也不同。在七氟醚麻醉狀態下，離體實驗中第一數位分佈曲線馮家陡峭，而活體腦電圖資料較爲平坦。在高頻雜訊存在條件下，Benford 分佈消失。

結論：離體實驗和 EEG 資料都顯示 Benford 樣分佈。該分佈可被七氟醚麻醉所改變，也可被人工類比產生的噪音消除。這些發現表明基於 Benford 法則的運算可以成功用於檢測七氟醚介導的電生理記錄的信號調製。

（李春譯 薛張綱校）

BACKGROUND: Monitoring and automated online analysis of brain electrical activity are frequently used for verifying brain diseases and for estimating anesthetic depth in subjects undergoing surgery. However, false diagnosis with potentially catastrophic consequences for patients such as intraoperative awareness may result from unnoticed irregularities in the process of signal analysis. Here we ask whether Benford's Law can be applied to detect accidental or intended modulation of neurophysiologic signals. This law states that the first digits of many datasets such as atomic weights or river lengths are distributed logarithmically and not equally. In particular, we tested whether data obtained from electrophysiological recordings of human patients representing global activity and organotypic slice cultures representing pure cortical activity follow the predictions of Benford's Law in the absence and in the presence of an anesthetic drug.

METHODS: Electroencephalographic (EEG) recordings from human subjects and local field potential recordings from cultured cortical brain slices were obtained before and after administration of sevoflurane. The first digit distribution of the datasets was compared with the Benford distribution.

RESULTS: All datasets showed a Benford-like distribution. Nevertheless, distributions belonging to different anesthetic levels could be distinguished in vitro and in human EEGs. With sevoflurane, the first digit distribution of the in vitro data becomes steeper, while it flattens for EEG data. In the presence of high frequency noise, the Benford distribution falls apart.

CONCLUSIONS: In vitro and EEG data show a Benford-like distribution which is altered by sevoflurane or destroyed by noise used to simulate artefacts. These findings suggest that algorithms based on Benford's Law can be successfully used to detect sevoflurane-induced signal modulations in electrophysiological recordings.

基於麻醉資訊管理系統的接近即時決策支援用於管理術中低血壓和高血壓

Anesthesia Information Management System-Based Near Real-Time Decision Support To Manage Intraoperative Hypotension And Hypertension.

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Anesthesia & Analgesia 2014 118 206–214

背景：術中低血壓和高血壓都與不良的臨床結果和發病率有關。通過麻醉資訊管理系統（AIMS）干預的臨床決策支援已被證明能夠提高醫療品質。我們假設一個以 AIMS 爲基礎的臨床決策支援系統可以用來改善術中低血壓和高血壓的管理。

方法：一個以 AIMS 爲基礎接近即時的決策支援模組，智慧麻醉管理器（SAM）被用於檢測事先選定的造成低血壓和高血壓的情景。分別使用低血壓（收縮壓<80 毫米汞柱）與高濃度吸入麻醉藥（>1.25 最低肺泡有效濃度[MAC]）、高血壓（收縮壓>160 毫米汞柱）與輸注去氧腎上腺素進行場景匹配來用於檢測。麻醉工作人員通過電腦螢幕上的“彈出”資訊獲得通知。 對 AIMS 的資料進行回顧性分析，以評估 SAM 的通知消息對低血壓和高血壓事件發生情況的影響。

結果：收集和比較了建立 SAM 資訊系統前 12 個月（N = 16913）及後 12 個月（N = 17132）的麻醉病例資料，使用資訊系統通知後低血壓合併高 MAC 的中位持續時間明顯縮短（曼惠特尼秩和檢驗，P = 0.031）。然而，高血壓事件合併輸注苯腎上腺素的中位持續時間並無顯著性減少（P = 0.47）。持續時間超過 6 分鐘（SAM 的採樣週期）的低血壓發生頻率（δ= -0.26 ％ [可信區間，-0.38 ％至-0.11 ％]，P <0.001）或高血壓發生頻率（δ= -0.92 ％ [可信區間，-1.79 ％至-0.04 ％] ，P = 0.035），以每 100 例手術（或百分比發生）發生的該類事件數量來表達，在使用資訊系統通知後都顯著減少。對於低血壓事件，在接到通知資訊後 81％的情況下麻醉工作人員會將吸入麻醉藥濃度降至 1.25 MAC 以下，無通知時則只有 59％（P = 0.003）。對於高血壓發作，雖然麻醉人員在接到通知資訊後，降低或中止注射苯腎上腺素的情況從 22％提高到 37％（P = 0.030），但整體反應較對低血壓發作的反應不太一致。

結論：在具有自動採集動脈血壓和吸入麻醉藥濃度變數的麻醉資訊管理系統時，接近即時的通知資訊可以有效減少低血壓合併>1.25 MAC 吸入麻醉藥事件的持續時間和頻率。然而，由於苯腎上腺素是手動記錄在 AIMS 中的，通知消息對減少高血壓合併注射苯腎上腺素的事件發生作用不太明顯。自動資料獲取和 AIMS 較高頻率的資料獲取可以提高術中臨床決策支援系統的有效性。

（淩曉敏譯 薛張綱校）

BACKGROUND: Intraoperative hypotension and hypertension are associated with adverse clinical outcomes and morbidity. Clinical decision support mediated through an anesthesia information management system (AIMS) has been shown to improve quality of care. We hypothesized that an AIMS-based clinical decision support system could be used to improve management of intraoperative hypotension and hypertension.

METHODS:A near real-time AIMS-based decision support module, Smart Anesthesia Manager (SAM), was used to detect selected scenarios contributing to hypotension and hypertension. Specifically, hypotension (systolic blood pressure <80 mm Hg) with a concurrent high concentration (>1.25 minimum alveolar concentration [MAC]) of inhaled drug and hypertension(systolic blood pressure >160 mm Hg) with concurrent phenylephrine infusion were

detected, and anesthesia providers were notified via "pop-up" computer screen messages. AIMS data were retrospectively analyzed to evaluate the effect of SAM notification messages on hypotensive and hypertensive episodes.

RESULTS: For anesthetic cases 12 months before (N = 16913) and after (N = 17132) institution of SAM messages, the median duration of hypotensive episodes with concurrent high MAC decreased with notifications (Mann Whitney rank sum test, P = 0.031). However, the reduction in the median duration of hypertensive episodes with concurrent phenylephrine infusion was not significant (P = 0.47). The frequency of prolonged episodes that lasted >6 minutes (sampling period of SAM), represented in terms of the number of cases with episodes per 100 surgical cases (or percentage occurrence), declined with notifications for both hypotension with >1.25 MAC inhaled drug episodes (δ = -0.26% [confidence interval, -0.38% to -0.11%], P < 0.001) and hypertension with phenylephrine infusion episodes (δ = -0.92% [confidence interval, -1.79% to -0.04%], P = 0.035). For hypotensive events, the anesthesia providers reduced the inhaled drug concentrations to <1.25 MAC 81% of the time with notifications compared with 59% without notifications (P = 0.003). For hypertensive episodes, although the anesthesia providers' reduction or discontinuation of the phenylephrine infusion increased from 22% to 37% (P = 0.030) with notification messages, the overall response was less consistent than the response to hypotensive episodes.

CONCLUSIONS: With automatic acquisition of arterial blood pressure and inhaled drug concentration variables in an AIMS, near real-time notification was effective in reducing the duration and frequency of hypotension with concurrent >1.25 MAC inhaled drug episodes. However, since phenylephrine infusion is manually documented in an AIMS, the impact of notification messages was less pronounced in reducing episodes of hypertension with concurrent phenylephrine infusion. Automated data capture and a higher frequency of data acquisition in an AIMS can improve the effectiveness of an intraoperative clinical decision support system.

術後嘔心嘔吐管理的共識指南

Consensus Guidelines for the Management of Postoperative Nausea and Vomiting

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Anesthesia & Analgesia 2014 118 85–113

摘要：現有指南包含關於術後噁心嘔吐的最新資料，以及對 2003 年和 2007 年版指南的更新。這些指南是在非住院患者麻醉學會的主持下，由各 PONV 專家組成的一個多學科國際工作組編撰而成。工作組成員系統地對現有的 PONV 醫學文獻進行評價，以便對那些接收手術並有 PONV 高危風險的成人和兒童如何進行管理提出循證醫學的參考工具。這些指南確認有 PONV 風險的成年和兒童患者，推薦減少發生 PONV 風險的方法，確認包括非藥物方法在內的最有效的止吐單一治療和預防 PONV 的聯合治療方案; 推薦 PONV 發生時的治療策略，爲管理有 PONV 高危風險的個體以及確保預防和治療 PONV 應用於臨床的步驟提出一種演算法。

（談婧華 譯 陳傑 校）

The present guidelines are the most recent data on postoperative nausea and vomiting (PONV) and an update on the 2 previous sets of guidelines published in 2003 and 2007. These guidelines were compiled by a multidisciplinary international panel of individuals with interest and expertise in PONV under the auspices of the Society for Ambulatory Anesthesia. The panel members critically and systematically evaluated the current medical literature on PONV to provide an evidence-based reference tool for the management of adults and children who are undergoing surgery and are at increased risk for PONV. These guidelines identify patients at risk for PONV in adults and children; recommend approaches for reducing baseline risks for PONV; identify the most effective antiemetic single therapy and combination therapy regimens for PONV prophylaxis, including nonpharmacologic approaches; recommend strategies for treatment of PONV when it occurs; provide an algorithm for the management of individuals at increased risk for PONV as well as steps to ensure PONV prevention and treatment are implemented in the clinical setting.

病態肥胖病人肺複張的無創監測：脈搏血氧飽和度儀和容積二氧化碳圖的作用

Noninvasive Monitoring of Lung Recruitment Maneuvers in Morbidly Obese Patients: The Role of Pulse Oximetry and Volumetric Capnography

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Anesthesia & Analgesia 2014 118 137–144

背景：此研究目的是探討脈搏血氧飽和度監測和容積二氧化碳圖(VCap)能否測定麻醉狀態下病態肥胖患者肺開放和關閉壓。

方法：研究 20 位行氣腹下腹腔鏡減肥手術的病態肥胖患者。控制通氣壓力的肺複張手法如下：（1）在升支測量肺的開放壓。呼氣末正壓(PEEP)從 8 cm H2O 增至 16cmH2O 後，吸入氧濃度(FIO2)開始下降直到脈搏血氧飽和度(SpO2)小於 92%。然後，吸氣末壓力以 2 cm H2O 遞增，可從 36 cm H2O 增加到 50 cm H2O 高限。當 SpO2 超過 97%時達到開放壓。（2）在隨後的降支，確認肺的關閉壓。PEEP 以 2cm H2O 爲單位從 22 cm H2O 遞降至 10 cm H2O。關閉壓定義爲呼吸順應性從其最大值開始下降的 PEEP 值。持續的記錄肺力學參數、SpO2 和 VCap。

結果：肺的開放壓爲 44(4) cm H2O（中位數和四分位間距），關閉壓爲 14（2）cm H2O。因此，維持肺不塌陷的 PEEP 水準爲 16（3）cm H2O。利用呼吸順應性作參考，受試者工作特徵分析表明 SpO2（曲線下面積[AUC] 0.80 [SE 0.07]，敏感性 0.65，特異性 0.94)；每次呼吸的 CO2 清除(AUC 0.91 [SE 0.05], 敏感性 0.85, 特異性 0.98)；Bohr 死腔(AUC 0.83 [SE 0.06], 敏感性 0.70, 特異性 0.95)。在複張手法的下降支，這些資料對於探測肺塌陷相對準確。

結論：通過結合脈搏血氧飽和度測定和 Vcap 的無創方法，對病態肥胖患者的肺複張可進行有效監測。SpO2、CO2 清除和 Bohr 死腔可判定個體的開放壓和關閉壓。

（朱浩 譯 陳傑 校）

BACKGROUND: We conducted this study to determine whether pulse oximetry and volumetric capnography (VCap) can determine the opening and closing pressures of lungs of anesthetized morbidly obese patients.

METHODS: Twenty morbidly obese patients undergoing laparoscopic bariatric surgery with capnoperitoneum were studied. A lung recruitment maneuver was performed in pressure control ventilation as follows: (1) During an ascending limb, the lungs' opening pressure was detected.

After increasing positive end-expiratory pressure (PEEP) from 8 to 16 cm H2O, fraction of inspired oxygen (FIO2) was decreased until pulse oximetric arterial saturation (SpO2) was <92%. Thereafter, end-inspiratory pressure was increased in steps of 2 cm H2O, from 36 to a maximum of 50 cm H2O. The opening pressure was attained when SpO2 exceeded 97%. (2) During a subsequent decreasing limb, the lungs' closing pressure was identified. PEEP was decreased from 22 to 10 cm H2O in steps of 2 cm H2O. The closing pressure was determined as the PEEP value at which respiratory compliance decreased from its maximum value. We continuously recorded lung mechanics, SpO2, and VCap.

RESULTS: The lungs' opening pressures were detected at 44 (4) cm H2O (median and interquartile range) and the closing pressure at 14 (2) cm H2O. Therefore, the level of PEEP that kept the lungs without collapse was found to be 16 (3) cm H2O. Using respiratory compliance as a reference, receiver operating characteristic analysis showed that SpO2 (area under the curve [AUC] 0.80 [SE 0.07], sensitivity 0.65, and specificity 0.94), the elimination of CO2 per breath (AUC 0.91 [SE 0.05], sensitivity 0.85, and specificity 0.98), and Bohr's dead space (AUC 0.83 [SE 0.06], sensitivity 0.70, and specificity 0.95] were relatively accurate for detecting lung collapse during the decreasing limb of a recruitment maneuver.

CONCLUSIONS: Lung recruitment in morbidly obese patients could be effectively monitored by combining noninvasive pulse oximetry and VCap. SpO2, the elimination of CO2, and Bohr's dead space detected the individual's opening and closing pressures.

先天性心臟病患者進行心導管術時心跳驟停的發生率

The Frequency of Cardiac Arrests in Patients with Congenital Heart Disease Undergoing Cardiac Catheterization

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Anesthesia & Analgesia 2014 118 175–182

背景：因爲導管技術的發展，心導管術對於有先天性心臟病的患者已經從診斷法轉變成主要用於介入治療。接受治療性心導管術的兒童可能會有更高的不良事件發生風險，本研究目的是確定在一個大型的三級兒童轉診中心，先天性心臟病患者接受心導管術時心跳驟停（CA）的發生率。

方法：回顧從 2004 年 1 月至 2009 年 12 月所有在心導管實驗室中發生的 CA。心跳驟停定義爲需要進行胸外按壓的迴圈停止。調查手術、患者、醫生和系統相關的因素。

結果：研究期間共行 7289 例導管手術，70 例手術與心跳驟停相關(0.96 [99% 可信區間, 0.7–1.3]每 100 例手術)；48 例（69%）成功復蘇至灌注節律，18 例（26%）需要行體外膜肺氧合，4 例（6%）導致復蘇失敗。38 例（54%）繼發於突然產生的心律失常。在 CA 發生後 71%的復蘇時間≤11 min（71%）。心跳驟停的發生與介入治療和更小的年齡(P < 0.001)相關(P < 0.001)。病例規劃和溝通系統的改變有效降低了心跳驟停的發生率(1.5% vs 0.7%; P = 0.002)。

結論：與非兒科心臟手術相比，接受心導管術兒童的 CA 發生率更高。在此群體中，程式和系統性因素也與心跳驟停的發生相關。這些問題強調密切溝通、預見和準備的必要性。

（李峰日 譯 陳傑 校）

BACKGROUND: Cardiac catheterization for patients with congenital heart disease has shifted from diagnostic to predominantly interventional procedures because of advances in catheter-based technologies. Children undergoing therapeutic catheterization may be at higher risk of adverse events, and the purpose of our study was to determine the incidence of cardiac arrest

(CA) in patients with congenital heart disease undergoing cardiac catheterization at a large pediatric tertiary referral center.

METHODS: All CAs from January 2004 through December 2009 occurring in the cardiac catheterization laboratory were reviewed. A CA was defined as an event in which cessation of circulation required chest compressions. Procedure, patient, practitioner, and system-related factors were examined.

RESULTS: Over the study period, during 7289 catheterization procedures, 70 procedures were associated with a CA (0.96 [99% confidence interval, 0.7–1.3] per 100 procedures); 48 events (69%) were successfully resuscitated to a perfusing rhythm, 18 events (26%) resulted in need for extracorporeal membrane oxygenation, and 4 events (6%) resulted in unsuccessful resuscitation. Sudden onset of cardiac arrhythmia led to CA during 38 events (54%). The duration of resuscitation after CA was ≤11 minutes in 71%. Occurrence of CA was associated with interventional procedures ($P < 0.001$) and younger age ($P < 0.001$). A change in systems for scheduling and communication of cases was associated with a significant reduction in the incidence of CA (1.5% vs 0.7%; $P = 0.002$).

CONCLUSIONS: The incidence of CA in children undergoing cardiac catheterization is high compared with pediatric noncardiac surgery. Procedural and system factors were associated with occurrence of CA in this cohort. These issues highlight the need for close communication, anticipation, and preparation.

畢業後醫學教育評鑒委員會（ACGME）授權的外科及麻醉住院醫師專案中負責人的學術生產力研究

Academic Productivity of Directors of ACGME-Accredited Residency Programs in Surgery and Anesthesiology

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Anesthesia & Analgesia 2014 118 200–205

背景：畢業後醫學教育評鑒委員會（ACGME）授權的住院醫師訓練計畫中，要求項目負責人參與學術活動。由於相對外科項目而言，麻醉科住院醫師計畫往往被提及在學術生產力方面相對不足。猜測這一定程度上反映了麻醉與外科培訓計畫的負責人之間參與學術活動的不同。爲驗證此猜想，本研究以 PubMed 引用和國家衛生研究院（NIH）的資助作爲學術活動的標準，檢查了同一個機構內，目前經過 ACGME 授權的麻醉、外科住院醫師計畫負責人的執業記錄。

方法：在 2011 年 11 月 1 日至 12 月 31 日之間，從完全公開的網站上收集了來自 127 個機構中的，擁有 ACGME 授權的麻醉學、外科學專案負責人資料。針對個人資訊的收集包括證書登錄年份、被任命爲負責人的年份、學銜、NIH 承認的資金支援記錄以及 PubMed 的引用數。同時計算了隨機抽選的 25 位對應機構的負責人組成的子集中的 h 指數。

結果：各組之間負責人的證書登錄年份（P=0.42）、學銜（P=0.38）以及作爲項目負責人的年限（P=0.22）之間沒有統計學差異。然而，麻醉學的項目負責人在過去或現在獲得的 NIH 資助上較少（P=0.002）。在總體或與教學相關的 PubMed 引用上也較少（P 均＜0.001）。在 h 指數上也相對於外科學的負責人們要少（P=0.001）。多變數分析顯示，在其他變數保持不變時，麻醉學負責人的發表率是相對應的外科學負責人的 43%（95%置信區間，0.31-0.58）。

結論：根據同行評議的發表數以及聯邦研究基金，麻醉學住院醫師計畫項目的負責人相對于外科學專案的負責人而言，其學術活動明顯較少。如此，本研究亦顯示了在麻醉研究的學術結構中存在系統性弱點的進一步證據。

（賀加貝 譯 陳傑 校）

BACKGROUND: Scholarly activity is expected of program directors of Accreditation Council for Graduate Medical Education (ACGME)-accredited residency training programs. Anesthesiology residency programs are cited more often than surgical programs for deficiencies in academic productivity. We hypothesized that this may in part reflect differences in scholarly activity between program directors of anesthesiology and surgical trainings programs. To test the hypothesis, we examined the career track record of current program directors of ACGME-accredited anesthesiology and surgical residency programs at the same institutions using PubMed citations and funding from the National Institutes of Health (NIH) as metrics of scholarly activity.

METHODS: Between November 1, 2011 and December 31, 2011, we obtained data from publicly available Web sites on program directors at 127 institutions that had ACGME-accredited programs in both anesthesiology and surgery. Information gathered on each individual included year of board certification, year first appointed program director, academic rank, history of NIH grant funding, and number of PubMed citations. We also calculated the h-index for a randomly selected subset of 25 institution-matched program directors.

RESULTS: There were no differences between the groups in number of years since board certification ($P = 0.42$), academic rank ($P = 0.38$), or years as a program director ($P = 0.22$). However, program directors in anesthesiology had less prior or current NIH funding ($P = 0.002$), fewer total and education-related PubMed citations (both $P < 0.001$), and a lower h-index ($P = 0.001$) than surgery program directors. Multivariate analysis revealed that the publication rate for anesthesiology program directors was 43% (95% confidence interval, 0.31–0.58) that of the corresponding program directors of surgical residency programs, holding other variables constant.

CONCLUSIONS: Program directors of anesthesiology residency programs have considerably less scholarly activity in terms of peer-reviewed publications and federal research funding than directors of surgical residency programs. As such, this study provides further evidence for a systemic weakness in the scholarly fabric of academic anesthesiology.

連續外周神經阻滯患者的血清游離羅呱卡因濃度：長期輸注是否安全？

Serum Free Ropivacaine Concentrations Among Patients Receiving Continuous Peripheral Nerve Block Catheters: Is It Safe for Long-Term Infusions?

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Anesthesia & Analgesia 2014 118 225–229

背景：羅呱卡因是一種用於持續外周神經阻滯導管輸注的長效藥物。導管可以長期原位留置。在本研究中，入組患者給予持續外周神經置管並測定游離血清羅呱卡因濃度。

方法：放置外周神經導管用於創傷患者的術後疼痛管理，對其輸注 0.2%的羅呱卡因或單次次給予 0.5%的劑量。取每個患者術後當天（預輸注）、第 3、5、7、10 和隨後每隔兩天直至導管拔除的血液標本。使用高效液相色譜法測定游離血清羅呱卡因濃度並用 wilcoxon 符號秩檢驗對樣本進行統計分析。

結果：對 35 位元患者的 133 個血液樣本進行了分析：開始輸注後所有血清游離羅呱卡因的濃度（35 位元患者中的 99 個樣本）均低於 0.34 mg/L（先前設定的中毒閾值）。血液

樣本中最高濃度爲 0.19 mg/L；所有其他樣本值都小於 0.09 mg/L。研究中藥物使用量在 1146~22320mg 範圍內（中位數爲 3722mg）。導管留置的平均時間爲 7 天（範圍：3~23 天）。從術後當天到第 3 天（預輸注），77%的患者血清游離羅呱卡因濃度有所增加。第 3 天的平均濃度爲 0.025 mg/L（95%均值的置信上限爲: 0.05, 範圍：<0.01–0.19；與預輸注水平相比，P < 0.001）。從術後第 3 天到第 5 天，68%的患者血清游離羅呱卡因濃度下降(平均水準爲 0.016 mg/L[95%均值的置信上限爲: 0.021]，術後第 5 天與第 3 天相比，P = 0.007)。

結論：在本研究中，儘管戰傷患者大劑量使用羅呱卡因，但該藥物血清游離濃度一直低於中毒劑量。長時間持續羅呱卡因輸注以及聯合多種藥物單次劑量給藥，並不產生中毒或接近中毒的血清藥物濃度。

（邊文玉 譯 陳傑 校）

BACKGROUND: Ropivacaine is a long-acting local anesthetic used for continuous peripheral nerve catheter infusions. Catheters may remain in situ for prolonged time periods. In the present study, patients were enrolled to receive continuous peripheral nerve catheters with measurement of free serum ropivacaine concentrations.

METHODS: Peripheral nerve catheters were placed for postoperative pain management in trauma patients and infused with ropivacaine 0.2% or bolused with 0.5%. Blood samples were obtained from each subject on days 0 (preinfusion), 3, 5, 7, 10, and every third day until catheter removal. Serum free ropivacaine concentrations were measured via high-performance liquid chromatography and were compared using the Wilcoxon signed rank test.

RESULTS: One hundred thirty-three blood samples were analyzed in 35 patients; all serum free ropivacaine concentrations after infusion initiation (99 samples from 35 subjects) were below 0.34 mg/L (previously determined toxic threshold). The highest concentration achieved in a blood sample was 0.19 mg/L; all other values were <0.09 mg/L. The total amount of drug received during the study ranged from 1146 to 22,320 mg (median of 3722 mg). Catheters remained in situ for a median of 7 days (range: 3–23). From day 0 to 3 (preinfusion), 77% of the study participants had an increase in the serum free-fraction ropivacaine concentrations. The median concentration on day 3 was 0.025 mg/L (95% upper confidence limit for mean: 0.05, range: <0.01–0.19); P < 0.001 compared with preinfusion levels). From day 3 to 5, 68% of the participants had a decrease in the serum free ropivacaine concentrations (median level 0.016 mg/L [95% upper confidence limit for mean: 0.021] P = 0.007 for day 5 compared with day 3).

CONCLUSIONS: In this study, free serum ropivacaine concentrations remained well below toxic values despite large amounts of drug administration in combat-wounded patients. The administration of continuous ropivacaine infusions over prolonged time periods, coupled with multiple drug boluses, did not produce toxic or near-toxic serum concentrations.