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關於藥物治療在病人血液保護方面的當前狀況

Current Status of Pharmacologic Therapies in Patient Blood Management

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病人血液管理包括以病人為中心、循證醫學及外科途徑並同時通過應用病人自體血而非同種異體血來改善病人結局。對那些首要措施需特別注意，例如貧血治療。強調以病人為中心，是有區別於原先輸血醫學（強調血製品製造，關注其風險，代價，庫存方面而不是病人的預後）。病人血製品管理目標是避免輸血，選擇有效地替代品避免同種異體血的應用。替代措施包括自體血儲存，術前自體血儲備，急性等容性血液稀釋，術中或術後紅細胞回收洗滌和回輸。這樣對於貧血及血液管理應用藥物措施有：促紅細胞生成素，鐵劑治療，止凝血藥，人工氧載體。

(鄧利兵譯 薛張綱校)

Patient blood management^{1,2} incorporates patient-centered, evidence-based medical and surgical approaches to improve patient outcomes by relying on the patient's own (autologous) blood rather than allogeneic blood. Particular attention is paid to preemptive measures such as anemia management. The emphasis on the approaches being "patient-centered" is to distinguish them from previous approaches in transfusion medicine, which have been "product-centered" and focused on blood risks, costs, and inventory concerns rather than on patient outcomes. Patient blood management³ structures its goals by avoiding blood transfusion⁴ with effective use of alternatives to allogeneic blood transfusion.⁵ These alternatives include autologous blood procurement, preoperative autologous blood donation, acute normovolemic hemodilution, and intra/postoperative red blood cell (RBC) salvage and reinfusion. Reviewed here are the available

pharmacologic tools for anemia and blood management:erythropoiesis-stimulating agents (ESAs), iron therapy, hemostatic agents, and potentially, artificial oxygen carriers.

預注低劑量氯胺酮的阿片類藥物節省效應為接受體外衝擊波碎石術的阿片類藥物濫用者中度鎮靜：一項隨機臨床實驗

Opioid-Sparing Effect of Preemptive Bolus Low-Dose Ketamine for Moderate Sedation in Opioid Abusers Undergoing Extracorporeal Shock Wave Lithotripsy: A Randomized Clinical Trial

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背景：氯胺酮已被用作阿片類藥物濫用者接受全身麻醉的多模式鎮痛機制的一部分。我們研究了氯胺酮靜脈推注一個極低劑量在阿片類藥物濫用者接受體外衝擊波碎石術中中度鎮靜的阿片類藥物節省效應。

方法：有 190 名阿片類藥物濫用者參與了這項隨機、安慰劑對照的臨床試驗。根據他們日常阿片類藥物用藥量分成 2 組。2 組隨機接受 0.1 mg/kg 氯胺酮靜脈注射（K 組）或安慰劑（P 組）。在間歇靜脈推注瑞芬太尼（0.2 μg/kg）減輕疼痛來中度鎮靜下進行體外碎石術。在這 2 組中比較瑞芬太尼總量（主要結果）和呼吸系統不良事件（次要結果）。

結果：在低劑量阿片類藥物濫用者中使用瑞芬太尼 $1.6 \pm 0.4 \mu\text{g/kg}$ （P 組），相較 K 組為 $1.0 \pm 0.2 \mu\text{g/kg}$ （95%的置信區間[CI]，0.4–0.7; $P < 0.001$ ）。高劑量阿片類藥物濫用者中使用瑞芬太尼 $2.0 \pm 0.5 \mu\text{g/kg}$ （P 組），相較 K 組為 $1.5 \pm 0.3 \mu\text{g/kg}$ （95%的置信區間，0.40–0.75; $P < 0.001$ ）。統計出在高劑量阿片類藥物濫用者中接受安慰劑相較 K 組的準備排出時間更長（ 55 ± 13 分鐘 vs 44 ± 8 分鐘, 95% 置信區間, 6–15; $P < 0.001$ ）。在氯胺酮組和安慰劑組中呼吸緩慢、呼吸暫停、噁心、嘔吐和血流動力學變化的發生率無明顯統計學意義。

結論：在阿片類藥物濫用者中度鎮靜中預注低劑量氯胺酮（0.1 mg/kg）有阿片類藥物節省效應。

（方昕譯 薛張綱校）

BACKGROUND: Ketamine has been used as part of a multimodal analgesia regime in opioid abusers undergoing general anesthesia. We studied the opioid-sparing effect of a very low-dose bolus of ketamine as part of moderate sedation for opioid abuse patients undergoing extracorporeal shock wave lithotripsy.

METHODS: In this randomized, placebo-controlled clinical trial, 190 opioid abusers were enrolled. They were stratified into 2 blocks based on their daily opioid consumption. Both blocks were then randomized to receive 0.1 mg/kg IV ketamine (group K) or placebo (group P). Lithotripsy was performed under moderate sedation with intermittent bolus doses of remifentanyl (0.2 μg/kg) to alleviate pain. The total remifentanyl dose (primary outcome) and respiratory adverse events (secondary outcome) were compared in the 2 groups.

RESULTS: Remifentanil administration in the group with low-opioid consumers was 1.6 ± 0.4 $\mu\text{g}/\text{kg}$ (group P) compared with 1.0 ± 0.2 $\mu\text{g}/\text{kg}$ in group K (confidence interval [CI] of difference 95%, 0.4–0.7; $P < 0.001$). Patients who had high-opioid consumption received 2.0 ± 0.5 $\mu\text{g}/\text{kg}$ (group P) vs 1.5 ± 0.3 $\mu\text{g}/\text{kg}$ (group K) remifentanil (CI of difference 95%, 0.40–0.75; $P < 0.001$). Ready to discharge time was statistically longer in high-consumption opioid abusers who received placebo compared with group K (55 ± 13 minutes vs 44 ± 8 minutes, CI of difference 95%, 6–15; $P < 0.001$). The incidences of bradypnea, apnea, nausea, vomiting, and hemodynamic changes were not statistically different between the ketamine and placebo groups.

CONCLUSION: Preemptive low-dose ketamine (0.1 mg/kg) as a bolus has opioid-sparing effects in opioid abusers undergoing moderate sedation.

多腔輸液設備對於已知藥物物理不相溶現象的影響：一項控制性體外研究

The impact of multilumen infusion devices on the occurrence of known physical drug incompatibility: a controlled in vitro study.

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背景：藥物不相溶性如今已成為一個問題，這個問題尤其存在於ICU病人的管理中。我們設計了這項控制性體外研究用於評估多腔輸液設備對於已知藥物物理不相溶現象的影響。

方法：通過給一個單腔導管連接三種不同的輸液設備進行研究：標準設備由2個分支和1個延長支組成，2組多腔設備分別是：一個3腔延長設備和一個9腔延長設備(Edelvaiss-MultilineTM; Doran International, Toussieu, France)。對於9腔延長設備，我們將3輸液設備拼接進行研究。我們將速尿、咪達唑侖和鹽水同時通過3組輸液設備滴注，並對3種不同濃度速尿進行測試。鹽水（載體）的輸注速度初始設定為100ml/h，以10ml/h逐漸降低滴速直至沉澱形成。根據歐洲藥典通過2項測試評估物理不溶：視覺評估和可視粒子數計數。每組設備都得到一個最低鹽水輸注速率，此時剛剛好無可視沉澱且無可視粒子沉澱（即通過2項測試）。

結果：標準組顯示即使是在最高鹽水流速（100ml/h）時，可見沉澱依然存在。3腔設備通過最低濃度的速尿與同其濃度一同下降的鹽水滴注速率來防止沉澱。9腔設備在無論組合前兩項速尿濃度為多少時只要鹽水注射速度在20–60ml/h之間即能防止沉澱，但組合第三項中即使鹽水滴速達到100ml/h也無法避免沉澱。

結論：輸液設備看上去似乎會對2種藥物的物理相容性產生影響。在特定條件下，9腔輸液設備能防止速尿—咪達唑侖的物理不相溶性。

（郭晨躍譯 薛張綱校）

BACKGROUND: Drug incompatibility is a problem, especially when managing patients in intensive care units. We designed the present study to assess the impact of multilumen infusion access devices on the occurrence of known physical drug incompatibility through a controlled in vitro study.

METHODS: Three infusion devices connected to a single-lumen catheter were studied: a standard set with 2-port manifold and 1-m extension set and 2 multilumen infusion access

devices: a 3-lumen extension set and a 9-lumen extension set (Edelvaiss-Multiline™; Doran International, Toussieu, France). For the 9-lumen extension set, 3 infusion access combinations were studied. Furosemide, midazolam, and saline were infused simultaneously through 3 infusion devices. Three concentrations of furosemide were tested. The infusion rate of saline (carrier) was initially set at 100 mL/h and stepwise decreased by 10 mL/h until precipitate formation. Physical incompatibility was assessed by 2 tests: visual inspection and the subvisible particle count test according to the European Pharmacopeia. The lowest saline infusion rate to prevent visible precipitate and attain an acceptable particle count (i.e., to pass "the 2 tests") was reported for each infusion set.

RESULTS:The standard set revealed visible precipitate even at the highest saline flow rate (100 mL/h). The 3-lumen device prevented drug precipitation using the 2 lowest furosemide concentrations with a saline infusion rate that decreased with furosemide concentration. The 9-lumen infusion access device prevented drug precipitation whatever the furosemide concentration for 2 access combinations using saline infusion rates of between 20 and 60 mL/h but not for a third access combination, despite saline infusion rates equal to 100 mL/h.

CONCLUSIONS:Infusion device characteristics appear to have an impact on the physical compatibility of the 2 drugs. Under specified conditions, the 9-lumen infusion access device prevents physical furosemide-midazolam incompatibility.

評估琥珀膽鹼引發惡性高熱的風險

Estimate of the relative risk of succinylcholine for triggering malignant hyperthermia.

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背景：惡性高熱 MH 應用丹曲林和吸入麻醉藥治療，麻醉中出現的惡性高熱，應用丹曲林只需 1 天 1 個劑量即可起效；不用吸入麻醉劑，通過已註冊資料和麻醉期間使用司可林的次數，估計丹曲林的需要量，以此判斷司可林引起 MH 的幾率。

方法：司可林引發 MH 的原因有兩個，來自 MHAUS 的 284 名患者分別被分為 2 組，一組接受司可林的 MH 患者，另一種不給予司可林的 MH 患者，麻醉劑與琥珀膽鹼的比例的估計，使用麻醉資訊管理系統的資料來自一個典型的北美醫院由三級手術室、產科、門診手術中心、和內鏡和放射室。

結果：用司可林引起 MH 的相對危險度比沒用司可林組高 19.6（低 95% 可信區間大於 16.1）。揮發性麻醉藥的相對風險為 9.1（大於 7.5）。兩個相對風險超過 1.0 (P < 0.0001)。在北美，使用司可林的患者超過一半出現 MH，而沒使用司可林的患者出現 MH 的不足一半。與揮發性麻醉藥相比，琥珀膽鹼的發生率在醫院使用分別為 5.8% 和 11.6%。

結論：我們的結果不能洞察的觸發機制 MH(即。琥珀膽鹼引起 MH 的發病率極低,但明顯增加聯合揮發性麻醉藥誘導時 MH 的風險)。需要更多的流行病學資料的收集和分析,丹曲林在琥珀膽鹼引起的 MH 有效果,是合理的,這種做法應該保持。

(韓敘譯 薛張綱校)

BACKGROUND: Facilities with volatile anesthetic agents stock dantrolene for the treatment of malignant hyperthermia (MH). The availability of dantrolene at these facilities satisfies cost-utility norms even for sites with as few as 1 anesthetic per workday, based on the overall incidence of MH per anesthetic. We considered the stocking of dantrolene at facilities with succinylcholine alone (i.e., where volatile anesthetics are not available), by using registry data and estimates of the frequency of administration of succinylcholine during anesthesia. We determine the magnitude of the relative risk of the administration of succinylcholine for triggering MH.

METHODS: The relative risk of triggering MH by succinylcholine versus volatile agents was calculated using data from 2 sources. The ratio of the number of cases of MH among patients receiving succinylcholine to number among patients not receiving succinylcholine was estimated from the previously published cohort of 284 cases of MH from the North American MH Registry of the MH Association of the United States (MHAUS). The percentage of anesthetics with succinylcholine was estimated using anesthesia information management system data from a typical North American hospital comprising tertiary operating rooms, obstetrics unit, ambulatory surgical center, and endoscopy and radiological suites.

RESULTS: The relative risk of MH with versus without succinylcholine was 19.6 (lower 95% confidence limit > 16.1). Limiting to cases with volatile anesthetics, the relative risk was 9.1 (>7.5). Both relative risks exceed 1.0 ($P < 0.0001$). Because more than half of the reported cases of MH included the use of succinylcholine, the relative risk exceeded 1.0 provided fewer than half of anesthetics in North America included the use of succinylcholine. The incidences of succinylcholine use at the hospital were 5.8% and 11.6% for all anesthetics and for anesthetics with volatile agents, respectively.

CONCLUSIONS: Our results provide no insight into the triggering mechanism for MH (i.e., succinylcholine could in isolation have an extremely low incidence of inducing MH, yet markedly increase the risk when administered in combination with volatile anesthetics). Until more epidemiologic data are collected and analyzed, having dantrolene available, where succinylcholine may be used, is reasonable, and this practice should be maintained..

使用 Episure™自動檢測™注射器與傳統的玻璃注射器實施硬膜外技術相關的學習曲線：經驗豐富的麻醉醫師對產科病人實施的一個非盲，隨機，對照，交叉試驗。

The Learning Curve Associated with the Epidural Technique Using the Episure™ AutoDetect™ Versus Conventional Glass Syringe: An Open-Label, Randomized, Controlled, Crossover Trial of Experienced Anesthesiologists in Obstetric Patients.

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背景：在 2 相初步研究中，我們已經觀察到使用 Episure™自動檢測™（彈簧）注射器能成功地確定硬膜外腔。在這項研究中，我們評估經驗豐富的麻醉醫師使用彈簧式注射器對建立成功的硬膜外分娩鎮痛（主要結果），放置硬膜外導管的時間，以及學習曲線（累計匯總分析，即 CUSUM）的影響。

方法：14 位麻醉科主治醫生隨機使用帶彈簧式注射器或傳統的玻璃注射器每人實施 50 個連續硬膜外麻醉技術。10 位參加者使用這兩種注射器每人完成另外一個 50 個連續硬膜外麻醉技術。

結果：一共實施了 1200 個硬膜外技術。使用彈簧式注射器與使用傳統的玻璃注射器實施硬膜外麻醉相比在獲得鎮痛成功方面兩者成功率無顯著差異，（絕對差異為 1.0%，95% 可信區間，CI：-8.9%至 10.8%），前者硬膜外導管放置平均時間更短（比為 0.92 95% CI:0.89-0.96）， $P = 0.003$ ）兩者有類似累積曲線相。麻醉科醫生鎮痛成功更常見（絕對差為 34.6%，95%CI，14.9%-54.3%， $P < 0.001$ ），首選連續生理鹽水阻力消失法與使用間歇空氣法相比鎮痛成功更常見（絕對差為 33.8% 95%CI，12.6%-55.0%， $P < 0.001$ ）。我們也觀察到首先使用彈簧式注射器組所用的平均時間更短（比為 0.65 95% CI，0.62 - 0.67， $P = 0.02$ ）。

結論：在建立成功的硬膜外分娩鎮痛方面，經驗豐富的產科麻醉醫師使用彈簧式注射器與使用常規的玻璃注射器相比有類似的整體比率，硬膜外導管插入時間更短，有類似的累積曲線，尤其是當麻醉師第一次隨機使用新型注射器時。參加的麻醉師使用新型注射器時偏愛連續生理鹽水阻力消失法時鎮痛成功率更高。

（賀盼譯 薛張綱校）

BACKGROUND: The Episure™ AutoDetect™ (spring-loaded) syringe has been observed to successfully identify the epidural space in 2 pilot studies. In this study we evaluated the impact of the spring-loaded syringe on the establishment of successful epidural labor analgesia (primary outcome), elapsed time for catheter placement, and learning curve (cumulative summary analysis, i.e., Cusum) of experienced anesthesiologists.

METHODS: Fourteen attending and fellow anesthesiologists were randomized to perform 50 consecutive epidural technique attempts using a spring-loaded or conventional glass syringe. Ten participants completed an additional 50 attempts with the alternate syringe in a crossover design.

RESULTS: A total of 1200 epidural placement attempts were performed. Use of the spring-loaded syringe was associated with a nonsignificant difference of estimated success rate in obtaining analgesia success (absolute difference of 1.0% 95% confidence interval, CI: -8.9% to 10.8%), shorter elapsed mean time to epidural catheter placement (ratio of 0.92 95% CI, 0.89-0.96); $P = 0.003$) and similar Cusum curves when compared with a conventional glass syringe. Analgesia success was more common with attending versus fellow anesthesiologists (absolute difference of 34.6% 95% CI, 14.9% to 54.3%; $P < 0.001$), and when the initial preferred technique was loss-of-resistance to continuous saline versus intermittent air (absolute difference of 33.8% 95% CI, 12.6% to 55.0%; $P < 0.001$). Shorter elapsed mean times were also observed in the group exposed to the spring-loaded syringe first (ratio of 0.65 95% CI, 0.62-0.67; $P = 0.02$).

CONCLUSIONS: When used by experienced obstetric anesthesiologists, the spring-loaded syringe was associated with a similar overall rate for establishing successful epidural labor analgesia, a shorter elapsed time to epidural catheter insertion, particularly when the anesthesiologist was randomized to use the novel syringe first, and a similar Cusum curve when compared with a conventional glass syringe. Attending versus fellow anesthesiologists and an

initial technique preference for loss-of-resistance to continuous saline were associated with greater analgesia success with the novel syringe.

一項關於處理產後出血的新鮮冰凍血漿與紅細胞比率的觀察研究

An observational study of the fresh frozen plasma:red blood cell ratio in postpartum hemorrhage.

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背景：產後出血是全世界產婦死亡的首要原因。最近一些關於創傷性病人和創傷後失血性休克的病人資料表明增加的新鮮冰凍血漿與紅細胞比率對大量失血有利。我們解決這個問題來處理嚴峻的產後出血。

方法：我們回顧了 4 年間（2006-2009）被診斷為產後出血病人的所有相關資料。在這項研究中，病人獲得前列磺酮及在 6 小時內輸血處理，根據她們對前列磺酮的反應分成 2 個組：出血僅需前列磺酮控制（前列磺酮組）和出血需要進一步的介入手段包括動脈血管栓塞和/或外科手術（B-Lynch 縫合術，動脈結紮術或全子宮切除術；干預組）。進一步介入手段的需要與否決定該研究的終點。利用傾向評分標準來評估高的新鮮冰凍血漿與紅細胞比率在控制出血方面的作用。

結果：在 12226 名被研究人員中，142（占 1.1%）人併發了嚴重的產後出血。僅用前列磺酮控制住出血的有 90 位病人（占 63%）。需要進一步介入手術的有 52 人（占 37%）。41 位病人同時輸注了紅細胞和新鮮冰凍血漿。新鮮冰凍血漿：紅細胞的比例增加，在整個研究中（ $P < 0.001$ ）從最初的 1:1.8 到最後 1:1.1。傾向評分模型（相反概率的處理），對於行進一步介入手術（比率[95%可信區間]，1.25[1.07-1.47]； $P = 0.008$ ）而言，高的新鮮冰凍血漿：紅細胞比率是不需要的。研究病例中沒有死亡，重要器官功能衰竭或者其他因產後出血造成的併發症。

結論：在這項回顧性研究中看出，對於產後出血而進行的進一步介入手術並不需要輸入高的新鮮冰凍血漿：紅細胞比率的血。使用高的新鮮冰凍血漿：紅細胞比率輸血的益處需要通過隨機對照試驗來證實。

（胡曉清譯 薛張綱校）

BACKGROUND: Postpartum hemorrhage is the leading cause of maternal death worldwide. Recent data from trauma patients and patients with hemorrhagic shock have suggested that an increased fresh frozen plasma:red blood cell (FFP:RBC) ratio may be of benefit in massive bleeding. We addressed this issue in cases of severe postpartum hemorrhage.

METHODS: We reviewed data from all patients diagnosed with severe postpartum hemorrhage during a 4-year period (2006-2009). Patients who were treated with sulprostone and required transfusion within 6 hours of delivery were included in the study and were divided into 2 groups according to their response to sulprostone: bleeding controlled with sulprostone alone (sulprostone group) and bleeding requiring an additional advanced interventional procedure including arterial angiographic embolization and/or surgical procedures (arterial ligation, B-Lynch suture, or hysterectomy; intervention group). The requirement or no requirement for advanced procedures constituted the primary end point of the study. Propensity scoring was used to assess the effect of a high FFP:RBC ratio on bleeding control.

RESULTS: patients were transfused with both RBCs and FFP. The FFP:RBC ratio increased over the study period ($P < 0.001$), from 1:1.8 at the start to 1:1.1 at the end of the study period. After propensity score modeling (inverse probability of treatment weighting), a high FFP:RBC ratio was associated with lower odds for advanced interventional procedures (odds ratio [95% confidence interval], 1.25 [1.07-1.47]; $P = 0.008$). There were no deaths, severe organ dysfunction, or other complications as a consequence of severe postpartum hemorrhage.

CONCLUSIONS: In this retrospective study, a higher FFP:RBC ratio was associated with a lower requirement for advanced interventional procedures in the setting of postpartum hemorrhage. The benefits of transfusion using a higher FFP:RBC ratio should be confirmed by randomized-controlled trials.

蛛網膜下腔出血和腦出血患者的複極異常：發病誘因和預後

Repolarization abnormalities in patients with subarachnoid and intracerebral hemorrhage: predisposing factors and association with outcome

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背景：顱內病變患者中心電圖異常十分常見。在本研究中，我們評估了複極異常的誘發因素，例如，校正的QT (QTc)間期延長，心電圖缺血樣改變和複極末形態異常，並且考查了需要重症監護的蛛網膜下腔出血和腦出血患者中這些異常指標的預示價值。

方法：本研究在重症監護室進行，是一個前瞻性、觀察性的研究。入院時記錄患者的臨床特徵，意識水準，早期的頭顱CT結果。研究分為三階段，各兩天。每個階段均記錄12導聯心電圖、經胸心超、電解質和肌鈣蛋白I等指標，以及血管活性藥物和鎮靜藥物輸注速度。複極異常比如QTc間期延長（毫秒），心電圖缺血樣改變，複極末形態異常（存在/缺失）等被評估和分析。格拉斯哥預後評分評估一年功能恢復。

結果：本研究歷時兩年，共108名患者參加研究。在兩種出血類型中不同的複極異常均頻繁發生。QTc間期延長易發生於女性(β , 24.5; $P = 0.010$)和使用異丙酚者(β , 30.5; $P = 0.001$)。心電圖缺血樣改變易發生於男性(比值比[OR], 5.9; $P = 0.003$)，複極末形態異常易

發生於動脈瘤出血(OR, 13.0; P = 0.002)。心電圖缺血樣改變比較常見，占研究的 87/108，並且與一年功能恢復較差相關(OR, 4.7; 較低的 95% 可信區間, 1.5; P = 0.010)。

結論：每一種複雜異常都有特有的發病誘因。心電圖缺血樣改變比較常見，並且與一年功能恢復較差相關。

(郁玲玲譯 薛張綱校)

BACKGROUND: Electrocardiographic (ECG) abnormalities are frequent in patients with intracranial insult. In this study, we evaluated the factors predisposing to the repolarization abnormalities, i.e., prolonged corrected QT (QTc) interval, ischemic-like ECG changes and morphologic end-repolarization abnormalities, and examined the prognostic value of these abnormalities in patients with subarachnoid and intracerebral hemorrhages requiring intensive care.

METHODS: This was a prospective, observational clinical study in a university-level intensive care unit. Clinical characteristics, the level of consciousness, and findings in primary head computed tomography were recorded on admission. The study period was divided into three 2-day sections. In each section, a 12-lead ECG, transthoracic echocardiography, the results of standard blood electrolytes and cardiac troponin I, as well as the rate of vasoactive and sedative drug infusions were recorded. Repolarization abnormalities such as prolongation of the QTc interval (millisecond), ischemic-like ECG changes, and morphologic end-repolarization abnormalities (present/absent) were evaluated and analyzed. The 1-year functional outcome was determined using the Glasgow Outcome Score.

RESULTS: During the 2-year study period, 108 patients were included in the study. Different repolarization abnormalities were frequent in both types of hemorrhage. Prolongation of the QTc interval was predisposed by female gender (β , 24.5; P = 0.010) and the use of propofol (β , 30.5; P = 0.001). The predisposing factor for ischemic-like ECG changes were male gender (odds ratio [OR], 5.9; P = 0.003) and for morphological end-repolarization abnormalities aneurysmatic bleeding (OR, 13.0; P = 0.002). Ischemic-like ECG changes were common, in 87/108 patients during the study period, and were associated with a poorer 1-year functional outcome (OR, 4.7; lower 95% confidence interval, 1.5; P = 0.010).

CONCLUSIONS: Each repolarization abnormality has characteristic predisposing factors. Ischemic-like ECG changes are common and are associated with a poorer 1-year functional outcome.

pan-caspase 抑制劑可減少患坐骨神經慢性擠壓傷的大鼠的心肌細胞凋亡和神經病理性疼痛

A pan-caspase inhibitor reduces myocyte apoptosis and neuropathic pain in rats with chronic constriction injury of the sciatic nerve.

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背景：慢性壓迫性損傷是一種廣泛使用的用於研究神經病理性疼痛的大鼠模型。它表現出了類似人類神經病理性疼痛的症狀，如自發性疼痛，痛覺過敏和異常痛覺。最近，神經

病理性疼痛的大鼠中，細胞凋亡被認為可能是疼痛和運動障礙的一個啓動子。我們的這項研究是要證明在此動物模型中，肌肉細胞凋亡是否會引起神經病理性疼痛。

方法：爲了弄清這個問題，我們對患有由坐骨神經的慢性擠壓傷而產生神經病理性疼痛的大鼠進行疼痛、營養灌注、肌肉組織的炎症以及心肌細胞凋亡的研究。動物接受 pan-caspase 抑制劑 ZVAD (OMe)-fmk (N =5) 或相等劑量的賦形藥 (n =6)。假手術組作爲對照組 (n =6)。

結果：在神經結紮後第 4 天，各實驗組沒有任何灌注異常或肌肉組織炎症的跡象。然而，賦形藥組出現明顯的細胞凋亡，而這在用 ZVA-D 治療的動物中是幾乎完全阻斷的。與假手術對照組的結果相比，用 ZVA-D 治療的動物對由熱、冷和機械性刺激引起的疼痛明顯減少。

結論：從本次神經病理性疼痛的實驗模型發現，細胞凋亡可能有助於產生溫度和機械性異常痛覺。神經病理性疼痛的症狀發展並不依賴於微循環紊亂或肌肉組織的炎症。

(周玲譯 薛張綱校)

BACKGROUND: Chronic constriction injury is a widely used model for neuropathic pain in rats. It presents with symptoms resembling human neuropathic pain, such as spontaneous pain, hyperalgesia, and allodynia. Recently, myocyte apoptosis was found in neuropathic rats as a possible promoter of pain and motor dysfunction. Our aim in this study was to demonstrate whether muscle cell apoptosis contributes to neuropathic pain in this animal model.

METHODS: To clarify this issue, we examined pain, nutritive perfusion, and inflammation in muscle tissue as well as myocyte apoptosis in rats with neuropathic pain established by chronic constriction injury of the sciatic nerve. Animals received either the pan-caspase inhibitor zVAD (OMe)-fmk (n = 5) or equivalent volumes of vehicle (n = 6). Sham-operated rats served as controls (n = 6).

RESULTS: At day 4 after nerve ligation, there were no signs of perfusion failure or muscle tissue inflammation in all experimental groups. However, animals treated with the vehicle had marked myocyte apoptosis, which was found almost completely blocked in zVA-Dtreated animals. The zVA-Dtreated animals presented with a significant reduction of pain upon heat, cold, and mechanical stimulation comparable with values found in sham controls.

CONCLUSIONS: Myocyte apoptosis possibly contributes to thermal and mechanical allodynia in this experimental model for neuropathic pain. The development of neuropathic pain symptoms did not depend on disturbances in microcirculation or muscle tissue inflammation.

細胞外信號調節激酶 1/2/P2X3 信號轉導通路在慢性坐骨神經損傷的大鼠脊髓的電針影響。

The Effects of Electroacupuncture on the Extracellular Signal-Regulated Kinase 1/2/P2X3 Signal Pathway in the Spinal Cord of Rats with Chronic Constriction Injury.

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背景:作為傳統的治療疼痛的方法，電針（EA）被廣泛用於臨床，但其鎮痛療效尚未確切。在本研究中，我們探討 EA 對慢性疼痛的療效以及患有慢性壓迫性脊髓損傷的大鼠 P2X3 受體的表達。

方法:本研究分 2 部分，第 1 部分，將 SD 大鼠分成 6 組（n=10）：假-CCI，CCI，LEA，CCI+2Hz，電針穴位），HEA，CCI+15Hz 電針刺激穴位），NA-LEA（CCI+2Hz 電針非穴位）以及 NA-LEA（CCI+15Hz 電針非穴位）。4 至 9 天 CCI 後電針治療隔天一次，傷害性刺激由電子觸覺測量儀和熱板裝置執行。印記檢查測量脊髓內蛋白質和 P2X3 受體的 mRNA 以及即時聚合酶鏈反應。第 2 部分，大鼠被分成 5 組（n=10）：假-CCI, CCI, EA (CCI+EA 電針穴位)，NA-EA (CCI+EA 非穴位) 以及 U0126 (CCI+鞘內注射 U0126)。EA 治療和第一部分相似，給予 U0126 組大鼠鞘內注射 5ug U0126 和 5% 二甲基亞砷。十微升作為其他四組的載體在 CCI 治療後 4 至 9 天每兩天給一次。使用印跡法檢驗細胞外信號調節激酶 1/2（ERK1/2）和其磷酸化。

結果:電針治療具有很顯著的鎮痛效果，減少了 CCI 引起的脊髓 P2X3 受體蛋白和 mRNA 表達增加。此外，相比 15Hz，2Hz 電針具有較好的止痛效果，同時 15Hz 電針穴位的取穴比 2Hz 電針治療大鼠脊髓 P2X3 受體在蛋白和 mRNA 水準的降低。無論是 EA 在穴位或鞘內注射 U0126 釋然異常性疼痛和痛覺過敏和降低 P2X3 受體的表達和 ERK1/2 磷酸化的脊髓。

結論:本研究顯示，EA 能部分緩解神經性疼痛的行為，並通過 ERK1/2 信號通路在脊髓 P2X3 受體的表達減少。相比高頻 EA，低頻 EA 對神經病理性疼痛有較好的止痛效果。
（楊琰譯 薛張綱校）

BACKGROUND: Electroacupuncture (EA), as a traditional clinical method, is widely accepted in pain clinics, but the analgesic effect of EA has not been fully demonstrated. In the present study, we investigated the effect of EA on chronic pain and expression of P2X3 receptors in the spinal cord of rats with chronic constriction injury (CCI).

METHODS: The study was conducted in 2 parts. In part 1, Sprague Dawley rats were divided into 6 groups (n = 10): sham-CCI, CCI, LEA; CCI + 2 Hz EA at acupoints), HEA; CCI + 15 Hz EA at acupoints), NA-LEA (CCI + 2 Hz EA at nonacupoints), and NA-HEA (CCI + 15 Hz EA at nonacupoints). EA treatment was performed once a day on days 4 to 9 after CCI. Nociception was assessed using von Frey filaments and a hotplate apparatus. The protein and the messenger RNA (mRNA) levels of P2X3 receptors in the spinal cord were assayed by Western blotting and real-time polymerase chain reaction, respectively. In part 2, rats were divided into 5 groups (n = 10): sham-CCI, CCI, EA (CCI + EA at acupoints), NA-EA (CCI + EA at nonacupoints), and U0126 (CCI + intrathecal injection of U0126). EA treatment was conducted similar to part 1. Rats were given 5 μg U0126 in the U0126 group and 5% dimethyl sulfoxide intrathecally. Ten microliters was used as a vehicle for the other 4 groups twice a day on days 4 to 9 after CCI. Extracellular signal-regulated kinase 1/2 (ERK1/2) and ERK1/2 phosphorylation in the spinal cord were also assayed by Western blotting.

RESULTS: EA treatment exhibited significant antinociceptive effects and reduced the CCI-induced increase of both protein and mRNA expression of P2X3 receptors in the spinal cord. Furthermore, 2 Hz EA had a better analgesic effect than 15 Hz EA, and the protein and mRNA level of P2X3 receptor in spinal cord were lower in rats treated with 2 Hz EA at acupoints than 15 Hz EA at acupoints. Either EA at acupoints or intrathecal injection of U0126 relieved allodynia and hyperalgesia and reduced the expression of P2X3 receptors and ERK1/2 phosphorylation in the spinal cord.

CONCLUSIONS: The data demonstrated that EA alleviates neuropathic pain behavior, at least in part, by reducing P2X3 receptor expression in spinal cord via the ERK1/2 signaling pathway. Low frequency EA has a better analgesic effect than high frequency HEA on neuropathic pain.

綜述：現代澱粉在外科手術中應用的安全性

Review Article: Safety of Modern Starches Used During Surgery

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各種以增加血容量為目的的羥乙基澱粉（HES）製劑已被使用了幾十年。在重症監護病房使用 HES，尤其應用於感染性休克患者，可能出現不良後果是最近備受關注的話題。然而，HES 製劑的藥代動力學和藥效學性質取決於其化學成分和原材料。因此，不同的臨床條件可導致這些製劑不同的有效性和安全性。通過一項對符合納入標準的 59 個已發表研究進行的正規調查，4529 個物件隨機接受羥乙基澱粉（2139 名）和對照製劑（2390 名）處理，來評估外科手術中使用低替代級羥乙基澱粉的安全性。沒有證據表明手術過程中使用低替代級澱粉會引起腎臟的不良反應（這一影響使用血肌酐濃度變化或其絕對值或需要腎臟替代治療來評估，39 項實驗，3389 名物件），失血量增加（38 項試驗，3280 個患者），異體紅細胞輸注（20 項試驗，2151 個病人；羥乙基澱粉輸注比值比為 0.73，95% 可信區間=0.61-0.87]p=0.0005）或死亡率增加（羥乙基澱粉死亡比值比=0.51[0.24-1.05]，p=0.079）。

（鄭華容 譯 陳傑 校）

Various hydroxyethyl starch (HES) preparations have been used for decades to augment blood volume. There has been concern recently regarding possible adverse outcomes when using HES in the intensive care setting, especially in patients with septic shock. However, the pharmacokinetic and pharmacodynamic properties of HES preparations depend on their chemical composition and source material. Thus, different clinical conditions could result in differing effectiveness and safety for these preparations. Consequently, we assessed the safety of tetrastarches when used during surgery, using a formal search, that yielded 59 primary full publications of studies that met a priori inclusion criteria and randomly allocated 4529 patients with 2139 patients treated with tetrastarch compared with 2390 patients treated with a comparator. There were no indications that the use of tetrastarches during surgery induces adverse renal effects as assessed by change or absolute concentrations of serum creatinine or need for renal replacement therapy (39 trials, 3389 patients), increased blood loss (38 trials, 3280 patients), allogeneic erythrocyte transfusion (20 trials, 2151 patients; odds ratio for HES transfusion 0.73 [95% confidence interval = 0.61–0.87], P = 0.0005), or increased mortality (odds ratio for HES mortality = 0.51 [0.24–1.05], P = 0.079).

布比卡因和羅哌卡因的心肌蓄積與線粒體逆轉效應和心功能降低相關

Myocardial Accumulation of Bupivacaine and Ropivacaine Is Associated with Reversible Effects on Mitochondria and Reduced Myocardial Function

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背景：局麻藥引起心臟毒性的機理至今仍未完全清楚。此項研究分析了能引起臨床毒性的局麻藥濃度是否會影響心肌線粒體結構和氧耗。

方法：游離出豚鼠心臟建立 Langendorff 離體心臟模型，將其暴露於布比卡因(3.0 和 7.5 $\mu\text{g}/\text{mL}$) 和羅哌卡因(3.6 和 9.0 $\mu\text{g}/\text{mL}$) 10min。記錄心率，收縮壓，左室內壓變化速率，心電圖和冠脈流量。給藥後即刻或 20min 洗脫期、60min 洗脫期後測量組織的局麻藥濃度。另外，使用電子顯微鏡觀察心肌線粒體並對其結構損傷進行評分。將心肌細胞放入布比卡因液進行培養，測定氧耗率、細胞外酸化情況和 PGC-1 α mRNA 相對量（一種細胞能量代謝的調節因數）的表達。

結果：布比卡因和羅哌卡因引起 PR 間期及 QRS 可逆性延長，左室內壓及其變化率降低。心肌組織中局麻藥濃度是動脈濃度的 3 倍。局麻藥應用後線粒體表現出顯著的濃度依賴性形態腫脹。對於羅哌卡因和布比卡因，這些變化分別在進行 20min、60min 洗脫期後被逆轉。布比卡因在乳鼠心肌細胞培養中，降低線粒體氧耗，增加 PGC-1 α 的表達，而脂肪酸代謝不受影響。

結論：布比卡因和羅哌卡因可在心肌組織中蓄積。當達到負性肌力作用的濃度時，局麻藥可逆性引起線粒體腫脹。布比卡因降低細胞代謝，然而此效應可被脂肪酸逆轉。與線粒體的相互作用可能是導致局麻藥負性肌力作用的原因。

（諸琳婕 譯 陳傑 校）

BACKGROUND: Mechanisms of local anesthetic cardiac toxicity are still not completely understood. In this study, we analyzed whether concentrations of local anesthetics found in clinical toxicity affect myocardial mitochondrial structure and oxygen consumption.

METHODS: Guinea pig isolated heart Langendorff preparations were exposed to bupivacaine (3.0 and 7.5 $\mu\text{g}/\text{mL}$) and ropivacaine (3.6 and 9.0 $\mu\text{g}/\text{mL}$) for 10 minutes. Heart rate, systolic blood pressure, the first derivative of left ventricular pressure (+dP/dt), electrocardiogram, and coronary flow were recorded. The local anesthetic tissue concentration was measured either immediately after local anesthetic exposure, or after 20- and 60-minute washout periods. In addition, electron microscopy of myocardial mitochondria was performed using a scoring system for structural damage of mitochondria. Cardiomyocyte cell culture was incubated with bupivacaine, and oxygen consumption ratio, extracellular acidification, and relative amounts of PGC-1 α mRNA, a regulator of cellular energy metabolism, were determined.

RESULTS: Bupivacaine and ropivacaine induced reversible PR interval and QRS prolongation, and left ventricular pressure and +dP/dt reduction. Myocardial tissue concentration of local

anesthetics was 3-fold the arterial concentration. Mitochondria showed a significant concentration-dependent morphological swelling after local anesthetic application. These changes were reversed by a 20-minute washout period for ropivacaine and by a 60-minute washout for bupivacaine. Bupivacaine reduced mitochondrial oxygen consumption and increased PGC-1 α expression in neonatal cardiomyocyte cell cultures, whereas fatty acid metabolism remained unaffected.

CONCLUSIONS: Bupivacaine and ropivacaine accumulate in the myocardium. Reversible local anesthetic-induced mitochondrial swelling occurs at concentrations that induce a negative inotropic effect. Bupivacaine reduces cellular metabolism, whereas this reduction is reversible by fatty acids. Interaction with mitochondria may contribute to the negative inotropic effect of local anesthetics.

特稿：疼痛醫療危機資源管理教育課程和案例

Special Article: Curriculum and Cases for Pain Medicine Crisis Resource Management Education

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在疼痛醫療機構可能發生的罕見緊急醫療事件需要技巧以及協作來保證病人的安全預後。環境模擬對於獲得和增強這方面的知識和技能是一個理想的設施。本文中為疼痛醫學專科醫師以及主治醫師介紹一項疼痛醫療危機資源管理教學課程，以及這項試驗計畫的成果。
(瞿亦楓 譯 陳傑 校)

Medical crises that may occur in the setting of a pain medicine service are rare events that require skillful action and teamwork to ensure safe patient outcome. A simulated environment is an ideal venue for both acquisition and reinforcement of this knowledge and skill set. Here, we present an educational curriculum in pain medicine crisis resource management for both pain medicine fellows and attending physicians as well as the results of a successful pilot program.

比較鞘內注射 30mg 利多卡因和 45mg 利多卡因試驗劑量對產科人群影響的一項前瞻性隨機實驗

A Prospective Randomized Trial of Lidocaine 30 mg Versus 45 mg for Epidural Test Dose for Intrathecal Injection in the Obstetric Population

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背景：硬膜外試驗劑量，用於排除意外的鞘內置管，在對患者不造成危險的前提下應產生確切的脊髓阻滯效果。大多數的麻醉醫生通常會用 45mg 的利多卡因作為局麻試驗劑量。孕婦對局麻藥更為敏感，相關報導提示這個劑量在孕婦人群中更容易出現麻醉平面過高以及全脊麻現象。因此本實驗假設與 45mg 利多卡因相比，30mg 劑量可產生相同的感覺和運動阻滯作用。

方法：在這個前瞻性隨機雙盲實驗中，將擇期行剖宮產病人分成四組：30mg 利多卡因鞘內或硬膜外給藥組，或 45mg 利多卡因鞘內或硬膜外給藥組。然後不知情的觀察者對四組病人的感覺和運動阻滯的程度進行評估。比較各劑量對鞘內注射的預測能力。高於 T6 節段的感覺阻滯或低血壓被記錄為不良事件。

結果：鞘內注射 30mg 利多卡因能在 3min 內迅速產生主觀與客觀的神經阻滯症狀（100%，95% 可信區間 CI，分別為 85%–100%）。而 45mg 的利多卡因也能產生相同作用。兩組中所有病人都描述了在 3min 後下肢發熱和沉重的感覺及 5min 後的運動阻滯作用。基於鞘內置管發生率為 1：380，如果患者在 3 分鐘後沒有感覺的改變，則 30mg 和 45mg 利多卡因給藥對於鞘內置管的陰性預測值分別為 100% (95% CI, 99.95%–100%) and 100% (95% CI, 99.93%–100%)，同時本研究未發現低劑量組的不良事件發生率降低。

結論：本研究結果指出這兩組劑量在確認導管誤置鞘內方面沒有顯著差異。兩組的鞘內注射的陰性預測值都非常高。這兩個劑量敏感度的 95% 可信區間太寬以至於不能明確所有誤置導管來保障臨床安全性。因此還需要進行大量研究來評價 30mg 的劑量是否具有較低的靈敏度，或者 45mg 的劑量能產生較高平面的運動阻滯。

（馬霄雯 譯 陳傑 校）

BACKGROUND: The epidural test dose, used to identify unintended intrathecal placement, should reliably produce a spinal block without posing a threat to the patient. Most anesthesiologists administer a dose of local anesthetic, commonly lidocaine 45 mg. Pregnant patients are more sensitive to local anesthetics; high and total spinal anesthesia have been reported in the pregnant population with this dose. We hypothesized that lidocaine 30 mg was as effective as lidocaine 45 mg in creating rapid objective evidence of a sensory or motor block.

METHODS: In this prospective, randomized, double-blind trial, patients scheduled for cesarean delivery were assigned to 1 of 4 groups: lidocaine 30 mg in the spinal or epidural space, or lidocaine 45 mg by the same routes. A blinded observer assessed the degree of sensory and motor block. The ability to identify intrathecal injection of each dose was compared. Sensory block above T6 dermatome and hypotension were recorded as side effects.

RESULTS: Intrathecal administration of lidocaine 30 mg produced rapid subjective and objective signs of neuroblockade within 3 minutes (100%, 95% confidence interval CI, 85%–100% for each). Lidocaine 45 mg produced similar results. All patients in both groups described their legs as warm or heavy after 3 minutes and had a motor block by 5 minutes. On the basis of an intrathecal catheter rate of 1:380, the observed negative predictive value for intrathecal placement if the patient described no sensory changes at 3 minutes was 100% (95% CI, 99.95%–100%) for 30 mg and 100% (95% CI, 99.93%–100%) for 45 mg. We did not identify a decrease in the rate of side effects with the lower dose.

CONCLUSIONS: Our results suggest that there is unlikely to be a large difference in the ability of these doses to detect unintentional intrathecal catheter placement. While the negative predictive value for intrathecal injection is very high for both doses, the 95% CI for the sensitivity of either dose is too wide to demonstrate clinical safety to identify all intrathecal catheters. A much larger study is warranted to assess whether there is a lower sensitivity with the 30-mg dose, or a propensity toward high cephalad motor block levels with the 45-mg dose.

疼痛多基因易感性的首要證據：一項兒童佇列研究

First Evidence of a Polygenic Susceptibility to Pain in a Pediatric Cohort

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背景：目前還沒有證據表明兒童術後疼痛變異的遺傳基礎。

方法：本研究前瞻性地隨訪 168 名接受整形或腹部手術並在術後使用嗎啡自控鎮痛的兒童。將孩子及其父母有關痛覺和阿片藥物代謝的基因歸為 6 個候選基因多態性分型（單核苷酸多態性[SNPs]），分別是：ABCB1C3435T, COMTVal158Met, NTRK1His40Tyr, OPRMA118G, POMCArG236Gln 和單倍型 CYP2D6，術後 24 小時內分別進行 11 次靜息和活動時表情疼痛評分（FPS）來評估術後疼痛。

結果：靜息時和較小程度上在活動時，ABCB1_CC 基因的兒童比 ABCB1_CT 和 ABCB1_TT 基因的兒童在 24 小時內至少 4 個 FPS 峰值大於 6 的發生率更高（調整後風險比= 4.5；95% 可信區間[CI]，1.5–13.4；多重比較的校正可信區間，0.98–20.55），且 OPRM_GA 基因的兒童比 OPRM_AA 基因的兒童發生率更高（調整後的危險比= 3.5；95% 可信區間，1.1–11.2；校正可信區間：0.70–17.30）。對親本交配型和多次比較校正後，靜息時 OPRM_GA 基因兒童術後 24 小時人平均 FPS 得分高於 OPRM_AA 基因兒童（ $P < 0.0002$ ），在活動期 NTRK1_CT 基因或者 NTRK1_TT 基因比 NTRK1_CC 基因的平均 FPS 值更高（ $P = 0.002$ ），而在活動時 COMT_GG 基因比 COMT_AA 基因和 COMT_GA 基因平均 FPS 值更低（ $P = 0.005$ ）。

結論：ABCB1 和 OPRM 基因型與臨床意義的疼痛變異有關，而 NTRK1 和 COMT 與亞臨床效應相關。首個小樣本量研究為進一步探討小兒疼痛的遺傳基礎提供了線索。

（孫莉荔 譯 陳傑 校）

BACKGROUND: There is currently no evidence about the genetic bases of postoperative pain variability in children.

METHODS: We prospectively followed a cohort of 168 children after orthopedic or abdominal surgery, who were under morphine patient-controlled analgesia. The children and their parents were genotyped for 6 candidate-gene polymorphisms (single-nucleotide polymorphisms [SNPs]) implicated in nociception and opiate metabolism: ABCB1C3435T, COMTVal158Met, NTRK1His40Tyr, OPRMA118G, POMCArG236Gln, and a haplotype of CYP2D6. Postoperative pain was assessed using the Faces Pain Scale (FPS), at rest and during mobilization, 11 times during the first 24 postoperative hours.

RESULTS: At rest, and to a lesser extent, at mobilization, having at least 4 pain peaks of FPS score >6 in 24 hours was more frequent in children with ABCB1_CC than in children with ABCB1_CT and ABCB1_TT (adjusted risk ratio = 4.5; 95% confidence interval [CI], 1.5–13.4; corrected CI for multiple comparisons, 0.98–20.55) and was more frequent in children with OPRM_GA than those with OPRM_AA (adjusted risk ratio = 3.5; 95% CI, 1.1–11.2; corrected CI, 0.70–17.30). After adjusting for parental mating type and correcting for multiple comparisons, mean FPS scores across the 24 postoperative hours were higher for OPRM_GA

than for OPRM_AA at rest ($P < 0.0002$), higher for NTRK1_CT or NTRK1_TT than NTRK1_CC during mobilization ($P = 0.002$), and lower for COMT_GG than COMT_AA and COMT_GA, during mobilization ($P = 0.005$).

CONCLUSIONS: ABCB1 and OPRM genotypes are associated with clinically meaningful pain variability, whereas NTRK1 and COMT are linked to subclinical effects. This first but small cohort study provides clues to further explore the genetic foundations of pediatric pain.

進化早期暴露於吸入麻醉藥導致秀麗隱杆線蟲行為學異常

Early Developmental Exposure to Volatile Anesthetics Causes Behavioral Defects in *Caenorhabditis elegans*

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背景：越來越多的動物實驗證據表明生命早期暴露於麻醉藥會導致發展中的神經系統凋亡，神經元的減少會引起成人階段的功能性不良後果。臨床回顧綜述表明兒童時期暴露於多種麻醉藥與學習能力障礙也有著緊密的關聯。儘管很多人關注過這個現象，但很少人知道麻醉藥引起神經細胞死亡的機理。秀麗隱杆線蟲，一個非常有力的基因動物模型，具有神經系統發育和細胞凋亡路徑的特徵性表現，提供了一個非常好的機會來研究麻醉引起的神經毒性。本研究假設這種線蟲在其生命早期暴露於吸入麻醉藥下會引起神經細胞的死亡，會產生一種成年期的行為學異常。

方法：在同步孵化後，幼蟲被暴露於 95% 有效濃度的吸入麻醉藥中持續 4 小時，在出生後第四天，測試暴露和對照組幼蟲的感知和向引誘物（趨化劑）移動的能力。使用標準趨化指數來測定成功趨化的比例。

結果：野生型線蟲在暴露於異氟醚或七氟醚後在其第一幼蟲期出現了趨化指數的顯著異常（趨化指數：未暴露組， 85 ± 2 ；異氟醚組， 52 ± 2 ；七氟醚組， 47 ± 2 ；兩暴露組 $P < 0.05$ ）。線粒體突變型 *gas-1* 對暴露產生更強效果（趨化性指數：未暴露組， 71 ± 2 ；異氟醚組， 29 ± 12 ；七氟醚組， 24 ± 13 ；兩暴露組 $P < 0.05$ ）。相反，介導細胞死亡程式通路突變的動物（*ced-3*）保留其感知和向引誘物移動的能力而不產生凋亡（趨化指數：未暴露組， 76 ± 10 ；異氟醚組， 73 ± 9 ；七氟醚組， 76 ± 10 ）。另外，本研究發現線蟲對麻醉藥神經毒性最敏感的視窗期發生於孵化後的第一幼蟲期(L1)，這與此模型種神經形成期相一致。所有數值以平均數±標準差表示。

結論：這些資料表明，麻醉劑影響線蟲的神經習性，延伸到這一門的範圍，早期暴露於吸入麻醉藥可導致功能上的神經學的異常。這意味著麻藥相關的神經毒性通過古老的根本的機制發生。秀麗隱杆線蟲是一個易控制的生物模型用來調查整個分子基因引起的發展中的神經系統的吸入麻醉藥的毒性效應。

（詹愷 譯 陳傑 校）

BACKGROUND: Mounting evidence from animal studies shows that anesthetic exposure in early life leads to apoptosis in the developing nervous system. This loss of neurons has

functional consequences in adulthood. Clinical retrospective reviews have suggested that multiple anesthetic exposures in early childhood are associated with learning disabilities later in life as well. Despite much concern about this phenomenon, little is known about the mechanism by which anesthetics initiate neuronal cell death. *Caenorhabditis elegans*, a powerful genetic animal model, with precisely characterized neural development and cell death pathways, affords an excellent opportunity to study anesthetic-induced neurotoxicity. We hypothesized that exposing the nematode to volatile anesthetics early in life would induce neuron cell death, producing a behavioral defect that would be manifested in adulthood.

METHODS: After synchronization and hatching, larval worms were exposed to volatile anesthetics at their 95% effective concentration for 4 hours. On day 4 of life, exposed and control worms were tested for their ability to sense and move to an attractant (i.e., to chemotax). We determined the rate of successful chemotaxis using a standardized chemotaxis index.

RESULTS: Wild-type nematodes demonstrated striking deficits in chemotaxis indices after exposure to isoflurane (ISO) or sevoflurane (SEVO) in the first larval stage (chemotaxis index: untreated, 85 ± 2 ; ISO, 52 ± 2 ; SEVO, 47 ± 2 ; $P < 0.05$ for both exposures). The mitochondrial mutant *gas-1* had a heightened effect from the anesthetic exposure (chemotaxis index: untreated, 71 ± 2 ; ISO, 29 ± 12 ; SEVO, 24 ± 13 ; $P < 0.05$ for both exposures). In contrast, animals unable to undergo apoptosis because of a mutation in the pathway that mediates programmed cell death (*ced-3*) retained their ability to sense and move toward an attractant (chemotaxis index: untreated, 76 ± 10 ; ISO, 73 ± 9 ; SEVO, 76 ± 10). Furthermore, we discovered that the window of greatest susceptibility to anesthetic neurotoxicity in nematodes occurs in the first larval stage after hatching (L1). This coincides with a period of neurogenesis in this model. All values are means \pm SD.

CONCLUSION: These data indicate that anesthetics affect neurobehavior in nematodes, extending the range of phyla in which early exposure to volatile anesthetics has been shown to cause functional neurological deficits. This implies that anesthetic-induced neurotoxicity occurs via an ancient underlying mechanism. *C. elegans* is a tractable model organism with which to survey an entire genome for molecules that mediate the toxic effects of volatile anesthetics on the developing nervous system.

技術交流: 驗證單機近紅外光譜系統在心臟手術中監測腦血流自動調節的作用

Technical Communication: Validation of a Stand-Alone Near-Infrared Spectroscopy System for Monitoring Cerebral Autoregulation During Cardiac Surgery

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背景:在體外迴圈(CPB)期間基於腦血流(CBF)自動調節功能監測的動脈血壓 (ABP) 個體化控制, 可以提供一個比現行使用的監護標準更為有效的預防腦血流灌注不足的方法。經顱多普勒(TCD)可即時監測血流自動調節功能。之前研究證實近紅外光譜(NIRS)衍生出的局部腦氧飽和度(rScO2)監測可以在臨床上替代腦血流(CBF)自動調節功能的監測。本研

究目的是確定單機“隨插即用”血流自動調節監控的臨床試用系統的準確性，此調節監控使用市售的近紅外光譜(NIRS)監測儀以及 TCD 方法。

方法：對 70 例病人在體外迴圈(CPB)期進行大腦中動脈血流速率的 TCD 監測和近紅外光譜(NIRS)監測。通過一台基於個人電腦的系統，和一台基於監控近紅外光譜(NIRS)的監測儀，計算血流自動調節指數。ABP 的慢波和腦血流(CBF)速率（平均速率指數[Mx]）之間的動態的線性相關性指數，以及 ABP 與局部腦氧飽和度 rScO₂（腦氧飽和度指數[COx]）之間的動態的線性相關性指數被計算出。當 CBF（腦血流）在自動調節範圍，腦血流(CBF)和 ABP 之間就不會有相關性；當腦血流(CBF)失調時，平均速率指數（Mx）和腦氧飽和度指數（COx）接近 1（即腦血流[CBF]和 ABP 相關）。通過基於個人電腦的系統和腦氧飽和度指數（COx）監測儀得出平均速率指數（Mx）和腦氧飽和度指數（COx）值，進行後兩者之間的時間平均值的線性回歸和方差分析。每一個病人的 Mx 和 COx 的值都以 5mmHg 為單位的 ABP 條柱進行分類。CBF 的下限自動被定義為當 Mx 逐步增加到大於或等於 0.4 時 ABP。

結果：在 Mx 和原型監測儀得到的 COx 之間有相關性和良好的一致性（ $r=0.510$ ，95%的可信區間為 0.414-0.595； $p<0.001$ ，偏差在 -0.07 ± 0.19 之間）。基於個人電腦的 COx 值與基於原型 NIRS 監測儀的 COx 值之間的相關性和偏差為 $r=0.957$ (95%的可信區間為 0.945-0.966； $p<0.001$ ， -0.06 ± 0.06)。在自動調節下限的 ABP 平均值為 63 ± 11 mm Hg(95%的預測區間為 52-74 mm Hg)。雖然通過原型監測儀監測到的 COx 的下限-APB 平均值與來自 Mx 測定的 APB 平均值（ 59 ± 9 mm Hg; 95%的預測區間為 50-68 mm Hg; $p=0.026$ ）有統計學差異性，但是這個差異性似乎不具有臨床意義。

結論：通過研究單機 NIRS 監測儀和以 TCD 為基礎的監測方法監測的 CBF 自動調節之間有相關性和良好的一致性。這種裝置可使血流自動調節監測廣泛用於 CPB 期間對 ABP 的個性化監測成為可能。

（王苑 譯 陳傑 校）

BACKGROUND: Individualizing arterial blood pressure (ABP) targets during cardiopulmonary bypass (CPB) based on cerebral blood flow (CBF) autoregulation monitoring may provide a more effective means for preventing cerebral hypoperfusion than the current standard of care. Autoregulation can be monitored in real time with transcranial Doppler (TCD). We have previously demonstrated that near-infrared spectroscopy (NIRS)-derived regional cerebral oxygen saturation (rScO₂) provides a clinically suitable surrogate of CBF for autoregulation monitoring. The purpose of this study was to determine the accuracy of a stand-alone “plug-and-play” investigational system for autoregulation monitoring that uses a commercially available NIRS monitor with TCD methods.

METHODS: TCD monitoring of middle cerebral artery CBF velocity and NIRS monitoring were performed in 70 patients during CPB. Indices of autoregulation were computed by both a personal computer-based system and an investigational prototype NIRS-based monitor. A moving linear correlation coefficient between slow waves of ABP and CBF velocity (mean velocity index [Mx]) and between ABP and rScO₂ (cerebral oximetry index [COx]) were calculated. When CBF is autoregulated, there is no correlation between CBF and ABP; when CBF is dysregulated, Mx and COx approach 1 (i.e., CBF and ABP are correlated). Linear regression and bias analysis were performed between time-averaged values of Mx and COx derived from the personal computer-based system and from COx measured with the prototype monitor. Values for Mx and COx were categorized in 5 mm Hg bins of ABP for each patient.

The lower limit of CBF autoregulation was defined as the ABP where Mx incrementally increased to ≥ 0.4 .

RESULTS: There was correlation and good agreement between COx derived from the prototype monitor and Mx ($r = 0.510$; 95% confidence interval, 0.414–0.595; $P < 0.001$; bias, -0.07 ± 0.19). The correlation and bias between the personal computer-based COx and the COx from the prototype NIRS monitor were $r = 0.957$ (95% confidence interval, 0.945–0.966; $P < 0.001$ and 0.06 ± 0.06 , respectively). The average ABP at the lower limit of autoregulation was 63 ± 11 mm Hg (95% prediction interval, 52–74 mm Hg). Although the mean ABP at the COx-determined lower limit of autoregulation determined with the prototype monitor was statistically different from that determined by Mx (59 ± 9 mm Hg; 95% prediction interval, 50–68 mm Hg; $P = 0.026$), the difference was not likely clinically meaningful.

CONCLUSIONS: Monitoring CBF autoregulation with an investigational stand-alone NIRS monitor is correlated and in good agreement with TCD-based methods. The availability of such a device would allow widespread autoregulation monitoring as a means of individualizing ABP targets during CPB.

通過閾值測定、條件性位置偏愛（CPP）圖及背根神經節啟動的轉錄因數 3 變化來研究順鉑誘發持續性痛覺過敏的小鼠模型中加巴噴丁，酮咯酸和依那西普的作用

Persistent Hyperalgesia in the Cisplatin-Treated Mouse as Defined by Threshold Measures, the Conditioned Place Preference Paradigm, and Changes in Dorsal Root Ganglia

Activated Transcription Factor 3: The Effects of Gabapentin, Ketorolac, and Etanercept

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背景：疼痛性神經病變是一種癌症化療中導致劑量限制的副作用。為了描述此現象，對順鉑處理的多發性神經病變小鼠模型進行疼痛行為和鎮痛作用研究。

方法：對雄性 C57BL/6 小鼠每隔一日進行腹腔注射順鉑或生理鹽水（2.3mg/kg/d）6 次，持續 2 周，總劑量 13.8mg/kg。對熱逃逸潛伏期，von Frey hairs 觸發機械痛覺，行為/發病率以及體重進行評估。觸發痛覺過敏後，檢測腹腔內注射加巴噴丁(100 mg/kg)、依那西普(20 and 40 mg/kg)、酮咯酸(15 mg/kg)和嗎啡(1, 3, and 10 mg/kg)各自作用。此外，採用 CPP 方法，研究加巴噴丁和酮咯酸對由順鉑觸發的疼痛狀態的影響。另外，還研究了順鉑處理小鼠的脊髓和背根神經節（DRG）。

結果：順鉑而非生理鹽水產生持續 46 天的後肢痛覺過敏，但對熱逃逸現象無影響。加巴噴丁和嗎啡而非依那西普或酮咯酸可產生完全但短暫（2 小時）的痛覺過敏逆轉。依那西普(40 mg/kg) 預處理使機械性痛覺過敏延遲觸發。加巴噴丁而非酮咯酸用於順鉑處理小鼠，基於 CPP 發現存在對藥物相關治療室的顯著偏愛行為。加巴噴丁注射後，在非順鉑處理小鼠（無痛覺過敏）中沒有發現位置偏愛行為。順鉑處理小鼠的免疫組織化學未顯示膠質纖維酸性蛋白（星形膠質細胞）或 Iba1（離子鈣結合調節分子 1）小膠質神經細胞啟動狀態的變化，但在 DRG 中觀察到啟動的轉錄因數 3 顯著增加。

結論：與其對 CPP 系統中行爲效應一致，順鉑處理小鼠表現痛覺過敏和 DRG 活化的轉錄因數 3 啟動，然而加巴噴丁而非酮咯酸在順鉑引起的多發性神經病中是有積極作用的，明確了神經病變是一種負面（痛苦的）狀態，且加巴噴丁可以緩解。

(黃萍 譯 陳傑 校)

BACKGROUND: Painful neuropathy is a dose-limiting side effect in cancer chemotherapy. To characterize this phenomenon, we examined pain behavior and analgesic actions in a mouse model of cisplatin polyneuropathy.

METHODS: Male C57BL/6 mice received intraperitoneal cisplatin or saline (2.3 mg/kg/d) every other day 6 times over 2 weeks for a total dose of 13.8 mg/kg. Thermal escape latencies, mechanical allodynia using von Frey hairs, and observation of behavior/morbidity and body weights were assessed. After onset of allodynia, we examined the actions of intraperitoneal gabapentin (100 mg/kg), etanercept (20 and 40 mg/kg), ketorolac (15 mg/kg), and morphine (1, 3, and 10 mg/kg). Additionally, using the conditioned place preference (CPP) paradigm, we examined the effects of gabapentin and ketorolac on the presumed pain state initiated by cisplatin. Additionally, we examined the spinal cord and dorsal root ganglia (DRG) of cisplatin-treated mice.

RESULTS: Cisplatin, but not saline treatment, produced persistent hindpaw tactile allodynia, which persisted 46 days with no effect on thermal escape. Gabapentin and morphine, but neither etanercept nor ketorolac, produced a complete but transient (2-hour) reversal of the allodynia. Etanercept (40 mg/kg) pretreatment resulted in a delay in onset of mechanical allodynia. Using CPP, gabapentin, but not ketorolac, in cisplatin animals resulted in a significant preference for the drug-associated treatment compartment. There was no place preference in non-cisplatin-treated (nonallodynic) mice after gabapentin injection. Immunohistochemistry in cisplatin-treated mice showed no change in glial fibrillary acidic protein (astrocyte) or Iba1 (ionized calcium binding adaptor molecule 1) (microglia) activation states, but a significant increase in activated transcription factor 3 was observed in the DRG.

CONCLUSIONS: Cisplatin-treated mice display allodynia and an activation of DRG activated transcription factor 3, which is paralleled by its effects on behavior in the CPP system, wherein gabapentin, but not ketorolac, in the presence of the cisplatin polyneuropathy, is positively rewarding, confirming that this neuropathy is an aversive (painful) state that is ameliorated by gabapentin.

用於腋路臂叢阻滯的高低刺激電流閾值對比：一項對 205 名病人的前瞻隨機三盲非劣效性試驗

High- Versus Low-Stimulation Current Threshold for Axillary Plexus Blocks: A Prospective Randomized Triple-Blinded Noninferiority Trial in 205 Patients

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背景：對於神經刺激器引導下的局部麻醉，麻醉醫師必須在假定低成功率（使用高電流閾值）和假定增加神經損傷風險（使用低電流閾值）這二者之間做出權衡。針對神經刺激

引導的臂叢神經阻滯，本研究假設使用 0.9 至 1.1mA 範圍內的高電流閾值在操作和起效時間方面並不比 0.3 至 0.5mA 範圍內的低電流閾值要差。

方法： 205 名計畫擇期手術病人被隨機分為低刺激電流閾值組（0.3-0.5mA，n=103）或者高刺激電流閾值組（0.9-1.1mA，n=102），兩組都使用 40mL 局麻藥混合液（1% 丙胺卡因和 0.75% 羅呱卡因各 20mL）進行腋路臂叢神經阻滯。研究主要終點為感覺完全阻滯時間。次要結果是手術準備時間（定義為從開始阻滯至感覺完全阻滯時間）和操作時間。非劣效性邊界設為 5 分鐘並且以雙邊 95% 的自舉置信區間（[CIs] 100,000 次重複）均數差來評價。

結果： 低刺激電流閾值組的感覺完全阻滯平均時間顯著減少（ (17.9 ± 12.1) (平均值 \pm 標準差) 對 22.8 ± 12.4 分鐘; 95% 置信區間, 1.1 至 8.6; $p = 0.012$.)。低刺激電流閾值組的手術準備時間為 30.3 ± 13.8 分鐘而高刺激電流閾值組為 31.7 ± 12.9 分鐘（95% 置信區間, -2.7 至 5.5; $p = 0.49$ ）。高刺激電流閾值組的操作時間明顯縮短（ 9.5 ± 4.7 對 11.9 ± 5.7 分鐘; 95% 置信區間, -4 至 1.1; $p = 0.001$ ）。

結論： 主次要終點都不能確認高電流閾值技術的非劣效性。但考慮到臨床實踐，在滿足手術要求的平均花費時間方面約 8.5 分鐘的差異是可以接受的。

（孫曉瓊 譯 陳傑 校）

BACKGROUND: For nerve stimulator-guided regional anesthesia, one has to compromise between a presumed low success rate (using a high-current threshold) and a presumed increased risk of nerve damage (using a low-current threshold). We hypothesized that high-current thresholds in the range of 0.9 to 1.1 mA are not inferior with respect to the procedural and latency times compared with low threshold currents in the range of 0.3 to 0.5 mA for nerve stimulation in brachial plexus blocks.

METHODS: Two hundred five patients scheduled for elective surgery were randomized to a low (0.3–0.5 mA, n = 103) or a high (0.9–1.1 mA, n = 102) stimulation current threshold for the axillary plexus block with 40 mL local anesthetic mixture (20 mL, each of prilocaine 1% and ropivacaine 0.75%). The primary end point was the time to complete sensory block. The secondary outcome measures were the time to readiness for surgery (defined as the time from the start of block procedure to complete sensory block) and the block performance time. The noninferiority margin was set at 5 minutes and was evaluated using the two-sided 95% bootstrap-confidence intervals ([CIs] 100,000 replications) for differences in means.

RESULTS: The mean times to complete sensory block revealed a significant decrease with the low-current group (17.9 ± 12.1 (mean \pm SD) versus 22.8 ± 12.4 minutes; 95% CI, 1.1 to 8.6; $p = 0.012$). The time to readiness for surgery was 30.3 ± 13.8 minutes in the low-current group and 31.7 ± 12.9 minutes in the high-current group (95% CI, -2.7 to 5.5; $p = 0.49$). The performance time was significantly shorter in the high-current threshold group (9.5 ± 4.7 versus 11.9 ± 5.7 minutes; 95% CI, -4 to 1.1; $p = 0.001$).

CONCLUSION: Noninferiority for the high-current threshold technique could neither be confirmed for the primary end point nor for secondary end points. However, we consider a difference in mean times of approximately 8.5 minutes to achieve readiness for surgery acceptable for clinical practice.

地塞米松預防術後噁心嘔吐：一項隨機對照試驗的最新 Meta 分析

Dexamethasone to Prevent Postoperative Nausea and Vomiting: An Updated Meta-Analysis of Randomized Controlled Trials

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背景：地塞米松確實可以減少術後噁心嘔吐（PONV）的發生，然而，地塞米松用作單一或者聯合預防性用藥時減少 PONV 的最佳劑量未清楚闡明。這項研究中，我們評估了靜脈內注射 4-5mg 和 8-10mg 作為單一或者聯合預防用藥的一部分預防 PONV 的應用。

方法：為了鑒定全身性給予地塞米松預防術後噁心和/或嘔吐的隨機臨床試驗，開展了一項廣泛的研究。過把集中起來的試驗分為兩組來地塞米松劑量的效應：4-5mg 和 8-10mg。第一組是非住院麻醉學會（SAMBA）指南預防 PONV 的推薦地塞米松劑量，第二組是兩倍的推薦劑量。SAMBA 指南是根據那些檢查地塞米松不同劑量的研究所發展起來的。

結果：入選了 60 個隨機臨床試驗包含 6696 個受試者。和對照組比，4-5mg 地塞米松劑量組降低了 24 小時 PONV 發生率(OR, 0.31; 95% 可信區間, 0.23-0.41)和需要處理的病例數 (NNT, 3.7; 95% 可信區間, 3.0-4.7)。和另一種止吐藥合用時，4-5mg 地塞米松組的 24 小時 PONV 發生率也較對照組低 (OR, 0.50; 95% 可信區間, 0.35-0.72; NNT, 6.6; 95% 可信區間, 4.3-12.8)。8-10mg 地塞米劑量松組的 24 小時 PONV 發生率比對照組少 (OR, 0.26; 95% CI, 0.20–0.32; NNT, 3.8; 95% CI, 3.0–4.3)。在對 8-10mg 劑量組的分析中發現了不對稱漏斗曲線圖，提示有發表偏倚的可能。和另一種止吐藥合用時，8-10mg 劑量組的 24 小時 PONV 的發生率也降低了 (OR, 0.35; 95% CI, 0.22–0.53; NNT, 6.2; 95% CI, 4.5–10)。在兩組之間直接對比的研究顯示，對於術後噁心和/或嘔吐的發生率，8-10mg 地塞米松沒有比 4-5mg 的劑量有臨床優勢。

結論：我們的結果表明地塞米松作為單一或者聯合用藥在降低 PONV 的發生方面，好像 4-5mg 與 8-10mg 有相似的臨床效應。這些發現支援了 SAMBA 指南目前推薦的全身性給予 4-5mg 地塞米松降低 PONV 的發生率。

（王曉莉 譯 馬皓琳 李士通 校）

BACKGROUND: Dexamethasone has an established role in decreasing postoperative nausea and vomiting (PONV); however, the optimal dexamethasone dose for reducing PONV when it is used as a single or combination prophylactic strategy has not been clearly defined. In this study, we evaluated the use of 4 mg to 5 mg and 8 mg to 10 mg IV doses of dexamethasone to prevent PONV when used as a single drug or as part of a combination preventive therapy.

METHODS: A wide search was performed to identify randomized clinical trials that evaluated systemic dexamethasone as a prophylactic drug to reduce postoperative nausea and/or vomiting. The effects of dexamethasone dose were evaluated by pooling studies into 2 groups: 4 mg to 5 mg and 8 mg to 10 mg. The first group represents the suggested dexamethasone dose to prevent PONV by the Society for Ambulatory Anesthesia (SAMBA) guidelines, and the second group represents twice the dose range recommended by the guidelines. The SAMBA guidelines were developed in response to studies, which have been performed to examine different dosages of dexamethasone.

RESULTS: Sixty randomized clinical trials with 6696 subjects were included. The 4-mg to 5-mg dose dexamethasone group experienced reduced 24-hour PONV compared with control, odds ratio (OR, 0.31; 95% confidence interval [CI], 0.23–0.41), and number needed to treat (NNT, 3.7; 95% CI, 3.0–4.7). When used together with a second antiemetic, the 4-mg to 5-mg

dexamethasone group also experienced reduced 24-hour PONV compared with control (OR, 0.50; 95% CI, 0.35–0.72; NNT, 6.6; 95% CI, 4.3–12.8). The 8-mg to 10-mg dose dexamethasone group experienced decreased 24-hour PONV compared with control (OR, 0.26; 95% CI, 0.20–0.32; NNT, 3.8; 95% CI, 3.0–4.3). Asymmetric funnel plots were observed in the 8-mg to 10-mg dose analysis, suggesting the possibility of publication bias. When used together with a second antiemetic, the 8-mg to 10-mg dose group also experienced reduced incidence of 24-hour PONV (OR, 0.35; 95% CI, 0.22–0.53; NNT, 6.2; 95% CI, 4.5–10). In studies that provided a direct comparison between groups, there was no clinical advantage of the 8-mg to 10-mg dexamethasone dose compared with the 4-mg to 5-mg dose on the incidence of postoperative nausea and/or vomiting.

CONCLUSIONS: Our results showed that a 4-mg to 5-mg dose of dexamethasone seems to have similar clinical effects in the reduction of PONV as the 8-mg to 10-mg dose when dexamethasone was used as a single drug or as a combination therapy. These findings support the current recommendation of the SAMBA guidelines for PONV, which favors the 4-mg to 5-mg dose regimen of systemic dexamethasone.

在高血壓病人麻醉誘導期間使用無創性脈搏傳導時間監測每搏收縮壓

Beat-to-Beat Tracking of Systolic Blood Pressure Using Noninvasive Pulse Transit Time During Anesthesia Induction in Hypertensive Patients

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背景：已有研究報導脈搏傳導時間（PPT）在清醒的人中，與動脈血壓（BP）有較好的相關性。我們測量了高血壓病人麻醉誘導期間，無創每搏 PPT 是否與持續有創動脈血壓監測有精確的相關性。

方法：23 名擇期行腎移植手術的高血壓病人被選入組。同步記錄橈動脈 BP、心電圖和指脈血氧體積描記。PTT 定義為從心電圖上的 R 波的波峰到光電容積描記的最大上升支的時間間隔。每搏 PTT 和 BP 之間的關係用相關性和受試者工作特徵（ROC）曲線分析來進行評價。

結果：在麻醉誘導期間，PPT 的變化與 BP 的變化是成正比的：當 BP 下降時，PPT 延長，反之亦然。PPT 的改變與收縮壓的相關性顯著優於與平均動脈壓（ $r = 0.81 \pm 0.11$ vs $r = 0.72 \pm 0.17$; $P < 0.001$ ）和舒張壓（ $r = 0.81 \pm 0.11$ vs $r = 0.52 \pm 0.24$; $P < 0.001$ ）的相關性。PPT 的改變與舒張壓下降的相關性比與舒張壓上升的相關性明顯（ $r = 0.83 \pm 0.12$ vs $r = 0.68 \pm 0.20$; $P = 0.001$ ）。ROC 曲線分析表明，在麻醉誘導期間，PTT 增加 15% 可以發現收縮壓下降 $\geq 30\%$ ，ROC 曲線下面積為 0.85。

結論：每搏 PPT 與有創收縮壓有良好的相關性，並且可以預測麻醉誘導期間的收縮壓下降。在高風險的高血壓患者不可用有創血壓時，每搏 PPT 可以作為潛在有用的收縮壓無創性監測指標。

（安光惠 譯 馬皓琳 李士通 校）

BACKGROUND: Pulse transit time (PTT) has been reported to show good agreement with arterial blood pressure (BP) in awake humans. We evaluated whether noninvasive beat-to-beat

PTT accurately correlated with invasively measured continuous arterial BP during anesthesia induction in hypertensive patients.

METHODS: Twenty-three hypertensive patients who were scheduled for kidney transplant were enrolled. Radial arterial BP, electrocardiogram, and finger pulse oximetric plethysmography were simultaneously recorded. PTT was measured as the time interval from the R-wave peak on the electrocardiogram to the maximal upslope of the photoplethysmogram. Relationships between beat-to-beat PTT and BP were evaluated by correlation and receiver operating characteristic (ROC) curve analysis.

RESULTS: During anesthesia induction, changes in PTT were directly proportional to changes in BP: when BP decreased, PTT lengthened, and vice versa. The inverse of PTT demonstrated significantly better correlation with systolic BP than with mean BP ($r = 0.81 \pm 0.11$ vs $r = 0.72 \pm 0.17$; $P < 0.001$) or diastolic BP ($r = 0.81 \pm 0.11$ vs $r = 0.52 \pm 0.24$; $P < 0.001$). The inverse of PTT was more highly correlated with decreasing than with increasing changes in systolic BP ($r = 0.83 \pm 0.12$ vs $r = 0.68 \pm 0.20$; $P = 0.001$). The ROC curve analysis revealed that a 15% increase in PTT during anesthesia induction could detect a $\geq 30\%$ decrease in systolic BP, with an area under the ROC curve of 0.85.

CONCLUSION: Beat-to-beat PTT was fairly well correlated with invasive systolic BP and could predict a reduction in systolic BP during anesthesia induction. Beat-to-beat PTT may show potential as a useful noninvasive index of systolic BP when invasive BP is unavailable in high-risk hypertensive patients.

心臟電生理學實驗中心對多名患者氣道損傷的研究

Airway Trauma in a High Patient Volume Academic Cardiac Electrophysiology Laboratory Center

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背景：在電生理治療過程中實施麻醉和氣道管理是有挑戰的，因為其獨特的設備需置於常規手術房間之外。我們報導了對於一些有氣道損傷，包括舌和咽部血腫及聲帶麻痺的病例中我們的經驗。

方法：我們分析了心臟電生理實驗中心 2009 年 12 月至 2011 年 1 月間所有報導的氣道損傷病例，並且與沒有氣道損傷的病例進行了比較。資料獲取通過回顧醫療記錄收集了來自于 87 例病人的資料，包括 16 例氣道損傷病人（損傷組）和 71 例沒有氣道損傷的來自同一時期相同病人群體的病人（控制組）。

結果：在 14 個月間 2434 例麻醉病人中，有 16 例（0.7%）報導了氣道損傷。所有這些病人都沒有發生威脅生命的氣道梗阻。我們發現對於體重指數小於 30 的病人誘導時不使用肌松藥是氣道損傷的顯著風險因素（ $P=0.04$ ；比值比，10；95%可信區間，1.1-482）。在

2 例未使用軟性咬口的心臟複律病人中發生了舌頭或軟組織咬傷。創傷組和控制組之間在操作前抗凝、操作期間抗凝及操作結束時逆轉肝素方面均未發現統計學顯著性差異。

結論：在我們的研究人群中，報導的氣道損傷的總體發生率為 0.7%。舌損傷是最常見的氣道損傷。原因可能為多因素；然而，不應用肌松藥的氣道管理顯現為一個潛在的危險因素。推薦在心臟複律前使用肌松藥行氣管插管和放置軟咬口，並且要保證牙齒間沒有軟組織。

（張怡 譯 馬皓琳 李士通校）

BACKGROUND: Providing anesthesia and managing airways in the electrophysiology suite can be challenging because of its unique setting outside of the conventional operating room. We report our experience of several cases of reported airway trauma including tongue and pharyngeal hematoma and vocal cord paralysis in this setting.

METHODS: We analyzed all of the reported airway trauma cases between December 2009 and January 2011 in our cardiac electrophysiology laboratories and compared these cases with those without airway trauma. Data from 87 cases, including 16 cases with reported airway trauma (trauma group) and 71 cases without reported airway trauma from the same patient population pool at the same period (control group), were collected via review of medical records.

RESULTS: Airway trauma was reported for 16 patients (0.7%) in 14 months among 2434 anesthetic cases. None of these patients had life-threatening airway obstruction. The avoidance of muscle relaxants during induction in patients with a body mass index less than 30 was found to be a significant risk factor for airway trauma ($P = 0.04$; odds ratio, 10; 95% confidence interval, 1.1–482). Tongue or soft tissue bite occurred in 2 cases where soft bite block was not used during cardioversion. No statistically significant difference was found between the trauma and the control groups for preprocedure anticoagulation, anticoagulation during the procedure, or reversal of heparin at the end of the procedure.

CONCLUSIONS: The overall incidence of reported airway trauma was 0.7% in our study population. Tongue injury was the most common airway trauma. The cause seems to have been multifactorial; however, airway management without muscle relaxant emerged as a potential risk factor. Intubation with muscle relaxant is recommended, as is placing a soft bite block and ensuring no soft tissue is between the teeth before cardioversion.

間歇性硬膜外注射與連續性硬膜外輸注用於分娩鎮痛的比較：一項系統回顧和薈萃分析

Intermittent Epidural Bolus Compared with Continuous Epidural Infusions for Labor Analgesia: A Systematic Review and Meta-Analysis

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背景：目前標準硬膜外分娩鎮痛方案為局麻藥結合阿片類藥物通過持續硬膜外輸注

（CEI）。使用 CEI 局麻藥鎮痛的劑量可能較大，產生深度運動阻滯，從而潛在影響器材輔助分娩發生率。在本隨機對照試驗（RCTs）的系統性回顧中，我們對採用硬膜外鎮痛分娩的健康產婦，比較了間斷硬膜外注射（IEB）和標準 CEI 使用或不使用患者自控硬膜外鎮痛，對患者滿意度、人為麻醉干預的需要、產程和分娩方式的影響。

方法：本研究為一項比較 CEI 和 IEB 分娩鎮痛的 RCTs 系統性評價。這些文章進行了有效性評估，資料由作者提取，並用比值比（ORs）、平均差（MDS）和 95% 可信區間（CIs）進行總結。

結果：9 項隨機對照試驗被納入該系統性回顧。344 名受試者接受了 CEI，350 名受試者接受了 IEB 分娩鎮痛。所有 9 個研究被認為為低偏倚風險。IEB 和 CEI 在剖腹產率(OR, 0.87; 95% CI, 0.56–1.35)、產程 (MD, -17 分; 95% CI, -42 to 7)和麻醉干預的需要 (OR, 0.56; 95% CI, 0.29–1.06)均無統計學差異。IEB 能輕度但統計學顯著性減少局麻藥使用量(MD, 每小時-1.2 mg 布比卡因; 95% CI, -2.2 到-0.3)。產婦的滿意度得分（100-mm 視覺類比評分法）IEB（MD, 7.0mm;95%CI, 6.2-7.8）較高。

結論：IEB 是一個有研究前景的概念，目前證據表明 IEB 稍微降低了局部麻醉劑使用量並提高產婦的滿意度。考慮到收集的很多結果中 CIs 較多，不能得出明確結論，但 IEB 仍是一個潛在改善器械助產率及麻醉干預需要的方法。需要更多研究來使理想的 IEB 方案概念化，並研究其對分娩鎮痛和產科轉歸的影響。

（許辛譯，馬皓琳，李士通校）

BACKGROUND: The current standard labor epidural analgesic regimens consist of a local anesthetic in combination with an opioid delivered via continuous epidural infusion (CEI). With CEI local anesthetic, doses may be large with resulting profound motor blockade potentially affecting the incidence of instrumental deliveries. In this systematic review of randomized controlled trials (RCTs), we compared the effect of intermittent epidural bolus (IEB) to standard CEI dosing with or without patient-controlled epidural analgesia on patient satisfaction, the need for manual anesthesia interventions, labor progression, and mode of delivery in healthy women receiving labor epidural analgesia.

METHODS: A systematic review of RCTs that compared CEI with IEB for labor analgesia was performed. The articles were evaluated for validity, and data were extracted by the authors and summarized using odds ratios (ORs), mean differences (MDs), and 95% confidence intervals (CIs).

RESULTS: Nine RCTs were included in this systematic review. Three hundred forty-four subjects received CEI, whereas 350 subjects received IEB labor analgesia. All 9 studies were deemed to be low risk of bias. There was no statistical difference detected between IEB and CEI in the rate of cesarean delivery (OR, 0.87; 95% CI, 0.56–1.35), duration of labor (MD, -17 minutes; 95% CI, -42 to 7), or the need for anesthetic intervention (OR, 0.56; 95% CI, 0.29–1.06). IEB did result in a small but statistically significant reduction in local anesthetic usage (MD, -1.2 mg bupivacaine equivalent per hour; 95% CI, -2.2 to -0.3). Maternal satisfaction score (100-mm visual analog scale) was higher with IEB (MD, 7.0 mm; 95% CI, 6.2–7.8).

CONCLUSIONS: IEB is an appealing concept; current evidence suggests IEB slightly reduces local anesthetic usage and improves maternal satisfaction. Given the wide CIs of the pooled results for many outcomes, definite conclusions cannot be drawn for those outcomes, but there is also a potential that IEB improves instrumental delivery rate and need of anesthesia interventions. More study is required to conceptualize the ideal IEB regimen and investigate its effect on labor analgesia and obstetric outcomes.

轉運降低模擬孕婦心跳驟停時的心肺復蘇品質

Transport Decreases the Quality of Cardiopulmonary Resuscitation During Simulated Maternal Cardiac Arrest

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背景：本研究的目的是為了比較對類比心跳驟停孕婦行心肺復蘇（CPR）時轉運至手術室和留在產房的復蘇效果。我們假設在轉運過程中心肺復蘇品質惡化。

方法：包括兩名實施者（產科醫師、護士或者麻醉醫師）的26人團隊隨機分組，分別在轉運時或者原地固定對 Laerdal Resusci Anne SkillReporter™ 人體模型行心肺復蘇。主要評測指標是正確的傳遞到模型的胸外按壓（定義為按壓頻率 ≥ 100 bpm，手掌按壓胸骨的位置正確，按壓深度 ≥ 1.5 英寸即3.8釐米及適當的釋放）的比例。次要指標包括按壓過程的中斷、轉運過程中按壓者相對於人體模型的位置和通氣潮氣量。

結果：在II期中正確的胸外按壓率的中位數（四分間距），轉運組是32%（10%-63%），固定組為93%（58%-100%）（ $P=0.002$ ，平均差異的95%可信區間是22%-58%）。轉運組的按壓頻率的中位數（四分間距）是124（110-140）bpm，固定組則為123（115-132）bpm（ $P=0.531$ ）。在心肺復蘇過程中，轉運組被打斷的發生率為92%，而固定組只有7%（ $P<0.001$ ，差異的95%可信區間是61%-92%）。轉運過程中，18名施救者跪在人體模型旁，2名跨坐在模型上，4名在跟著推床跑。轉運組的通氣潮氣量的中位數（四分間距）是270（166-430）ml，固定組為390（232-513）ml（ $P=0.03$ ）。

結論：我們的研究結果驗證了我們的假設，證實了轉運對類比孕婦心跳驟停模型的心肺復蘇總體品質帶來不利影響。這些結果和先前出版的有關從產房移到手術室時轉運相關延遲的資料進一步加強了這樣的建議：心跳驟停的產婦的剖腹產手術需在原地實施。

（方斌 譯 馬皓琳 李士通校）

BACKGROUND: The purpose of this study was to compare cardiopulmonary resuscitation (CPR) for simulated maternal cardiac arrest rendered during transport to the operating room with that rendered while stationary in the labor room. We hypothesized that the quality of CPR would deteriorate during transport.

METHODS: Twenty-six teams composed of 2 providers (obstetricians, nurses, or anesthesiologists) were randomized to perform CPR on the Laerdal Resusci Anne SkillReporter™ mannequin during transport or while stationary. The primary outcome measure was the percentage of correctly delivered compressions, defined as compression rate ≥ 100 beats per minute, correct sternal hand placement, compression depth ≥ 1.5 inches (3.8 cm), and proper release. Secondary outcomes included interruptions in compressions, position of providers relative to the mannequin during the transport phase, and ventilation tidal volume.

RESULTS: The median (interquartile range) percentage of correctly rendered compressions during phase II was 32% (10%–63%) in the transport group and 93% (58%–100%) in the stationary group ($P=0.002$, 95% confidence interval of mean difference = 22%–58%). The median (interquartile range) compression rates were 124 (110–140) beats per minute in the transport group and 123 (115–132) beats per minute in the stationary group ($P=0.531$). Interruptions in CPR were observed in 92% of transport and 7% of stationary drills ($P<0.001$, 95% confidence interval of difference = 61%–92%). During transport, 18 providers knelt next to the mannequin, 2 straddled the mannequin, and 4 ran alongside the gurney. Median

(interquartile range) tidal volume was 270 (166–430) mL in the transport group and 390 (232–513) mL in the stationary group ($P = 0.03$).

CONCLUSIONS: Our data confirm our hypothesis and demonstrate that transport negatively affects the overall quality of resuscitation on a mannequin during simulated maternal arrest. These findings, together with previously published data on transport-related delays when moving from the labor room to the operating room further strengthen recommendations that perimortem cesarean delivery should be performed at the site of maternal cardiac arrest.

被動腿抬高和/或頭低腳高位對接受手術治療的先天性心臟病嬰幼兒頸內靜脈截面積的影響

The Effect of Passive Leg Elevation and/or Trendelenburg Position on the Cross-Sectional Area of the Internal Jugular Vein in Infants and Young Children Undergoing Surgery for Congenital Heart Disease

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背景：在這項研究中，我們評估了被動腿抬高（LE）和頭低腳高位（T）對手術治療先天性心臟病的嬰幼兒頸內靜脈（IJV）截面積（CSA）的影響。另外一個目的是比較右向左（RL）和左向右（LR）分流的受試者之間頸內靜脈截面積的差異。

方法：將 90 例 10 天—31 個月大，重量 1.5 公斤—9.7 公斤的嬰兒和幼兒分配至 RL 組（ $n = 48$ ）或 LR 組（ $n = 42$ ）。在這兩個群體中，使用一個二維超聲感測器在以下體位時測量頸部兩側的 IJV 的橫截面積橫徑和垂直徑：仰臥位、15°T 位、LE 50°的仰臥位、15°T 位+LE 50°（TLE）。頸內靜脈的平均截面積增加超過 25% 被視為具有臨床意義。

結果：在 LR 組，T、LE 和 TLE 顯著增加右側 IJVs 的 CSA（至少分別為 12.3%、10.3% 和 18.3%，“至少”指的是 95% 置信度）和左側 IJVs 的 CSA（至少分別為 15.8%、15.0% 和 18.9%），而在 RL 組中只有 TLE 增加雙側 IJVs 的 CSA（右側和左側至少分別為 8.2% 和 7.7%）。LR 組中與 T 和 TLE 相關的右側 IJV 的 CSA 增加比 RL 組顯著（T 至少是 12.3% 比 1.2%，TLE 至少是 18.3% 比 8.2%）。在 LR 組中 TLE 時右側和左側 IJVs 的 CSA 有臨床意義的顯著增加（平均分別為 28.6% 和 26.3%）。在大部分病人中（至少為 69.2%），右側 IJV 的 CSA 比左側顯著大。

結論：被動 LE 和 T 體位一樣能有效增加 IJV 的 CSA，但是沒有任何一種單一的方法可以使 CSA 有臨床意義上的顯著增加。只有 LR 分流組中 T 體位+被動 LE 體位的嬰幼兒兩側 IJVs 的 CSA 有臨床意義上的顯著增加，但在 RL 組中相同年齡的嬰幼兒卻無此差別。

（崔曉娜 譯 馬皓琳 李士通 校）

BACKGROUND: In this study we evaluated the effect of passive leg elevation (LE) and Trendelenburg (T) position on the cross-sectional area (CSA) of the internal jugular vein (IJV) in infants and young children undergoing surgery for congenital heart disease. A secondary aim was to compare the CSA of the IJV between subjects with right-to-left (RL) shunt and left-to-right (LR) shunt.

METHODS: Ninety infants and small children from 10 days to 31 months old weighing from 1.5 to 9.7 kg were assigned to group RL ($n = 48$) or LR ($n = 42$). In both groups, the CSA, transverse, and vertical diameters of the IJV on both sides of the neck were measured using a 2-dimensional ultrasound transducer in the following positions: supine position, 15° of T position, supine position with 50° of LE, and 15° of Trendelenburg position with 50° of LE (TLE). A more than 25% increase in mean CSA of the IJV was considered clinically significant.

RESULTS: In group LR, T, LE, and TLE significantly increased CSA of both right (at least 12.3%, 10.3%, and 18.3%, respectively, “at least” refers to the lower 95% confidence limits) and left (at least 15.8%, 15.0%, and 18.9%, respectively) IJVs, whereas only TLE increased the CSA of both IJVs significantly in group RL (at least 8.2% and 7.7% in the right and left, respectively). The increase in the CSA of the right IJV related to T and TLE was larger in group LR than in group RL (at least 12.3% vs 1.2% for T and at least 18.3% vs 8.2% for TLE, respectively). A clinically significant increase in CSA was achieved in both right and left IJVs with TLE in group LR (mean 28.6% and 26.3%, respectively). The CSA of the right IJV was larger than that of the left IJV in most (at least 69.2%) patients.

CONCLUSIONS: Passive LE was as effective as T position to increase the CSA of the IJV, but there was no clinically significant increase in the CSA with any single maneuver. Only T position with passive LE achieved a clinically significant increase in the CSA of both IJVs in infants and young children with LR shunt, but not in the same age group with RL shunt.

鞘內注射巴氯芬對複雜性區域疼痛綜合征中不同性質疼痛的功效

Efficacy of Intrathecal Baclofen on Different Pain Qualities in Complex Regional Pain Syndrome

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背景：複雜性區域疼痛綜合征（CRPS）以使人嚴重衰弱的慢性疼痛為特點。患有 CRPS 的病人可能會經歷各種疼痛感覺，它們很可能體現了不同的病理生理機制。本研究中，我們評估了中樞 γ -氨基丁酸（B）受體刺激對患有肌張力障礙的 CRPS 患者中不同性質疼痛的獨特作用。

方法：在一個為期一年的開放性設計中，我們每 3 個月對接受滴定劑量鞘內注射巴氯芬（ITB）治療的 42 名有肌張力障礙的 CRPS 患者評估一次 10 項疼痛性質的神經病理性疼痛量表、肌張力障礙程度和鎮痛藥物使用情況的改變。

結果：我們使用一個線性混合模型分析並以總體肌張力障礙程度和追加鎮痛藥物的使用情況作為控制手段。在最初的 6 個月中，我們發現總體的劇烈痛、尖銳痛、鈍性痛和深部痛有顯著的改善。在這個時期之後，儘管肌張力障礙進一步改善並繼續提升 ITB 劑量但評分趨於平穩。

結論：ITB 刺激 γ -氨基丁酸（B）受體對有肌張力障礙的 CRPS 患者特定性質的疼痛表現出獨特的鎮痛效果。

（唐瑩 譯 馬皓琳 李士通 校）

BACKGROUND: Complex regional pain syndrome (CRPS) is characterized by severe debilitating chronic pain. Patients with CRPS may experience various pain sensations, which likely embody different pathophysiologic mechanisms. In this study, we evaluated the differential effects of central γ -aminobutyric acid (B) receptor stimulation on the different pain qualities in CRPS patients with dystonia.

METHODS: The 10 pain qualities of the neuropathic pain scale, dystonia severity, and changes in use of antinociceptive drugs were evaluated every 3 months for a period of 1 year in 42 CRPS patients with dystonia receiving titrated doses of intrathecal baclofen (ITB) treatment in an open design.

RESULTS: Using a linear mixed model analysis and controlling for global dystonia severity and the use of supplemental analgesics, we found a significant improvement in global intense pain, sharp pain, dull pain, and deep pain during the first 6 months. After this period, the scores leveled off despite further improvement of dystonia and continued ITB dose escalation.

CONCLUSIONS: γ -Aminobutyric acid (B) receptor stimulation by ITB exerts differential antinociceptive effects on specific pain qualities in CRPS patients with dystonia.

鉀離子通道在大鼠鞘內注射嗎啡所致抗外周水腫效應中的作用。

The Involvement of Potassium Channels in the Peripheral Antiedematogenic Effect of Intrathecally Injected Morphine in Rats

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背景：既往研究顯示鞘內注射嗎啡可通過啟動一氧化氮/環磷酸鳥苷酸通路減少大鼠實驗性炎性水腫。這個證據支持了這樣一個假設，即在這種情況下鉀通道的開放在調解嗎啡的效應中起重要作用。

方法：雄性韋氏大鼠接受鞘內注射藥物（20 微升）30 分鐘後，予角叉菜膠（150 微克）刺激爪。通過記錄爪體積的增加（以毫升為單位）來評估水腫情況，通過依藍染液滲出計算血漿滲漏。通過髓過氧化物酶分析來間接評價中性粒細胞遷移情況。通過組織學檢查來觀察炎性細胞浸潤和血管充血情況。

結果：與磷酸鹽緩衝液相比較，嗎啡（37nmol）可以抑制炎性水腫、血漿漏出及血管充血，但是對髓過氧化物酶活性及中性粒細胞數量無作用。同時注射 4-氨基吡啶（10 nmol）、格列本脲（5 nmol）和地喹鉍（10pmol）可逆轉嗎啡的作用，而尼克地爾（0.03nmol）可增強嗎啡的作用。

結論：這些結果支持這樣一個假設，即鞘內注射嗎啡所致的外周抗水腫效應由鉀通道的啟動所介導。而且，阿片類藥物不影響急性中性粒細胞遷移的抑制，但影響毛細血管募集反應的減小。

（王贊 譯 馬皓琳 李士通 校）

BACKGROUND: A previous study indicated that intrathecal administration of morphine reduces experimental inflammatory edema in rats by activating the nitric oxide/cyclic guanosine

monophosphate pathway. This evidence supports the hypothesis that potassium channel opening may play an important role in mediating morphine's effect under such conditions.

METHODS: Male Wistar rats received intrathecal injections of drugs (20 μ L) 30 minutes before paw stimulation with carrageenan (150 μ g). Edema was measured as paw volume increase (in milliliters), and plasma leakage was measured by Evans blue dye leakage. Neutrophil migration was evaluated indirectly by myeloperoxidase assay. The inflammatory infiltration and vascular congestion were observed by histologic examination.

RESULTS: Morphine (37 nmol) inhibited inflammatory edema, plasma leakage, and vascular congestion but had no effect on myeloperoxidase activity or neutrophil content compared with phosphate-buffered saline. Coinjection with 4-aminopyridine (10 nmol), glibenclamide (5 nmol), and dequalinium (10 pmol) reversed, but nicorandil (0.03 nmol) enhanced the effect of morphine.

CONCLUSIONS: These results support the hypothesis that the peripheral antiedematogenic effect produced by intrathecal morphine is mediated by potassium channel activation.

Furthermore, this opioid effect does not involve the inhibition of acute neutrophil migration but does involve a reduction in capillary recruitment.