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改良环糊精剂型丙泊酚：首次重点关注注射痛量效关系的人体研究

Propofol in a Modified Cyclodextrin Formulation: First Human Study of Dose-Response with Emphasis on Injection Pain

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背景：已经开发出一种新型的丙泊酚非脂制剂型，其中含有磺丁基-β-环糊精以及水。本研究的主要目的是比较脂制剂型以及新型环糊精剂型的丙泊酚注射时引起的疼痛差异。本研究假设环糊精剂型的丙泊酚可比脂剂丙泊酚引起更少的注射痛。

方法：本研究是一项运用完全交叉平衡设计的方法，针对健康志愿者的单中心，双盲，2-周期，随机，剂量阶梯式增加的研究。通过主观及客观的评估方法比较脂肪制剂以及环糊精结构的丙泊酚在多个不同的时间点的注射痛情况。记录分析了关于疼痛的五个反应变量。

结果：环糊精剂型的丙泊酚在所有五个疼痛变量中均显著升高。其他结果包括镇静作用等无差异。

结论：环糊精剂型的丙泊酚并不能减少于丙泊酚相关的注射时疼痛。

(龚寅 译 陈杰 校)

BACKGROUND: A new lipid-free preparation of propofol has been developed containing the drug, sulfobutylether β-cyclodextrin and water. The primary objective of this study was to compare the effects of propofol in the lipid formulation with those of the new cyclodextrin formulation, particularly with regard to pain on injection. We hypothesized that the propofol in cyclodextrin would be associated with less pain on injection than propofol in lipid.

METHODS: The study was a single-center, double-blind, 2-period, randomized, dose-escalating study using a completely balanced cross-over design in healthy volunteers. Pain on injection was compared between propofol in cyclodextrin and propofol in lipid using subject and observer assessments of pain rated at several different time points. Five response variables to pain were analyzed.

RESULTS: Propofol in cyclodextrin had significantly higher pain scores for all 5 variables. Other endpoints, including sedation, showed no difference.

CONCLUSION: The propofol in cyclodextrin formulation failed to reduce the pain on injection associated with propofol.

N2O 反常调节脑电图慢波振荡：麻醉监测的意义

Nitrous Oxide Paradoxically Modulates Slow Electroencephalogram Oscillations: Implications for Anesthesia Monitoring

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背景：氧化亚氮 (N₂O) 是最传统的镇痛药/辅助镇痛药之一，并一直沿用至今。然而，其对于脑电图 (EEG) 的影响却至今未明。有人提出，N₂O 可能增加术中高频的 EEG 活动(经常提示患者警戒状态和认知的改变) 这一可能的反常效果解释了为什么许多 EEG 监视器并不能捕捉到麻醉期间 N₂O 对于患者整体状态的影响。为了更好地了解为何使用现行 EEG 监测 N₂O 的波动会如此低效，本研究力求在最小噪音的实验环境中，对健康的志愿者使用多频道的 EEG 记录仪定量研究他们在静息状态的 EEG 变化。

方法：健康男性志愿者在隔绝噪音的 EEG 记录环境中，分别吸入氧气混合 20% ($n = 10$), 40% ($n = 10$), 或者 60% ($n = 5$) 的 N₂O。吸入 N₂O 20 分钟，其中包括 5 分钟平衡期和 5 分钟消退期。选择 EEG 的频谱边缘频率(SEF)(95%), 中位频率 (MF), 总功率和带限频率(δ , θ , α , β 和 γ) 作为定量的参数，在 N₂O 吸入期间可对这些参数的变化进行定量并对给药前，药物效应峰值和消除期不同时段进行比较。

结果：N₂O 吸入期间，频谱频率的定量变化仅仅显示了 SEF 和 MF 的微小变化，但额部的总功率在药物高峰期却显著降低($P = 0.001$; 平均降低[95% 置信区间]: $41.90 \mu V^2$ [18.19–65.61 μV^2])，在消除期反弹。总功率的这一系列变化是由于低频功率(δ/θ)的转换,而低频功率在额部最高。

结论：N₂O 只是维持静息状态 EEG 的清醒特征(α 谱带)，并且抑制了那些功率升高与镇静/催眠(δ 和 θ)密切相关的功率，而不是直接提高 EEG 的高频功率(β 或 γ 谱带)。这些数据显示，N₂O 对低频率 EEG 的抑制可能会帮助解释之前在 N₂O 麻醉期间使用 EEG 监测患者状态的困难原因。因为低频功率的升高代表性地提示了麻醉深度加深，N₂O 对这些活动的抑制及其消除期的反弹都反常地影响着 EEG 的监护参数。因此，对于这些影响的修正，有望在未来提升监测方法。

(俞劼晶 译 陈杰 校)

BACKGROUND: Nitrous oxide (N₂O) is one of the oldest analgesics/adjuvant agents still in use today; however, its effects on the human electroencephalogram (EEG) remain unclear. It has been proposed that N₂O may enhance higher-frequency EEG activity (often indicative of alert states and cognition) during sedation. This possibly paradoxical effect has been used to explain the failure of many EEG monitors to capture the effects of N₂O on patient state during anesthesia. To better understand the poor efficacy of current EEG approaches to monitoring N₂O action, we quantitatively studied the sole effect of N₂O on the resting EEG in healthy volunteers using multichannel EEG recordings under noise-minimized laboratory conditions.

METHODS: Healthy male volunteers were administered 20% ($n = 10$), 40% ($n = 10$), or 60% ($n = 5$) inspired N₂O mixed with oxygen during noise-shielded EEG recordings. N₂O was administered over a 20-minute period involving a 5-minute equilibration period and 5-minute washout. EEG spectral edge frequency (95%), median power frequency, total power, and band-limited power (δ , θ , α , β , and γ) were used as quantitative EEG parameters. The changes in these EEG parameters were quantified throughout N₂O inhalation and compared between predrug baseline, peak drug effect, and washout.

RESULTS: Quantification of changes in spectral power during N₂O inhalation showed only minor changes in estimates of spectral edge and median power frequency, whereas significant reductions in total power were observed at frontal sites during peak gas effect

($P = 0.001$; mean reduction [95% confidence interval]: $41.90 \mu V^2$ [18.19–65.61 μV^2]) that rebounded during N_2O washout. Such changes in total power were driven by shifts in low-frequency power (δ/θ), which were most elevated at frontal sites.

CONCLUSION: Rather than directly enhancing high-frequency EEG power (β or γ bands), N_2O seems to preserve the awake features of resting EEG (α band) and suppress power in those bands in which increases are typically associated with sedation/hypnosis (δ and θ). These data suggest that N_2O 's suppression of low-frequency EEG power may help to explain previously reported difficulties in attempting to monitor patient state with the EEG during anesthesia involving N_2O . Because increases in low-frequency power typically indicate increasing anesthesia, N_2O 's suppression of such activity and its rebound during washout would paradoxically influence EEG monitoring parameters. Therefore, correcting for such effects is expected to improve future monitoring methods.

双侧全膝关节置换术：主要并发症发病率和死亡率的危险因素

Bilateral Total Knee Arthroplasty: Risk Factors for Major Morbidity and Mortality

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背景：相同的住院时间，双侧全膝关节置换（Bilateral total knee arthroplasty，BTKA）较单侧膝关节置换相比发病率及死亡率较高。然而，目前没有层化分析的证据显示哪些患者具有发病和死亡的高风险。本研究目的是分析 BTKA 患者中主要发病率和死亡率的危险因素。

方法：收集 1998-2007 年全国住院病人的数据，从中随机选择 BTKA 的病人。统计分析其死亡率及主要并发症。然后进行多因素分析找出主要并发症发病率及死亡率的独立危险因素。

结果：从 42,003 个数据库条目中收集了 206,573 例 BTKA 病例。主要院内并发症及死亡的发生率是 9.5%。不良结局的危险因素包括高龄（与 45-65 岁组相比，65-74 岁组和 >75 岁组的比值比分别为 1.88[CI:1.72,2.05]和 2.66[CI:2.42,2.92]），男性 (OR: 1.54 [CI: 1.44, 1.66])，以及合并症。充血性心衰(OR: 5.55 [CI: 4.81, 6.39])和肺动脉高压 (OR: 4.10 [CI: 2.72, 6.10])是不良结局最主要的危险因素。

结论：研究证实了影响 BTKA 患者主要并发症发病率和死亡率的危险因素。本研究资料有助于该类患者的手术选择。

（丁佳 译 陈杰 校）

BACKGROUND: Bilateral total knee arthroplasty (BTKA) performed during the same hospitalization carries increased risk for morbidity and mortality compared with the unilateral approach. However, no evidence-based stratifications to identify patients at risk for major morbidity and mortality are available. Our objective was to determine the incidence and patient-related risk factors for major morbidity and mortality among patients undergoing BTKA.

METHODS: Nationwide Inpatient Survey data collected for the years 1998 to 2007 were analyzed and cases of elective BTKA procedures were included. Patient demographics, including comorbidities, were analyzed and frequencies of mortality and major complications were computed. Subsequently, a multivariate analysis was conducted to determine independent risk factors for major morbidity and mortality.

RESULTS: Included were 42,003 database entries, representing an estimated 206,573 elective BTKAs. The incidence of major in-hospital complications and mortality was 9.5%. Risk factors for adverse outcome included advanced age (odds ratios [ORs] for age groups 65–74 and >75 years were 1.88 [confidence interval, CI: 1.72, 2.05] and 2.66 [CI: 2.42, 2.92], respectively, compared with the 45–65 years group), male gender (OR: 1.54 [CI: 1.44, 1.66]), and a number of comorbidities. The presence of congestive heart failure (OR: 5.55 [CI: 4.81, 6.39]) and pulmonary hypertension (OR: 4.10 [CI: 2.72, 6.10]) were the most significant risk factors associated with increased odds for adverse outcome.

CONCLUSIONS: We identified patient-related risk factors for major morbidity and mortality in patients undergoing BTKA. Our data can be used to aid in the selection of patients for this procedure.

布比卡因的比重是否会影响在择期剖腹产术前长时间保持坐位时药物的鞘内扩散？
一项前瞻性、随机、对照研究

Does the Baricity of Bupivacaine Influence Intrathecal Spread in the Prolonged Sitting Position Before Elective Cesarean Delivery? A Prospective Randomized Controlled Study

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背景：在剖腹产腰硬联合麻醉时出现硬膜外置管困难可能会过分延长从混合局麻药注入到放置仰卧倾斜位的时间。本研究假定这种延迟可能会影响不同比重局麻药鞘内注射的分布，如低比重的药物会出现更高的感觉阻滞平面。

方法：选择在腰硬联合麻醉下行择期剖腹产的无妊娠合并症的健康临产妇纳入这项前瞻性、随机、双盲试验中。研究对象分别接受鞘内重比重（重比重组）、等比重（等比重组）和低比重（低比重组）布比卡因 10mg。鞘内注药后，研究对象在放置仰卧倾斜位前要保持坐位 5 分钟（模拟困难硬膜外置管）。主要观察指标是腰麻后 25 分钟内感觉阻滞平面。其他包括运动阻滞评分，母体低血压，升压药使用情况。

结果：分析了 89 位病人的数据。组间病人的特征无差异。腰麻后感觉阻滞水平随着药物比重的降低有明显的升高：重比重组 T10[T11-8](T10-9) 中位数[四分位数间

距] (95%可靠区间),等比重组 T9[T10-7](T9-7),和低比重组 T6[T8-4](T8-5) (Cuzick 趋势检验: $P < 0.001$).低比重组中所有的病人在腰麻后 25 分钟其感觉阻滞平面都到达了 T4,而在等比重和重比重组中都只有 80%的病人到达 T4 ($P=0.04$, 差异 20%, 差异的 95%可靠区间 4%-33%)。在低比重组中病人下肢的运动阻滞更加完全 (Bromage 评分=4) (重比重 43%,等比重 63%, 低比重 90%, $P<0.001$)。尽管母体出现低血压, 恶心, 呕吐的情况在各组中无差异, 但等比重和低比重组中麻黄素使用量较重比重分别高 1.83 和 3.0 倍 (Cuzick 趋势检验: $P < 0.001$)。

结论: 本研究显示当接受剖腹产术的临产妇行腰麻注入局麻药, 保持坐位 5 分钟后, 低比重的布比卡因所到达的感觉阻滞平面要比等比重和重比重更高。

(范逸辰 译 陈杰 校)

BACKGROUND: Difficulties in inserting an epidural catheter while performing combined spinal-epidural anesthesia for cesarean delivery may lead to undue delays between the spinal injection of the local anesthetic mixture and the adoption of the supine position with lateral tilt. We hypothesized that this delay may affect the intrathecal distribution of local anesthetic of different baricities such that hypobaric local anesthetic would lead to a higher sensory block level.

METHODS: Healthy parturients with uncomplicated pregnancies undergoing elective cesarean delivery under combined spinal-epidural anesthesia were enrolled in this prospective double-blind randomized controlled trial. The subjects were allocated to receive hyperbaric (hyperbaric group), isobaric (isobaric group), or hypobaric (hypobaric group) spinal bupivacaine 10 mg. After the spinal injection, the subjects remained in the sitting position for 5 minutes (to simulate difficulty in inserting the epidural catheter) before being helped into the supine lateral tilt position. The primary outcome was the sensory block level during the 25 minutes after the spinal injection. Other end points included motor block score, maternal hypotension, and vasopressor requirements.

RESULTS: Data from 89 patients were analyzed. Patient characteristics were similar in all groups. The median [interquartile range] (95% confidence interval) sensory levels after spinal injection were significantly higher with decreasing baricity: hyperbaric T10 [T11-8] (T10-9), isobaric T9 [T10-7] (T9-7), and hypobaric T6 [T8-4] (T8-5) ($P < 0.001$, Cuzick trend). All patients in the hypobaric group reached a sensory block level of T4 at 25 minutes after spinal injection compared with 80% of the patients in both the isobaric and hyperbaric groups ($P = 0.04$; difference 20%, 95% confidence interval of difference 4%–33%). Significantly more patients in the hypobaric group had complete lower limb motor block (Bromage score = 4) (hyperbaric 43%, isobaric 63%, and hypobaric 90%; $P < 0.001$). The incidences of maternal hypotension and nausea and vomiting were similar among groups, although the ephedrine requirements were significantly increased in the isobaric and hypobaric groups by factors of 1.83 and 3.0, respectively, compared with the hyperbaric group ($P < 0.001$, Cuzick trend).

CONCLUSIONS: We demonstrated that when parturients undergoing cesarean delivery were maintained in the sitting position for 5 minutes after spinal injection of the local anesthetic, hypobaric bupivacaine resulted in sensory block levels that were higher compared with isobaric and hyperbaric bupivacaine, respectively, during the study period.

预防性静脉给予纳洛酮来改善因中重度疼痛而接受吗啡静脉自控镇痛的儿童发生阿片类药物副作用的最佳剂量：一项探索剂量的研究

The Optimal Dose of Prophylactic Intravenous Naloxone in Ameliorating Opioid-Induced Side Effects in Children Receiving Intravenous Patient-Controlled Analgesia Morphine for Moderate to Severe Pain: A Dose Finding Study

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背景：阿片类药物引起的副作用，如皮肤瘙痒、恶心、呕吐，是常见的现象，可能比疼痛本身伤害更大。持续低剂量的纳洛酮输注（0.25 μg/kg/h）能改善很多而非全部患者如上的这些副作用，同时不影响镇痛效果。本研究目的在于确定使得阿片类药物副作用降到最低的纳洛酮最佳剂量，并采用剂量递增法测量相关的血浆吗啡和纳洛酮的浓度。

方法：59 位中重度术后疼痛的患儿（24 名男性/35 名女性；平均年龄 14.2 ± 2.2 岁）给予吗啡静脉自控镇痛（基础剂量 20 μg/kg/h，追加剂量 20 μg/kg，每小时最多 5 次），同时给予小剂量纳洛酮静脉持续输注（最初剂量 0.05 μg/kg/h，随后队列剂量依次为 0.10, 0.15, 0.25, 0.40, 0.65, 1, and 1.65 μg/kg/h）。如果有 2 例患者出现难以忍受的恶心、呕吐或皮肤瘙痒，随后患者的纳洛酮的剂量则增加。剂量/治疗成功被定义为 10 例患者在此纳洛酮剂量下副反应降到最小。使用电喷雾串联质谱法处理、储存并检测纳洛酮输注开始后收集到的血液样本，用于测定血浆吗啡和纳洛酮水平。

结果：成功治疗病人并将副作用/失败比降至 10% 以下的最低纳洛酮剂量为 1 μg/kg/h；每个队列的大小为 4-11 名患者不等。纳洛酮对预防皮肤瘙痒的有效性优于恶心呕吐。在所有纳洛酮输注剂量中，都需要有额外的药物来补充治疗阿片类药物的副作用。当纳洛酮输注速度 ≤ 0.15 μg/kg/h 时，血浆纳洛酮浓度低于试验测定下限 0.1 ng/ml。当输注速度 > 0.25 μg/kg/h 时，血浆浓度呈线性增加。在各个剂量的队列中，非成功治疗的患者的血浆纳洛酮浓度相当或高于成功治疗的患者的水平。血浆吗啡浓度介于 3.52 和 172 ng/ml 之间，其中 > 90% 的浓度介于 10.2 和 61.6 ng/ml 之间。成功治疗和非成功治疗患者血浆中的吗啡浓度相当。

结论：纳洛酮输注速度 ≥ 1 μg/kg/h 时可显著降低但不能消除术后接受吗啡静脉自控镇痛的患儿阿片类药物的副反应。非成功治疗患者血浆中纳洛酮和吗啡的浓度都与成功治疗患者的水平相近，这表明改善阿片类药物副作用的成败与血浆浓度无关。
(滕凌雅 译 陈杰 校)

BACKGROUND: Opioid-induced side effects, such as pruritus, nausea, and vomiting are common and may be more debilitating than pain itself. A continuous low-dose naloxone infusion (0.25 μg/kg/h) ameliorates some of these side effects in many but not all patients without adversely affecting analgesia. We sought to determine the optimal

dose of naloxone required to minimize opioid-induced side effects and to measure plasma morphine and naloxone levels in a dose escalation study.

METHODS: Fifty-nine pediatric patients (24 male/35 female; average age 14.2 ± 2.2 years) experiencing moderate to severe postoperative pain were started on IV patient-controlled analgesia morphine (basal infusion 20 $\mu\text{g}/\text{kg}/\text{h}$, demand dose 20 $\mu\text{g}/\text{kg}$, 5 doses/h) and a low-dose naloxone infusion (initial cohort: 0.05 $\mu\text{g}/\text{kg}/\text{h}$; subsequent cohorts: 0.10, 0.15, 0.25, 0.40, 0.65, 1, and 1.65 $\mu\text{g}/\text{kg}/\text{h}$). If 2 patients developed intolerable nausea, vomiting, or pruritus, the naloxone infusion was increased for subsequent patients. Dose/treatment success occurred when 10 patients had minimal side effects at a naloxone dose. Blood samples were obtained for measurement of plasma morphine and naloxone levels after initiation of the naloxone infusion, processed, stored, and measured by tandem mass spectrometry with electrospray positive ionization.

RESULTS: The minimum naloxone dose at which patients were successfully treated with a <10% side effect/failure rate was 1 $\mu\text{g}/\text{kg}/\text{h}$; cohort size varied between 4 and 11 patients. Naloxone was more effective in preventing pruritus than nausea and vomiting. Concomitant use of supplemental medicines to treat opioid-induced side effects was required at all naloxone infusion rates. Plasma naloxone levels were below the level of assay quantification (0.1 ng/mL) for infusion rates $\leq 0.15 \mu\text{g}/\text{kg}/\text{h}$. At rates $>0.25 \mu\text{g}/\text{kg}/\text{h}$, plasma levels increased linearly with increasing infusion rate. In each dose cohort, patients who failed therapy had comparable or higher plasma naloxone levels than those levels measured in patients who did not fail treatment. Plasma morphine levels ranged between 3.52 and 172 ng/mL, and >90% of levels ranged between 10.2 and 61.6 ng/mL. Plasma morphine levels were comparable between patients who failed therapy and those patients who achieved symptom control.

CONCLUSIONS: Naloxone infusion rates $\geq 1 \mu\text{g}/\text{kg}/\text{h}$ significantly reduced, but did not eliminate, the incidence of opioid-induced side effects in postoperative pediatric patients receiving IV patient-controlled analgesia morphine. Patients who failed therapy generally had plasma naloxone and morphine levels that were comparable to those who had good symptom relief suggesting that success or failure to ameliorate opioid-induced side effects was unrelated to plasma levels.

比较连续股神经与后路腰丛神经阻滞在髋关节术后的镇痛效果：一项随机对照研究

Continuous Femoral Versus Posterior Lumbar Plexus Nerve Blocks for Analgesia After Hip Arthroplasty: A Randomized, Controlled Study

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背景：髋关节成形术常需要有效的术后镇痛，通常采取硬膜外或者后路腰丛局部麻醉输注的方法。但是，美国区域麻醉学会指南现在不推荐对需要术后注射各种抗

凝药物的髋关节成形术患者采取硬膜外或者连续后路腰丛阻滞。连续股神经阻滞可能是一种镇痛选择，但是它是否能提供连续后路腰丛一样的镇痛效果尚不清楚。因此，本研究通过髋关节成形术后从不同位置置入导管（股神经和后路腰丛）验证此两种方法在术后镇痛上没有影响的假说。

方法：接受髋关节成形术的患者术前随机分为接受股神经阻滞（神经刺激导管头超过针尖 5-15cm）或者接受后路腰丛阻滞（神经刺激导管头超过针尖 0-1cm）。患者术后接受至少 2 天的 0.2% 的罗哌卡因镇痛（背景流量 6ml/hr，解救剂量 4ml，锁定时间 30min）。主要终点为以疼痛数字评价量表记录的 24 小时平均疼痛评分，时间从术后首日晨 7:30 开始记录，排除每天两次的理疗部分。次要终点包括在同一个 24 小时内的理疗时的疼痛评分，可行走距离，需要补充镇痛药的剂量以及住院期间对镇痛的满意程度。

结果 接受股神经浸润阻滞的患者（n=25）平均（标准差）疼痛评分为 3.6（1.8），而接受后路腰丛浸润阻滞的患者（n=22）评分为 3.5（1.8），组间差异 0.1（95% 可信区间 -0.9 ~ 1.2；P=0.78）。因为可信区间特异度预设设在 -1.6~ 1.6 宽度范围内，得出两种技术在术后镇痛上等效。同样，除了接受股神经导管的患者在术后首晨行走训练的中位数为 2 米（10-90 百分位数为 0-17 米），而接受后路腰丛导管的患者中位数为 11 米（10-90 百分位数为 0-31 米）（非参数数据，P=0.02）外，两种方法在次要终点上也没有差异。

结论 在髋关节成型术后，使用神经刺激导管引导技术时，可以选择采取连续股神经来代替连续后路腰丛镇痛。但是，股神经镇痛在早期进行行走锻炼时，镇痛效果欠佳。

(陆秉玮 译 陈杰 校)

BACKGROUND: Hip arthroplasty frequently requires potent postoperative analgesia, often provided with an epidural or posterior lumbar plexus local anesthetic infusion. However, American Society of Regional Anesthesia guidelines now recommend against epidural and continuous posterior lumbar plexus blocks during administration of various perioperative anticoagulants often administered after hip arthroplasty. A continuous femoral nerve block is a possible analgesic alternative, but whether it provides comparable analgesia to a continuous posterior lumbar plexus block after hip arthroplasty remains unclear. We therefore tested the hypothesis that differing the catheter insertion site (femoral versus posterior lumbar plexus) after hip arthroplasty has no impact on postoperative analgesia.

METHODS: Preoperatively, subjects undergoing hip arthroplasty were randomly assigned to receive either a femoral or a posterior lumbar plexus stimulating catheter inserted 5 to 15 cm or 0 to 1 cm past the needle tip, respectively. Postoperatively, patients received perineural ropivacaine, 0.2% (basal 6 mL/hr, bolus 4 mL, 30-minute lockout) for at least 2 days. The primary end point was the average daily pain scores as measured with a numeric rating scale (0–10) recorded in the 24-hour period beginning at 07:30 the morning after surgery, excluding twice-daily physical therapy sessions. Secondary end points included pain during physical therapy, ambulatory distance, and supplemental analgesic requirements during the same 24-hour period, as well as satisfaction with analgesia during hospitalization.

RESULTS: The mean (SD) pain scores for subjects receiving a femoral infusion ($n = 25$) were 3.6 (1.8) versus 3.5 (1.8) for patients receiving a posterior lumbar plexus infusion (n

= 22), resulting in a group difference of 0.1 (95% confidence interval -0.9 to 1.2; $P = 0.78$). Because the confidence interval was within a prespecified -1.6 to 1.6 range, we conclude that the effect of the 2 analgesic techniques on postoperative pain was equivalent. Similarly, we detected no differences between the 2 treatments with respect to the secondary end points, with one exception: subjects with a femoral catheter ambulated a median (10th–90th percentiles) 2 (0–17) m the morning after surgery, in comparison with 11 (0–31) m for subjects with a posterior lumbar plexus catheter (data nonparametric; $P = 0.02$).

CONCLUSIONS: After hip arthroplasty, a continuous femoral nerve block is an acceptable analgesic alternative to a continuous posterior lumbar plexus block when using a stimulating perineural catheter. However, early ambulatory ability suffers with a femoral infusion.

鞘内注射吗啡与局部浸润镇痛作为全膝关节置换术后疼痛管理的随机对照试验

Local Infiltration Analgesia Versus Intrathecal Morphine for Postoperative Pain Management After Total Knee Arthroplasty: A Randomized Controlled Trial

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背景：局部浸润镇痛（LIA），即手术期间在关节周围复合注射局部麻醉药、非甾体抗炎药和肾上腺素，LIA 已经在全膝关节置换术（TKA）术后疼痛管理中成了常规。本研究比较了 TKA 术后鞘内注射吗啡和 LIA 的效应。

方法：在这项双盲研究中，50 例椎管内麻醉下行 TKA 的患者随机分为 2 组：M 组，脊麻时鞘内注入 0.1mg 吗啡和脊麻药物；而 L 组，手术期间在膝关节处给予罗哌卡因、酮咯酸和肾上腺素行局部浸润镇痛，并术后两次通过关节内导管注入上述的混合物。记录术后疼痛，解救镇痛需要，活动度和出院时间。3 个月随访期间使用牛津膝关节评分和 EQ - 5D 评估病人的健康质量。主要终点是术后第 48 小时内的静脉吗啡用量。

结果：L 组术后第 48 小时平均吗啡消耗量显著低于 M 组：26 ± 15 比 54 ± 29mg，即每 24 小时平均相差 14.2mg（95% 可信区间为 7.6-20.9）。L 组在 48 小时内休息和运动时疼痛评分低于 M 组（ $P < 0.01$ ）。L 组在术后 24h 和 48h 行走时疼痛评分也比 M 组低（ $P < 0.001$ ）。L 组中，有更多患者在 24 小时内能够爬楼梯：50%（11/22）比 4%（1/23），即 46% 的差异（95% 可信区间 23.5%-68.5%），而在 48 小时内：70%（16/23）比 22%（5/23），即 48% 的差异（95% 可信区间为 23%-73%）。L 组的达到出院标准的中值（范围）时间比 M 组更短，分别为 51（24-166）h 比 72（51-170）h。时间差异 23h（95% 可信区间为 18%-42%）（ $P = 0.001$ ）。L 组的住院时间也短于 M 组：中位数分别为 3（2-17）天和 4（2-14）天（ $P = 0.029$ ）。L 组病人的满意度高于 M 组（ $P = 0.001$ ），但在膝关节功能、副作用、病人相关预后、牛津膝关节评分及 EQ - 5D 没有差异。

结论：TKA 术后，LIA 比鞘内注射吗啡提供了更好的术后镇痛及早期活动，并缩短住院时间。

(孙晓琼 译 陈杰 校)

BACKGROUND: Local infiltration analgesia (LIA)—using a combination of local anesthetics, nonsteroidal anti-inflammatory drugs, and epinephrine, injected periarticularly during surgery—has become popular in postoperative pain management after total knee arthroplasty (TKA). We compared intrathecal morphine with LIA after TKA.

METHODS: In this double-blind study, 50 patients scheduled to undergo TKA under spinal anesthesia were randomized into 2 groups: group M, 0.1 mg morphine was injected intrathecally together with the spinal anesthetic and in group L, LIA using ropivacaine, ketorolac, and epinephrine was infiltrated in the knee during the operation, and 2 bolus injections of the same mixture were given via an intraarticular catheter postoperatively. Postoperative pain, rescue analgesic requirements, mobilization, and home readiness were recorded. Patient-assessed health quality was recorded using the Oxford Knee Score and EQ-5D during 3 months follow-up. The primary endpoint was IV morphine consumption the first 48 postoperative hours.

RESULTS: Mean morphine consumption was significantly lower in group L than in group M during the first 48 postoperative hours: 26 ± 15 vs 54 ± 29 mg, i.e., a mean difference for each 24-hour period of 14.2 (95% confidence interval [CI] 7.6 to 20.9) mg. Pain scores at rest and on movement were lower during the first 48 hours in group L than in group M ($P < 0.001$). Pain score was also lower when walking in group L than in group M at 24 hours and 48 hours postoperatively ($P < 0.001$). In group L, more patients were able to climb stairs at 24 hours: 50% (11 of 22) versus 4% (1 of 23), i.e., a difference of 46% (95% CI 23.5 to 68.5) and at 48 hours: 70% (16 of 23) versus 22% (5 of 23), i.e., a difference of 48% (95% CI 23 to 73). Median (range) time to fulfillment of discharge criteria was shorter in group L than in group M, 51 (24–166) hours versus 72 (51–170) hours. The difference was 23 (95% CI 18 to 42) hours ($P = 0.001$). Length of hospital stay was also shorter in group L than in group M: median (range) 3 (2–17) versus 4 (2–14) days ($P = 0.029$). Patient satisfaction was greater in group L than in group M ($P = 0.001$), but no differences were found in knee function, side effects, or in patient-related outcomes, Oxford Knee score, or EQ-5D.

CONCLUSIONS: LIA technique provided better postoperative analgesia and earlier mobilization, resulting in shorter hospital stay, than did intrathecal morphine after TKA.

简报：对于用紫杉醇治疗的 C57B16 雌性大鼠，大麻二酚可以防止冷和机械刺激性痛觉超敏的发生

Brief Report: Cannabidiol Prevents the Development of Cold and Mechanical Allodynia in Paclitaxel-Treated Female C57B16 Mice

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给人行紫杉醇化疗通常会致周围性神经病变。对于研究周围性神经病变的机制和治疗方法的啮齿动物模型仅限于雄性大鼠，而雌性大鼠的研究还很有限。本实验研究了不同剂量的紫杉醇对于引起雌性 C57Bl/6 大鼠的冷刺激和机械性痛觉超敏的影响。由于无精神活性药物植物大麻素大麻二酚可以减少其他种类的神经性疼痛，作者评估了其对紫杉醇引起的痛觉超敏有无效果。紫杉醇会剂量依赖性地引起痛觉超敏，并对雌性大鼠影响更为明显。但是大麻二酚防止这种紫杉醇引起的痛觉超敏。本实验的结果表明：在大鼠中，大麻二酚可以阻止紫杉醇引起的痛觉过敏的发生。因此，大麻二酚可能预防人类由于使用有限剂量下的紫杉醇引起的神经性病变。
(张婷 译 陈杰 校)

The taxane chemotherapeutic paclitaxel frequently produces peripheral neuropathy in humans. Rodent models to investigate mechanisms and treatments are largely restricted to male rats, whereas female mouse studies are lacking. We characterized a range of paclitaxel doses on cold and mechanical allodynia in male and female C57Bl/6 mice. Because the nonpsychoactive phytocannabinoid cannabidiol attenuates other forms of neuropathic pain, we assessed its effect on paclitaxel-induced allodynia. Paclitaxel produced allodynia that was largely dose independent and more robust in female mice, and this effect was prevented by treatment with cannabidiol. Our preliminary findings therefore indicate that cannabidiol may prevent the development of paclitaxel-induced allodynia in mice and therefore be effective at preventing dose-limiting paclitaxel-induced peripheral neuropathy in humans.

在健康个体，rFVIIa 逆转氯吡格雷引起的出血作用：一项随机、安慰剂对照、双盲、探索性研究

Reversal of Clopidogrel-Induced Bleeding with rFVIIa in Healthy Subjects: A Randomized, Placebo-Controlled, Double-Blind, Exploratory Study

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背景：氯吡格雷(Plavix®)可以有效降低血栓性事件的发生，但同时也会增加出血的风险。在因自身抗体所致血友病患者，重组的 FVII 激活剂(rFVIIa, NovoSeven®)可用于治疗其出血现象，因此人们提出用该药物可以减轻氯吡格雷导致的出血副作用。

方法：在这项单中心、随机、安慰剂对照、双盲、剂量递增的 I 期探索试验，我们试验性地从健康个体穿刺活检，评估了 FVIIa 应用于逆转氯吡格雷引起出血增加效应的安全性及有效性。有效性评估包括逆转出血参数（出血持续时间[BD]，中止出血及穿刺活检导致的出血量[BV]，血栓弹力图参数），在氯吡格雷治疗后 rFVIIa 组及安慰剂组分别测定。

结果：一定比例的个体（56%）对氯吡格雷的反应有限（定义为 $\leq 30\%$ 血小板聚集受抑制）而中止了试验。余下的进一步进行试验，并做了4项活检。在40个体中，随机选择37个进行有效性评估。相比于基线的活检结果，氯吡格雷可以增加BD和BV。重组FVIIa（10和20 $\mu\text{g}/\text{kg}$ ）可以显著减轻氯吡格雷导致的BD延长效应（ $P = 0.007$ 和 $P = 0.001$ ，分别）。早期中止试验限制进一步评估大剂量rFVIIa的效果。同一医生对组织活检结果提示，20 $\mu\text{g}/\text{kg}$ 的rFVIIa可以显著减少氯吡格雷导致的BD延长（ $P = 0.048$ ）。体外试验通过血液凝固的动力学参数：凝血开始时间（TEG[®]-R）及凝血三角（TEG[®]-A）进一步证明了rFVIIa的作用（ $P < 0.005$ ）。

结论：在我们的临床试验中，rFVIIa（10和20 $\mu\text{g}/\text{kg}$ ）可以逆转氯吡格雷的出血效应。

（范羽译 薛张纲校）

BACKGROUND: Clopidogrel (Plavix[®]) therapy, although effective for minimizing risk of thrombotic events, is also associated with potential bleeding risk. Recombinant activated FVII (rFVIIa, NovoSeven[®]) induces hemostasis in hemophilia patients with inhibitors (alloantibodies) and has been proposed as potential treatment for mitigating clopidogrel therapy-mediated bleeding.

METHODS: In this single-center, randomized, placebo-controlled, double-blind, dose-escalation, exploratory phase I trial, we assessed the safety and effects of rFVIIa in reversing clopidogrel-enhanced bleeding in an experimentally induced punch biopsy in healthy subjects. Efficacy assessments included the reversal of bleeding characteristics (bleed duration [BD], the primary end point and blood loss volume [BV] induced by punch biopsy, and thromboelastograph [TEG[®]] parameters) with rFVIIa or placebo after clopidogrel treatment.

RESULTS: A significant number of subjects (56%) had limited response to clopidogrel (defined as $\leq 30\%$ platelet aggregation inhibition) and were discontinued from study. The remaining subjects continued and had 4 biopsies. Of 40 subjects randomized, 37 were evaluated for efficacy. Clopidogrel treatment increased BD and BV compared with the baseline biopsy. Recombinant FVIIa (10 and 20 $\mu\text{g}/\text{kg}$) significantly mitigated the clopidogrel-induced effects on BV ($P = 0.007$ and $P = 0.001$, respectively). Early trial termination limited the evaluation of effects of higher rFVIIa doses. Subgroup analyses of subjects biopsied by the same physician demonstrated significant reduction of clopidogrel-induced BD with 20 $\mu\text{g}/\text{kg}$ rFVIIa ($P = 0.048$). Ex vivo analysis of rFVIIa demonstrated clotting dynamics presented by parameters time to clot onset (TEG[®]-R) and clot angle (TEG[®]-A) ($P < 0.005$).

CONCLUSIONS: In this clinical study, rFVIIa (10 and 20 $\mu\text{g}/\text{kg}$) reversed the effect of clopidogrel on blood loss.

研究有外科感染风险的肥胖患者应用头孢西丁的药代动力学及组织渗透性

Pharmacokinetics and tissue penetration of cefoxitin in obesity: implications for risk of surgical site infection

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背景：肥胖是外科感染的重要危险因素之一，这个理由很不充分。SSIs 是发病的主要原因，延长住院时间，增加医疗费用。药物治疗常被作为肥胖患者的治疗手段。术前应用抗生素同时使切口获得足够的药物浓度，是预防手术部位感染的重要策略。虽然如此，关于肥胖患者手术的抗生素浓度的信息仍很少。这项研究检验预防性使用抗生素头孢西丁可能会延迟和或降低肥胖患者的组织渗透力的假设。

方法：对腹部及骨盆手术的肥胖患者（BMI 43 ± 10 kg/m²，n = 14，2 g 头孢西丁）、正常体重患者及健康志愿者（BMI 20 ± 2 kg/m²，n = 13，1 g 头孢西丁）的血浆及组织中头孢西丁的浓度进行检测。使用微量探测仪来检测腹部皮层及离体脂肪组织（同时测切口及愈合组织）的组织浓度。

结果：由于肥胖患者的剂量是两倍多，所以肥胖患者的血浆浓度及浓度-时间曲线下面积大约是两倍高。规范剂量的浓度会更高，虽然浓度-时间曲线下面积并没有显著的不同。检测的及规范剂量的皮下头孢西丁的浓度及浓度-时间曲线下面积肥胖患者远比正常体重患者低。头孢西丁组织渗透力和体重指数呈反比关系。肥胖者的组织渗透力更加低（ 0.08 ± 0.07 vs 0.37 ± 0.26 ， $P < 0.05$ ）。肥胖者脂肪组织的头孢西丁的切口及愈合组织的浓度分别仅有 7.8 ± 7.3 及 2.7 ± 1.4 $\mu\text{g/g}$ ，低于最低抑菌浓度需氧微生物是 $8\mu\text{g/mL}$ 和厌氧微生物是 $16\mu\text{g/mL}$ 。

结论：肥胖手术患者预防性使用抗生素头孢西丁的组织渗透力弱，足够的组织浓度尽管增加临床剂量（2g），足够的组织抗生素浓度可能是肥胖手术患者 ssis 风险增加的因素之一。需要进一步研究达到足够的组织浓度所需的确切的剂量。

（侯文婷译 薛张纲校）

BACKGROUND: Obesity is a significant risk factor for surgical site infections (SSIs), for poorly understood reasons. SSIs are a major cause of morbidity, prolonged hospitalization, and increased health care cost. Drug disposition in general is frequently altered in the obese. Preoperative antibiotic administration, achieving adequate tissue concentrations at the time of incision, is an essential strategy to prevent SSIs.

Nonetheless, there is little information regarding antibiotic concentrations in obese surgical patients. This investigation tested the hypothesis that the prophylactic antibiotic cefoxitin may have delayed and/or diminished tissue penetration in the obese.

METHODS: Plasma and tissue concentrations of cefoxitin were determined in obese patients undergoing abdominal and pelvic surgery (body mass index 43 ± 10 kg/m², n = 14, 2 g cefoxitin) and in normal-weight patients and healthy volunteers (body mass index 20 ± 2 kg/m², n = 13, 1 g cefoxitin). Tissue concentrations were measured using a microdialysis probe in the subcutaneous layer of the abdomen, and in adipose tissue excised at the time of incision and wound closure.

RESULTS: Plasma concentrations and area under the concentration-time curve (AUC) were approximately 2-fold higher in the obese patients because of the 2-fold-higher dose. Dose-normalized concentrations were higher, although AUCs were not significantly different. Measured and dose-normalized subcutaneous cefoxitin concentrations and AUCs in the obese patients were significantly lower than in the normal-weight subjects.

There was an inverse relationship between cefoxitin tissue penetration (AUC(tissue)/AUC(plasma) ratio) and body mass index. Tissue penetration was substantially lower in the obese patients (0.08 ± 0.07 vs 0.37 ± 0.26 , $P < 0.05$). Adipose

tissue cefoxitin concentrations in obese patients were only 7.8 ± 7.3 and 2.7 ± 1.4 $\mu\text{g/g}$, respectively, at incision and closure, below the minimum inhibitory concentration of 8 and 16 $\mu\text{g/mL}$, respectively, for aerobic and anaerobic microorganisms.

CONCLUSION : Obese surgical patients have impaired tissue penetration of the prophylactic antibiotic cefoxitin, and inadequate tissue concentrations despite increased clinical dose (2 g). Inadequate tissue antibiotic concentrations may be a factor in the increased risk of SSIs in obese surgical patients. Additional studies are needed to define doses achieving adequate tissue concentrations.

苯肾上腺素、麻黄碱和前负荷增加对于第三代Vigileo-FloTrac 与经食道多普勒在监测时心输出量变化时的影响

The Impact of Phenylephrine, Ephedrine, and Increased Preload on Third-Generation Vigileo-FloTrac and Esophageal Doppler Cardiac Output Measurements.

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背景：心输出量监测对于围手术期的目标导向性液体治疗具有潜在的指导意义。而Vigileo-FloTrac正是一种对脉搏波型进行分析从而监测心输出量的仪器。然而有些因素会影响Vigileo-FloTrac在监测心输出量变化时的可信度，如使用了血管加压素等。我们使用了血管加压素，测试第三代Vigileo-FloTrac系统是否可能精确测量出心输出量和前负荷的变化，并且与相同情况下的经食道超声多普勒测量情况进行比较。

方法：对33名麻醉后的病人，同时使用第三代Vigileo-FloTrac和经食道超声多普勒测量心输出量。引起血流动力学改变的措施包括：使用苯肾上腺素增加血管张力，使用麻黄碱增加心肌收缩力和心率以及放置头低脚高体位增加前负荷。每一项措施进行之前和之后分别用两种方法测量心输出量。

结果：总计得到了176对心输出量的测量结果。脉搏波形和多普勒法测量心输出量的配对差值为 0.14 ± 2.13 L/min，百分比误差为66%(2倍的标准差除以其方法所测得心输出量的平均值)。关于脉搏波形和多普勒在预测趋势变化时的能力，使用苯肾上腺素后两者的一致性为23%，使用麻黄碱后的一致性为69%，改变体位后的一致性为96%。

结论：当前负荷发生变化时，第三代Vigileo-FloTrac仪器所使用的根据脉搏波形分析法可以精确地监测和反应出心输出量的变化。但是脉搏波形分析法对于苯肾上腺素和麻黄碱引起的心输出量变化的监测不够精确。

(黄剑译 薛张纲校)

BACKGROUND: Cardiac output (CO) monitoring based on pulse contour analysis (Vigileo-FloTrac) has the potential to be used for goal-directed fluid therapy in the perioperative setting. However, factors such as vasopressor usage may impact Vigileo-

FloTrac's reliability in tracking CO changes. We tested third-generation Vigileo-FloTrac system's ability to accurately measure the changes in CO induced by vasopressor administration and increased preload in comparison with esophageal Doppler measurements.

METHODS:In 33 anesthetized patients, CO was monitored simultaneously by the third-generation Vigileo-FloTrac and esophageal Doppler. Hemodynamic challenges included phenylephrine (to increase vasomotor tone), ephedrine (to increase myocardial contractility and heart rate), and whole-body tilting (to increase preload). Measurements were performed before and after each intervention.

RESULTS:Overall, 176 pairs of CO measurements were obtained. The difference between paired pulse contour and Doppler measurements of CO was 0.14 ± 2.13 L/min (mean \pm SD), and the percentage error (2 SD of the difference divided by the mean CO of the reference method) was 66%. The trending ability of pulse contour versus Doppler was 23% (concordance, the percentage of the total number of data points that are in 1 of the 2 quadrants of agreement) after phenylephrine treatment, 69% (concordance) after ephedrine treatment, and 96% (concordance) after whole-body tilting.

CONCLUSIONS:The pulse contour method of measuring CO, as implemented in the third-generation Vigileo-FloTrac device, accurately tracks changes in CO when preload changes. However, the pulse contour method does not accurately track changes in CO induced with phenylephrine and ephedrine.

术后 5 年出现恶性疾病与使用七氟醚麻醉的时间和脑电双频指数小于 45 的时间的相关性

Malignant Disease Within 5 Years After Surgery in Relation to Duration of Sevoflurane Anesthesia and Time with Bispectral Index Under 45

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背景：手术、麻醉以及相关的事件已经被认为与促进癌细胞的增殖相关联。我们调查了术后 5 年之内的癌症的发生率与麻醉持续时间及作为麻醉深度检测指标——脑电双频指数小于 45 的时间之间的相关性。

方法：这是一项前瞻性队列研究，2972 例术前未发现任何恶性疾病的患者使用七氟醚麻醉，并监测 BIS 值，术后随访其是否新发恶性肿瘤。使用 COX 回归评估麻醉时间和 BIS<45 的时间与术后发生癌症风险的相关性。用标准比计算手术人群中癌症发生率与一般人群中发生率的比值。

结果：术后 5 年，129 位病人（4.3%）被诊断 136 个新的恶性肿瘤。没有证据显示 T_{ANESTH} or $T_{BIS<45}$ 或使用 BIS 其他阈值时（即分别<30，<40，<50）与新诊断的恶性疾病相关联。新的恶性疾病的标准发病比是 1.37。

结论：用七氟醚进行麻醉，麻醉持续时间与增加深麻醉累积时间都被证实都不会增加术前没有肿瘤而术后 5 年出现的新的恶性疾病的风险。

（刘珏莹译 薛张纲校）

Background: Surgery, general anesthesia, and related events have been implicated to promote cancer proliferation. We investigated the incidence of cancer within 5 years after surgery in relation to duration of anesthesia (T_{ANESTH}) and also by time with bispectral index (BIS) under 45 ($T_{BIS<45}$) serving as a proxy for more profound anesthesia exposure.

Methods: New malignant diagnoses after surgery under sevoflurane anesthesia were obtained in a prospective cohort of 2972 BIS-monitored patients without any clinically diagnosed malignant disease at the time of index surgery. The risk of cancer during follow-up in relation to T_{ANESTH} and $T_{BIS<45}$ was assessed by Cox regression. The cancer incidence in this surgical population was compared with the incidence in a standardized general population by calculation of standard incidence ratio.

Results: One hundred twenty-nine patients (4.3%) were assigned 136 new malignant diagnoses within 5 years after surgery. No relation between T_{ANESTH} or $T_{BIS<45}$ and new malignant disease was found, nor were any significant relations obtained when other thresholds for BIS (i.e., <30, <40, and <50, respectively) were used in the calculations. The standard incidence ratio for new malignant disease was 1.37 (confidence interval, 1.15–1.62).

Conclusion: Neither duration of anesthesia nor increased cumulative time with profound sevoflurane anesthesia was associated with an increased risk for new malignant disease within 5 years after surgery in previously cancer-free patients.

择期剖宫产产妇行腰麻后使用晶体或胶体对心输出量的影响

Maternal Cardiac Output Changes After Crystalloid or Colloid Coload Following Spinal Anesthesia for Elective Cesarean Delivery: A Randomized Controlled Trial
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背景: 行剖宫产产妇腰麻后会出现低血压, 通过静脉输液或使用升压药以减少胎儿和产妇低血压的发病率。大多数研究都集中在无创收缩压 (SBP) 的测量, 以评估这种疗法的效果。我们使用经胸多普勒技术, 分别测量使用新福林结合输注晶体或在麻醉开始即使用胶体溶扩容时产妇的心输出量 (CO)。我们假设与晶体相比, 胶体会增加心输出量从而减少对升压药的需求量。

方法: 我们招募了 60 名健康的择期在椎管内麻醉下行剖宫产手术的产妇作为这项随机双盲对照研究妇女。在左倾位置测定基线心率、基线收缩压和 CO 变量, 包括每搏输出量、纠正流动时间和收缩力。在腰麻后, 受试者分别给予快速输注 1L w/v 6% 羟乙基淀粉溶液 (HES) 或哈特曼晶液体 (HS)。滴定新福林保证产妇的收缩压维持在基准水平。腰麻后 20 分钟每隔 5 分钟测量 CO。主要比较两组间 CO 变量, 次要比较新福林用量和产妇血流动力学及胎儿的结果数据。

结果: 产妇的人口统计资料, 手术时间, 胎儿的结果数据两组相似。CO 变量的差异, 两组间无显著差异。HS 组 5 分钟时 CO 值及 HES 组 5 分钟及 10 分钟时的 CO 值暂时高于基准值 (范围 0.13-1.74L/分钟), 晶体组和胶体组间的 CO 在研究期间

的整体平均差异为 0.06L/分钟（95%置信区间：-0.46 至 0.58）。两组每搏输出量均高于基线。只有 HES 组流速峰值始终高于基线，两组的纠正流动时间均增加，上述效应在 HS 组时暂时的，但在 HES 组持续存在。任何时间心率在组内或两组之间是没有差异的，但随着时间延长下降。两组使用新福林剂量是相似的。

结论：我们发现腰麻后使用晶体或胶体液对 CO 没有明显差异。此外，在升压药求或血流动力学稳定方面也无差异性。我们的结论是：在择期腰麻下行剖宫产产妇使用胶体或晶体结合新福林没有显著差异。

（陆丽虹译 薛张纲校）

BACKGROUND: Minimizing hypotension associated with spinal anesthesia for cesarean delivery by administration of IV fluids and vasopressors reduces fetal and maternal morbidity. Most studies have concentrated on noninvasive systolic blood pressure (SBP) measurements to evaluate the effect of such regimens. We used a suprasternal Doppler flow technique to measure maternal cardiac output (CO) variables in parturients receiving a phenylephrine infusion combined with the rapid administration of crystalloid or colloid solution at the time of initiation of anesthesia (coload). We hypothesized that a colloid coload compared with a crystalloid coload would produce a larger sustained increase in CO and therefore reduce vasopressor requirements.

METHODS: We recruited 60 healthy term women scheduled for elective cesarean delivery under spinal anesthesia for this randomized double-blind study. Baseline heart rate, baseline SBP, and CO variables including stroke volume, corrected flow time, and contractility were recorded in the left lateral tilt position. At the time of spinal injection, subjects were allocated to receive a rapid 1-L coload of either 6% w/v hydroxyethyl starch solution (HES) or Hartmann (crystalloid) solution (HS). A phenylephrine infusion was titrated to maintain maternal baseline SBP. CO was measured at 5-minute intervals for 20 minutes after initiation of spinal anesthesia. The primary outcome, CO, was compared between groups, as were secondary outcomes: phenylephrine dose and maternal hemodynamic and fetal outcome data.

RESULTS: Maternal demographics, surgical times, and fetal outcome data were similar between groups. There were no significant differences between groups in any measured CO variable at any time point. CO was transiently higher than baseline at 5 minutes in the HS group and at 5 and 10 minutes in the HES group (range, 0.13–1.74 L/min); the overall mean difference in CO between crystalloid and colloid over the study period was 0.06 L/min (95% confidence interval: -0.46 to 0.58). Stroke volume was higher than baseline in both groups throughout; peak velocity was consistently higher than baseline only in the HES group; and corrected flow time increased in both groups; the effect was transient in the HS but sustained in the HES group. Heart rate was not different at any time point within or between groups but did decrease over time. The total phenylephrine dose from time of spinal anesthesia to delivery was similar between groups.

CONCLUSION: We found no difference in CO in women randomized to colloid or crystalloid coload. In addition, there were no differences in vasopressor requirements or hemodynamic stability. We conclude that there is no advantage in using colloid over crystalloid when used in combination with a phenylephrine infusion during spinal anesthesia for elective cesarean delivery.

程序性硬膜外间断给药对比持续给药用于分娩镇痛对母体运动功能和分娩结局的影响：一项对初产妇的随机双盲研究

Programmed intermittent epidural bolus versus continuous epidural infusion for labor analgesia: the effects on maternal motor function and labor outcome :

A randomized double-blind study in nulliparous women.

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背景：与持续硬膜外给药(CEI)相比，程序性的硬膜外间断给药(PIEB)可减少局麻药使用总量和手控给药次数，病人满意度更高。在此随机双盲研究中，我们比较了PIEB和CEI用于维持分娩镇痛对运动阻滞的发生率和分娩结局的影响。研究初期结果变量为母体运动功能，第二结果变量为分娩方式。

方法：本研究入选标准为：初产妇、顺产、宫口扩大<4cm。硬膜外镇痛负荷剂量和维持均使用0.0625%左旋布比卡因和0.5 µg/mL的舒芬太尼。硬膜外使用负荷剂量20ml后，产妇被随机分配接受PIEB(负荷剂量1小时后每小时单次推注10ml)或者CEI(负荷剂量后即刻开始持续推注每小时10ml)来维持镇痛。病人自控硬膜外镇痛(PCEA)由第二个输注泵实施来控制突发痛，药物为0.125%的左旋布比卡因。分娩期间规律使用Bromage评分来评估双下肢运动阻滞程度，任意侧下肢出现任何程度运动阻滞时评估结束。我们同样评估了病人自控硬膜外镇痛的单次注药量和总的镇痛药液使用量。

结果：研究样本量为145(PIEB = 75; CEI = 70)。运动阻滞在CEI组为37%，在PIEB为2.7%($P < 0.001$; 比值为21.2; 95%置信区间为4.9-129.3)；运动阻滞在CEI组中发生时间更早($P = 0.008$) (危害比为7.8; 95%置信区间为1.9-30.8; $P = 0.003$)且在宫口开全后发生更加频繁($P < 0.001$)。在CEI组中器械助产发生率为20%，而在PIEB组中为7% ($P = 0.03$)。PIEB组在总左旋布比卡因使用量、需要额外PCEA手控注药的病人数，每个病人PCEA手控注药平均次数方面均低于对照组($P < 0.001$)。在疼痛评分和产程镇痛方面组间无差异。

结论：与CEI相比，PIEB维持的分娩镇痛母体运动阻滞和器械阴道助产发生率较低。

(任云译 薛张纲校)

BACKGROUND: Programmed intermittent epidural anesthetic bolus (PIEB) technique may result in reduced total local anesthetic consumption, fewer manual boluses, and greater patient satisfaction compared with continuous epidural infusion(CEI). In this randomized, double-blind study, we compared the incidence of motor block and labor outcome in women who received PIEB or CEI for maintenance of labor analgesia. The primary outcome variable was maternal motor function and the secondary outcome was mode of delivery.

METHODS: Nulliparous, term women with spontaneous labor and cervical dilation <4 cm were eligible to participate in the study. Epidural analgesia was initiated and maintained with a solution of levobupivacaine 0.0625% with sufentanil 0.5 µg/mL. After

an initial epidural loading dose of 20 mL, patients were randomly assigned to receive PIEB (10 mL every hour beginning 60 minutes after the initial dose) or CEI (10 mL/h, beginning immediately after the initial dose) for the maintenance of analgesia. Patient-controlled epidural analgesia (PCEA) using a second infusion pump with levobupivacaine 0.125% was used to treat breakthrough pain. The degree of motor block was assessed in both lower extremities using the modified Bromage score at regular intervals throughout labor; the end point was any motor block in either limb. We also evaluated PCEA bolus doses and total analgesic solution consumption.

RESULTS: We studied 145 subjects (PIEB = 75; CEI = 70). Motor block was reported in 37% in the CEI group and in 2.7% in the PIEB group ($P < 0.001$; odds ratio = 21.2; 95% CI: 4.9-129.3); it occurred earlier ($P = 0.008$) (hazard ratio = 7.8; 95% CI: 1.9-30.8; $P = 0.003$) and was more frequent at full cervical dilation in the CEI group ($P < 0.001$). The incidence of instrumental delivery was 20% for the CEI group and 7% for the PIEB group ($P = 0.03$). Total levobupivacaine consumption, number of patients requiring additional PCEA boluses, and mean number of PCEA boluses per patient were lower in the PIEB group ($P < 0.001$). No differences in pain scores and duration of labor analgesia were observed.

CONCLUSION: Maintenance of epidural analgesia with PIEB compared with CEI resulted in a lower incidence of maternal motor block and instrumental vaginal delivery.

近红外线分光镜测量脑血管的反应性的局限性：低频振荡所扮演的角色。

The Limitations of Near-Infrared Spectroscopy to Assess Cerebrovascular Reactivity: The Role of Slow Frequency Oscillations

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背景：使用近红外线分光镜检查得到的总的血红蛋白反应指数已经被用于无创评估脑血管的反应性。与压力反应指数相似，总血红蛋白反应指数是由相关系数计算而来的，与动脉血压有关。然而，总血红蛋白指数在脑外伤病人中的可靠性仍不确定。虽然慢振荡可以被近红外线分光镜描述成信号，但是评估自动调节的重要性仍然不确定。在最近的研究中，我们研究了总血红蛋白低振荡在于脑血管反应性监测中的角色。

方法：这项研究是基于一项回顾性研究分析，这项研究曾经以不同的方案记载发表多次。在 2008 年 6 月-2009 年 6 月之间有 37 名脑外伤患者被收治于 Addenbrooke's 神经外监护室。在人工假体摘除后，我们使用光谱分析来研究组织的血红蛋白指数（THI，即测量结合氧的血红蛋白和未结合氧的血红蛋白）和颅内压信号。压力反应指数和总血红蛋白反应指数都与颅内压，动脉血压，组织血红蛋

白指数等动态相关。另外，我们也研究了来自左右大脑的总血红蛋白指数的相关性。

结果：压力反应指数和总血红蛋白反应指数的一致性依赖于输入信号的低振荡能力。对于标准慢波活动度 >0.4 ，组间比较显示总血红蛋白指数与压力反应指数有很大的相关性。（ $r=0.80$,95%可信区间是 $0.53-0.92$, $P<0.01$ ）。另外，组内比较提示只有当左右脑的总血红蛋白指数至少有中等程度的一致时，才能用总血红蛋白指数来代替压力反应指数。

结论：我们的研究提示脑血管反应指数总血红蛋白指数可以用于无创替代压力反应指数，但是只有在输入信号有足够的慢波能量时。另外，左右大脑的总血红蛋白指数的一致性是比较总压力反应指数和局部总血红蛋白指数的先决条件。最后，无创监测脑血管的反应性可以在患者无颅内压监测的条件下，理想地指导这些患者的动脉血压的管理。

（翁梅琳译 薛张纲校）

BACKGROUND: A total hemoglobin reactivity index (THx) derived from near-infrared spectroscopy (NIRS) has recently been introduced to assess cerebrovascular reactivity noninvasively. Analogously to the pressure reactivity index (PRx), THx is calculated as correlation coefficient with arterial blood pressure (ABP). However, the reliability of THx in the injured brain is uncertain. Although slow oscillations have been described in NIRS signals, their significance for assessment of autoregulation remains unclear. In the current study, we investigated the role of slow oscillations of total hemoglobin for NIRS-based cerebrovascular reactivity monitoring.

METHODS: This study was based on a retrospective analysis of data that were consecutively recorded for a different project published previously. Thirty-seven patients with traumatic brain injury and admitted to Addenbrooke's Neurosciences Critical Care Unit between June 2008 and June 2009 were included. After artifact removal, we performed spectral analysis of the tissue hemoglobin index (THI, a measure of oxy- and deoxygenated hemoglobin) and intracranial pressure (ICP) signal. PRx and THx were calculated as moving correlations between ICP and ABP, and THI and ABP, respectively. The agreement between PRx and THx as a function of normalized power of slow oscillations (0.015–0.055 Hz) contained in the input signals was assessed performing between-subject and within-subject correlation analyses. Furthermore, the correlation between the THx values derived from the right and left sides was analyzed.

RESULTS: The agreement between PRx and THx depended on the power of slow oscillations in the input signals. Between-subject comparisons revealed a significant correlation between THx and PRx ($r = 0.80$, 95% confidence interval $0.53-0.92$, $P < 0.01$) for patients with normalized slow wave activity >0.4 in the THI signal, compared with $r = 0.07$ (95% confidence interval -0.40 to 0.51 , $P = 0.79$) in the remaining files. Furthermore, within-subject comparisons suggested that THx may be used as a substitute for PRx only when there is an at least moderate agreement ($r = 0.36$) between the THx values derived from the right and left sides.

CONCLUSIONS: Our results suggest that the NIRS-based cerebrovascular reactivity index THx can be used as a noninvasive substitute for PRx, but only during phases with sufficient slow wave power in the input signal. Furthermore, a good agreement between the THx measures on both sides seems to be a prerequisite for comparison of a global (PRx) versus the more local (THx) index. Nevertheless, noninvasive assessment of

cerebrovascular reactivity may be desirable in patients without ICP monitoring and help to guide ABP management in these patients.

连续外周神经阻滞:一项基于发表证据的综述

Continuous Peripheral Nerve Blocks: A Review of the Published Evidence

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摘要：连续外周神经阻滞,又称为神经周围局麻药输注包括了经皮在外周神经周围置管,然后通过这根导管给予局麻药从而提供多天甚至数月的麻醉或镇痛。连续外周神经阻滞可以在医院进行,但轻便的便携式泵使得病人可以下床活动同时进行输注。这一技术最主要用于术后镇痛。同时,也可用于顽固性呃逆,血管意外后诱导交感神经切除和血管扩张来增加血流,断肢再植,或四肢的手术,缓解雷诺病的血管痉挛;治疗外周血管栓塞和慢性疼痛如复杂区域疼痛综合症、幻肢痛、三叉神经痛和癌性疼痛。创伤后连续外周神经阻滞能在病人转运至医疗中心前或者等待手术修复前给予镇痛。放置导管可以通过很多方法进行,包括神经刺激、超声引导、诱导异感,荧光影像或者简单的触觉进行。简单的硬膜外导管可以用于置管,或者能传输电流至其尖端的“可刺激的导管”也可用。输注的药物包括了稀释的长效局麻药,可通过仅给予单次剂量、背景剂量或者两者结合的方式进行。记录的益处有赖于成功缓解疼痛,包括减少安静痛、暴发痛和运动痛,减少辅助镇痛药和阿片类相关副作用和睡眠障碍。在一些病例中,病人的满意度增加,下床活动、功能均改善;被动关节运动功能恢复加速,同时病人达到出院标准或者实际出院时间均加快。最后,术后关节炎症和炎症指标均减少。输注本身带来了许多益处,但是在几个随机临床试验中得出导管拔除后仍具有延长的益处。一些小的并发症有时经常发生,但是大的风险例如临床相关的感染和神经损伤很少见。本文是关于连续周围神经阻滞的循证综述。

(姚敏敏译 薛张纲校)

Abstract : A continuous peripheral nerve block, also termed “perineural local anesthetic infusion,” involves the percutaneous insertion of a catheter adjacent to a peripheral nerve, followed by local anesthetic administration via the catheter, providing anesthesia/analgesia for multiple days or even months. Continuous peripheral nerve blocks may be provided in the hospital setting, but the use of lightweight, portable pumps permits ambulatory infusion as well. This technique's most common application is providing analgesia after surgical procedures. However, additional indications include treating intractable hiccups; inducing a sympathectomy and vasodilation to increase blood flow after a vascular accident, digit transfer/replantation, or limb salvage; alleviating vasospasm of Raynaud disease; and treating peripheral embolism and chronic pain such as complex regional pain syndrome, phantom limb pain, trigeminal neuralgia, and cancer-induced pain. After trauma, perineural infusion can provide analgesia during transportation to a distant treatment center, or while simply awaiting surgical repair. Catheter insertion may be accomplished using many possible modalities, including nerve

stimulation, ultrasound guidance, paresthesia induction, fluoroscopic imaging, and simple tactile perceptions (“facial click”). Either a nonstimulating epidural-type catheter may be used, or a “stimulating catheter” that delivers electrical current to its tip. Administered infusate generally includes exclusively long-acting, dilute, local anesthetic delivered as a bolus only, basal only, or basal-bolus combination. Documented benefits appear to be dependent on successfully improving analgesia, and include decreasing baseline/breakthrough/dynamic pain, supplemental analgesic requirements, opioid-related side effects, and sleep disturbances. In some cases, patient satisfaction and ambulation/functioning may be improved; an accelerated resumption of passive joint range-of-motion realized; and the time until discharge readiness as well as actual discharge from the hospital or rehabilitation center achieved. Lastly, postoperative joint inflammation and inflammatory markers may be decreased. Nearly all benefits occur during the infusion itself, but several randomized controlled trials suggest that in some situations there are prolonged benefits after catheter removal as well. Easily rectified minor complications occur somewhat frequently, but major risks including clinically relevant infection and nerve injury are relatively rare. This article is an evidence-based review of the published literature involving continuous peripheral nerve blocks.

利多卡因通过抑制小胶质细胞活化来减少糖尿病诱导触觉性疼痛过敏

Lidocaine Attenuates the Development of Diabetic-Induced Tactile Allodynia by Inhibiting Microglial Activation

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背景：利多卡因在临床上用来治疗与糖尿病神经病变相关的触觉性疼痛过敏。尽管利多卡因通过抑制小胶质细胞活化的镇痛效应与创伤诱导的神经性疼痛有相似之处，但他减少糖尿病诱导的触觉性疼痛过敏的机制还未完全阐明。

方法：为了评估利多卡因在糖尿病神经病变中对小胶质细胞的效应，小鼠在接受注射链脲霉素后 14 天到 21 天持续注射利多卡因。在第 21 天，评估脊髓背角内小胶质细胞的积聚及 p38 分裂活化蛋白激酶的活化。在体外，利多卡因对细胞存活，单核细胞趋化蛋白-1 的趋化作用和促炎症反应的影响通过干扰素- γ -激活的原始小胶质细胞来检测。

结果：STZ-小鼠中，在触觉性疼痛过敏的早期进程中持续全身应用利多卡因产生长时间的镇痛效果。利多卡因显著减少脊髓背角中小胶质细胞的积聚和 p38 磷酸化。在体外，利多卡因负调节干扰素- γ -诱导基因诱导氧化合酶和 interleukin-1 β 。利多卡因预处理显著减少干扰素- γ -活化小胶质细胞中单核细胞趋化蛋白-1 的趋化作用。

结论：利多卡因可能通过调节脊髓小胶质细胞的 P38 途径来缓解 STZ-诱导的触觉性疼痛过敏。在糖尿病神经病变早期通过利多卡因的治疗来抑制小胶质细胞活性显示了一种潜在可行的治疗触觉性疼痛过敏的策略。

(张玥琪译, 薛张纲校)

BACKGROUND: Lidocaine is used clinically for tactile allodynia associated with diabetes-induced neuropathy. Although the analgesic effect of lidocaine through suppression of microglial activation has been implicated in the development of injury-induced neuropathic pain, its mechanism of action in diabetes-induced tactile allodynia has not yet been completely elucidated.

METHODS: To evaluate the effects of lidocaine on microglial response in diabetic neuropathy, streptozotocin (STZ)-injected mice received a continuous infusion of lidocaine (vehicle, 2, or 10%) from day 14 to day 21 after STZ injection. On day 21, microglial accumulation and p38 mitogen-activated protein kinase activation in the dorsal horn were evaluated. In vitro, the effects of lidocaine on cell viability, chemotactic response to monocyte chemoattractant protein-1, and induction of proinflammatory mediators were examined in interferon (IFN)- γ -stimulated primary microglial cells.

RESULTS: Continuous systemic administration of lidocaine in the early progression of tactile allodynia produced long-lasting analgesic effects in STZ-treated mice. Lidocaine significantly reduced accumulation and p38 phosphorylation of microglial cells in the dorsal horn. In vitro, lidocaine down-regulated IFN- γ -induced gene induction of inducible nitric oxide synthase and interleukin-1 β . Pretreatment with lidocaine significantly reduced chemotactic response to monocyte chemoattractant protein-1 of IFN- γ -activated microglial cells.

CONCLUSION: Lidocaine alleviates STZ-induced tactile allodynia, possibly by modulating the p38 pathway in spinal microglial cells. Inhibiting microglial activation by lidocaine treatment early in the course of diabetes-induced neuropathy represents a potential therapeutic strategy for tactile allodynia.

结合临床和实验室方法对心胸外科重症监护病房内患者进行肝素诱导血小板减少症的诊断

A Diagnosis of Heparin-Induced Thrombocytopenia with Combined Clinical and Laboratory Methods in Cardiothoracic Surgical Intensive Care Unit Patients

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背景: 由于大量血小板减少症的发生与体外循环 (CPB) 有关, 所以在心胸外科手术患者中诊断术后肝素诱导血小板减少症 (HIT) 是比较复杂的。体外循环使患者发展成为直接针对血小板因子 4 (PF4)/肝素复合物的抗体和 HIT 的发生率较高。这种比较容易形成的免疫抗体的敏感性高, 但特异性十分低。同时使用临床概率评分和快速实验室免疫分析法已显示特异性有所增加, 这在体外循环的情况下尤其重要。及时的诊断是关键, 因为停止肝素和替代性抗凝药物治疗可以减少血栓栓塞事件的风险。

方法: 我们回顾性地研究了从 2007 年 1 月至 2010 年 12 月用血清素释放分析法 (SRA) 和 PF4/肝素免疫分析血清的心胸外科手术患者的记录。我们指定一个高

级、中级或低级临床“4Ts”概率评分来量化每一个病人的血小板减少症、血小板减少的时间和血栓性并发症。然后将临床评分和PF4/肝素免疫分析与“金标准”的诊断测试——SRA相比较。

结果：PF4/肝素光学密度 >0.40 的敏感性和特异性分别为100%和26%。结合PF4/肝素光学密度 >0.40 和高/中级4Ts评分诊断HIT的敏感性和特异性分别为100%和70%。低级4Ts评分阴性预测值为100%。

结论：我们证明了结合4Ts临床评分和PF4/肝素免疫分析用于诊断HIT与单独使用PF4/肝素免疫分析相比较增加了诊断HIT的敏感性和特异性。此外，一个中级4Ts评分和阳性的PF4/肝素抗体测试结果，确认性的血小板活化检测如SRA是必要的。医生治疗心胸外科手术后的患者时应该认识到，甚至HIT中级临床可能性的患者也需要抗体测试，并用血小板活化检测进行确认。

(唐亮译 马皓琳 李士通校)

BACKGROUND: Diagnosing postoperative heparin-induced thrombocytopenia (HIT) in cardiothoracic surgical patients is complicated because of the profound thrombocytopenia that occurs with cardiopulmonary bypass (CPB). CPB predisposes patients to develop a frequent incidence of antibodies directed against platelet factor 4 (PF4)/heparin complexes and HIT. The sensitivity of readily available antibody immunoassays is high, but specificity is quite low. The use of both a clinical probability score and rapid laboratory immunoassay has been shown to increase specificity, which is of particular importance in the CPB setting. Prompt diagnosis is crucial because cessation of heparin and treatment with alternative anticoagulation can reduce the risk of thromboembolic events.

METHODS: We retrospectively reviewed records from cardiothoracic surgical patients whose serum was tested with both the serotonin release assay (SRA) and the PF4/heparin immunoassay from January 2007 through December 2010. We assigned a high, intermediate, or low clinical “4Ts” probability score that quantifies thrombocytopenia, timing of platelet decrease, and thrombotic complications in each patient. We then compared the clinical score and the PF4/heparin immunoassay against the “gold standard” diagnostic test, the SRA.

RESULTS: The sensitivity and specificity for PF4/heparin optical density >0.40 were 100% and 26%, respectively. Sensitivity and specificity for the diagnosis of HIT with a combination of PF4/heparin optical density >0.40 and high/intermediate 4Ts score were 100% and 70%, respectively. The negative predictive value was 100% for low 4Ts score.

CONCLUSIONS: We demonstrated that the use of the 4Ts clinical score combined with the PF4/heparin immunoassay for HIT diagnosis increases the sensitivity and specificity of HIT testing compared with the PF4/heparin immunoassay alone. Furthermore, with an intermediate 4Ts score and positive PF4/heparin antibody test, a confirmatory platelet activation assay such as the SRA is necessary. Physicians treating patients after cardiothoracic surgery should recognize the need for an antibody test and confirmation with a platelet activation assay with even moderate clinical probability of HIT.

麻醉方式对于宫腔镜手术中甘氨酸吸收的影响：一项随机对照试验

The Impact of Anesthesia on Glycine Absorption in Operative Hysteroscopy: A Randomized Controlled Trial

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背景：宫腔镜手术需要使用膨胀性介质，它的吸收可能导致严重的并发症如血容量过多和水中毒。我们比较了两种麻醉方式（全身麻醉和局部麻醉联合镇静）对于宫腔镜手术中甘氨酸吸收的影响。

方法：这是一项为期超过 17 个月时间的随机对照试验。因异常子宫出血进行宫腔镜手术的符合条件的病人被随机分为两组：全身麻醉组和局部麻醉联合镇静组。主要观察指标是用自动化串联滤罐系统测量的甘氨酸溶液吸收中位数（第 10--第 90 百分位数）。次要观察指标包括吸收大于 1000ml 的发生率、因过度吸收中断手术、血清钠改变中位数、术后低钠血症和病人术后 24 小时时的生活质量（8 项短条目健康调查问卷）。应用非参数检验（曼-惠特尼 U 检验、 χ^2 检验和费舍尔确切检验）。

结果：在 142 个符合条件的病人中，95 人同意参与试验并被随机分组。全身麻醉组病人甘氨酸溶液的吸收中位数（第 10-第 90 百分位数）较局部麻醉联合镇静组高（480 mL [76–1300 mL] 比 253 mL [70–728 mL]; $P = 0.005$ ）。全身麻醉组甘氨酸溶液吸收大于 1000ml 的发生率较局部麻醉联合镇静组高(>1000 mL [20% 比 4%; $P = 0.009$])，血清钠降低速度也较快(≥ 10 mEq/L [8% 比 0%; $P = 0.005$])。患者分级的术后生活质量两组相比较差异不大。

结论：相对于全身麻醉，局部麻醉联合镇静时的甘氨酸溶液吸收较少，应作为宫腔镜手术优先考虑的麻醉方式。

（张怡译 马皓琳 李士通校）

BACKGROUND: Operative hysteroscopy requires the use of a distension medium and its absorption can lead to serious consequences from intravascular volume overload and water intoxication. We compared the impact of 2 types of anesthesia (general anesthesia and local anesthesia with sedation) on the absorption of glycine solution in operative hysteroscopy.

METHODS: A randomized controlled trial was conducted over a 17-month period. Eligible patients undergoing operative hysteroscopy for abnormal uterine bleeding were randomized in 2 groups: a general anesthesia group and a local anesthesia with sedation group. The primary outcome was the median absorption of the glycine solution (10th–90th percentile) measured with an automated tandem canister system. Secondary outcomes included incidence of absorption >1000 mL, discontinued surgery because of excessive absorption, median change in serum sodium, postoperative hyponatremia, and patients' postoperative quality of life at 24 hours (8-item Short Form Health Survey questionnaire). Nonparametric analyses (Mann-Whitney U test, χ^2 test, and Fisher exact test) were used.

RESULTS: Of 142 eligible patients, 95 agreed to participate and were randomized. Women who underwent general anesthesia had a higher median absorption of the glycine

solution (10th–90th percentile) compared with women who underwent local anesthesia with sedation (480 mL [76–1300 mL] vs 253 mL [70–728 mL]; $P = 0.005$). General anesthesia was also associated with a higher rate of glycine solution absorption (>1000 mL [20% vs 4%; $P = 0.009$]) and a more rapid rate of decrease in serum sodium (≥ 10 mEq/L [8% vs 0%; $P = 0.005$]) than local anesthesia with sedation. Postoperative quality of life measures as rated by the patients were comparable between the 2 groups.

CONCLUSION: Compared with general anesthesia, local anesthesia with sedation is associated with less glycine absorption and should be considered the preferred method of anesthesia for operative hysteroscopy.

七氟醚对猪自体肺移植模型预处理的效应

The Effects of Anesthetic Preconditioning with Sevoflurane in an Experimental Lung Autotransplant Model in Pigs

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背景：由于胸外科手术对一侧肺的通气损害，缺血再灌注肺损伤在胸外科手术中成倍的重要。我们在本项研究中评估了七氟醚对猪自体肺移植模型的细胞保护作用。

方法：我们根据使用的麻醉药物不同（七氟醚或丙泊酚）将 20 只行肺切除术加自体肺移植术的大白猪分为 2 组，每组 10 只。每 5 分钟测量一次促炎症反应介质、氧化应激、氧化亚氮代谢及血流动力学和血液数据。

结果：丙泊酚组氧化应激指标和促炎症反应介质升高，但两组血流动力学无显著差异。

结论：我们证明了在活体缺血再灌注肺损伤的模型中，七氟醚降低了炎症反应和氧化应激。

（刘伍译 马皓琳 李士通校）

BACKGROUND: Ischemia–reperfusion lung injury is doubly important in thoracic surgery because of the associated ventilation damage to 1 lung. In this study we evaluated the cytoprotective effects of sevoflurane in a pulmonary autotransplant model in pigs.

METHODS: Twenty Large White pigs undergoing pneumonectomy plus lung autotransplant were divided into 2 10-member groups on the basis of the anesthetic received (propofol or sevoflurane). Proinflammatory mediators, oxidative stress, nitric oxide metabolism, and hemodynamic and blood variables were measured at 5 different time points.

RESULTS: There was an increase of oxidative stress markers and proinflammatory mediators in the propofol group, whereas the hemodynamic variables were similar in both groups.

CONCLUSIONS: We demonstrated that sevoflurane decreased the inflammatory response and oxidative stress in a live ischemia–reperfusion lung model.

麻醉医生关于动脉波形分析过去、现在、将来的概念

Arterial Waveform Analysis for the Anesthesiologist: Past, Present, and Future Concepts

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定性的动脉波形分析已有千年历史，而可追溯到 18 世纪的欧拉的著作中的定量动脉波形分析技术却未被麻醉医生和其他临床工作者广泛应用。这可能部分归因于血压计的普及，它使得实际操作者评估动脉血压可不必开发一种监测装置来测定更高级的动脉波形的特性。测量这些特性的装置的开发延迟了 20 年正说明了我们对此信息的原始构想的正确。外周动脉血压波形的形状可能确实包含了对麻醉医生和重症监护医生的有用信息。外周动脉血压描记图的最大斜率似与左心室收缩性有关，虽然这种关系可能被其他血流动力学变量混杂。当负荷情况稳定时，外周动脉血压描记图的线下面积与每搏量有关，这个发现已被应用于一些连续心输出量监测的开发中。脉搏波传导速度可能与血管阻抗有关，并可能潜在提高基于波形的心搏量估计的精确性。通过广义传递函数可根据外周动脉（例如肱、桡）的描记图估计中心动脉压（例如主动脉），并融入一些连续心输出量监测仪的算法。

（毛祖旻 译 马皓琳 李士通 校）

Qualitative arterial waveform analysis has been in existence for millennia; quantitative arterial waveform analysis techniques, which can be traced back to Euler's work in the 18th century, have not been widely used by anesthesiologists and other clinicians. This is likely attributable, in part, to the widespread use of the sphygmomanometer, which allows the practitioner to assess arterial blood pressure without having to develop a sense for the higher-order characteristics of the arterial waveform. The 20-year delay in the development of devices that measure these traits is a testament to the primitiveness of our appreciation for this information. The shape of the peripheral arterial pressure waveform may indeed contain information useful to the anesthesiologist and intensivist. The maximal slope of the peripheral arterial pressure tracing seems to be related to left ventricular contractility, although the relationship may be confounded by other hemodynamic variables. The area under the peripheral arterial pressure tracing is related to stroke volume when loading conditions are stable; this finding has been used in the development of several continuous cardiac output monitors. Pulse wave velocity may be related to vascular impedance and could potentially improve the accuracy of waveform-based stroke volume estimates. Estimates of central arterial pressures (e.g., aortic) can be produced from peripheral (e.g., brachial, radial) tracings using a Generalized Transfer Function, and are incorporated into the algorithms of several continuous cardiac output monitors.

应用 AP Advance、GlideScope Ranger 可视喉镜和 Macintosh 喉镜在人体模型插管的研究

A Mannequin Study of Intubation with the AP Advance and GlideScope Ranger Videolaryngoscopes and the Macintosh Laryngoscope

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背景：AP Advance (APA)是一种可以互换镜片的可视喉镜：插管者可选用标准 Macintosh 镜片或增加了曲率和一条通道以引导导管进入喉部的困难气道镜片。因此 APA 可能在处理正常气道和困难气道时有着同等的有效性。我们验证了 APA 在正常气道模型插管不慢于 Macintosh 喉镜，在困难气道模型插管中不慢于 GlideScope Ranger 可视喉镜的假设。

方法：可能有气管插管职责的医学专业人员接受了每一种喉镜使用的培训。参加者用 APA、GlideScope 和传统的 Macintosh 喉镜对模拟的 (Laerdal SimMan) 正常和困难气道进行插管。应用 Cox 相对危险回归法来比较插管速度，当危害比 >0.8 时认为速度不慢。我们同时还比较了喉部显影、失败数以及参与者的偏好。

结果：未经校准的 APA 和 Macintosh 喉镜插管时间事实上是相等的 (中位数 22 比 23 秒)；在对经验、次序、阶段的影响进行校准后，APA 比 Macintosh 喉镜的危害比 (95%可信区间) 为 0.87 (0.65, 1.17),并不明显高于我们预先定义的非劣效性边界值 0.8 ($P = 0.26$)。APA 在困难气道的插管速度比 GlideScope 喉镜更快 (危害比 $=0.76$, [5.0, 11.3], $P < 0.001$, 中位数: 20 比 59 秒)。所有的受试者都用 APA 完成了困难气道模型的插管, 而用 GlideScope 和 Macintosh 者分别有 33%和 37%插管失败。在困难气道中, 99%受试者应用 APA 暴露声门达到了 Cormack and Lehane 评级 I 到 II 级, 而应用 GlideScope 和 Macintosh 者分别为 85%和 33%。请受试者选用其中一种喉镜时, 82%选择 APA。

结论：在正常气道模型, APA 和 Macintosh 喉镜的插管时间相似。然而在困难气道模型中, APA 插管速度显著快于 GlideScope 喉镜。

(瞿亦枫 译 马皓琳 李士通 校)

BACKGROUND: The AP Advance (APA) is a videolaryngoscope with interchangeable blades: intubators can choose standard Macintosh blades or a difficult-airway blade with increased curvature and a channel to guide the tube to the larynx. The APA may therefore be comparably effective in both normal and difficult airways. We tested the hypotheses that intubation with the APA is no slower than Macintosh laryngoscopy for normal mannequin airways, and that it is no slower than videolaryngoscopy using a GlideScope Ranger in difficult mannequin airways.

METHODS: Medical professionals whose roles potentially include tracheal intubation were trained with each device. Participants intubated simulated (Laerdal SimMan) normal and difficult airways with the APA, GlideScope, and a conventional Macintosh

blade. Speed of intubation was compared using Cox proportional hazards regression, with a hazard ratio >0.8 considered noninferior. We also compared laryngeal visualization, failures, and participant preferences.

RESULTS: Unadjusted intubation times in the normal airway with the APA and Macintosh were virtually identical (median, 22 vs 23 seconds); after adjustment for effects of experience, order, and period, the hazard ratio (95% confidence interval) comparing APA with Macintosh laryngoscopy was 0.87 (0.65, 1.17), which was not significantly more than our predefined noninferiority boundary of 0.8 ($P = 0.26$). Intubation with the APA was faster than with the GlideScope in difficult airways (hazard ratio = 7.6 [5.0, 11.3], $P < 0.001$; median, 20 vs 59 seconds). All participants intubated the difficult airway mannequin with the APA, whereas 33% and 37% failed with the GlideScope and Macintosh, respectively. In the difficult airway, 99% of participants achieved a Cormack and Lehane grade I to II view with the APA, versus 85% and 33% with the GlideScope and Macintosh, respectively. When asked to choose 1 device overall, 82% chose the APA.

CONCLUSIONS: Intubation times were similar with the APA and Macintosh laryngoscopes in mannequins with normal airways. However, intubation with the APA was significantly faster than with the GlideScope in the difficult mannequin simulation.

对比瑞芬太尼和哌替啶应用于分娩镇痛的一项系统综述

A Comparison Between Remifentanyl and Meperidine for Labor Analgesia: A Systematic Review

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背景: 瑞芬太尼是一超短效阿片类药物, 具有良好的药代动力学特性使它非常适合分娩镇痛。尽管瑞芬太尼自由通过胎盘, 但由于在新生儿体内快速代谢和重新分布使它快速消除。我们研究的目的是瑞芬太尼和哌替啶相比在降低分娩产妇疼痛评分是否有效。还观察了瑞芬太尼对母亲、产程和新生儿的影响。

方法: 用多个关键词 (如产科镇痛, 瑞芬太尼, 哌替啶) 没有语言限制搜索 MEDLINE、CINAHL、Embase、Cochrane CENTRAL 及母婴保健数据库。检查了来自于 5 个重要研究会议出版的摘要和来自检索文献的参考文献用来搜索额外的研究。选择了瑞芬太尼和哌替啶在分娩产妇做对比的随机对照试验。按照用于干预的系统回顾的循证医学手册中列出的标准来进行评估偏倚风险。我们评估序列产生是否合适、分配隐藏、盲法和随访的完整性。用标准化数据收集表从每一项研究提取数据。主要观察指标是疼痛评分的降低 (视觉模拟评分[VAS], 0-100mm)。我们也评估了产妇副作用 (镇静、血氧饱和度下降和呼吸减缓) 和对新生儿的影响 (Apgar 评分、脐带 pH 及神经病学和适应能力评分)

结果: 7 个研究 (349 个患者) 确认入组; 仅有 3 个研究适合在荟萃分析中用于定量合成 (233 例患者)。我们发现瑞芬太尼在 1 小时降低平均 VAS 评分比哌替

啖多 25mm (95%置信区间 19-31mm) ($P < 0.001$)。由于资料不充分导致关于瑞芬太尼副作用方面做出的结论有限。

结论：瑞芬太尼在降低 1 小时后的分娩疼痛平均视觉模拟评分方面优于哌替啶。

(刘朝辉译, 马皓琳, 李士通校)

BACKGROUND: Remifentanyl is an ultrashort-acting opioid with favorable pharmacokinetic properties that make it suitable as a labor analgesic. Although it crosses the placenta freely, it is eliminated quickly in the neonate by rapid metabolism and redistribution. We aimed to determine whether remifentanyl compared with meperidine is effective in reducing pain scores in laboring parturients. Other effects on the mother, the labor process, and the neonate were also examined.

METHODS: MEDLINE, CINAHL, Embase, Cochrane CENTRAL, and Maternity and Infant Care databases were searched without language restriction using multiple keywords for labor analgesia, remifentanyl, and meperidine. Published abstracts from 5 key research meetings and references from retrieved articles were examined for additional studies. Randomized controlled trials in laboring parturients comparing remifentanyl with meperidine were selected. Risk of bias was assessed using criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*. We assessed for adequacy of sequence generation, allocation concealment, blinding, and completeness of follow-up. Data were extracted from each study using a standardized data collection form. The primary outcome was reduction in pain scores (visual analog scale [VAS], 0–100 mm). We also evaluated maternal side effects (sedation, oxygen desaturation, and bradypnea) and effects on the neonate (Apgar scores, umbilical cord pH, and Neurologic and Adaptive Capacity Scores).

RESULTS: Seven studies (349 patients) were identified for inclusion; only 3 studies were suitable for quantitative synthesis in a meta-analysis (233 patients). We found that remifentanyl reduces the mean VAS score at 1 hour by 25 mm more than meperidine ($P < 0.001$) (95% confidence interval = 19–31 mm). Limited conclusions can be made regarding the side-effect profile of remifentanyl because of insufficient data.

CONCLUSION: Compared with meperidine, remifentanyl is superior in reducing mean VAS scores for labor pain after 1 hour.

青少年的氧化亚氮麻醉和血浆高半胱氨酸

Nitrous Oxide Anesthesia and Plasma Homocysteine in Adolescents

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背景：氧化亚氮可以使维生素 B₁₂ 灭活，抑制蛋氨酸合酶，从而升高血浆总高半胱氨酸量 (tHcy)。儿童长时间暴露于氧化亚氮可导致神经病变、脊髓变性，甚至导致死亡。我们对氧化亚氮麻醉导致儿童血浆 tHcy 明显增加的假设进行了研究。

方法：27 名 (年龄 10-18 岁) 择期行脊柱大手术的儿童入组，采取患者诱导后 0-96 h 一系列血浆样本。麻醉方案，包括氧化亚氮的使用，由麻醉师自由决定。使用标准酶法测定血浆 tHcy。

结果：血浆 tHcy 浓度中位数基线值为 5.1 $\mu\text{mol/L}$ (3.9-8.0 $\mu\text{mol/L}$ ，四分位距)，并且所有暴露于氧化亚氮的病人 ($n=26$) 血浆 tHcy 量均升高，平均升高 9.4 $\mu\text{mol/L}$ (几何平均数;95%置信区间 7.1-12.5 $\mu\text{mol/L}$) 或 228% (均值; 95%置信区间, 178%-279%)。血浆 tHcy 量在麻醉诱导后 6-8 小时出现峰值。一名没有接受氧化亚氮的病人血浆 tHcy 量未升高。一些患者血浆 tHcy 成倍增加 (最高+567%)。血浆 tHcy 的增加与氧化亚氮麻醉的持续时间和平均浓度密切相关 ($r=0.80$, $P<0.001$)。

结论：小儿患者接受氧化亚氮麻醉显著增加血浆 tHcy 浓度。这种影响程度似乎比成人要大，但临床意义不明。

(安光惠译 马皓琳 李士通校)

BACKGROUND: Nitrous oxide inactivates vitamin B₁₂, inhibits methionine synthase, and consequently increases plasma total homocysteine (tHcy). Prolonged exposure to nitrous oxide can lead to neuropathy, spinal cord degeneration, and even death in children. We tested the hypothesis that nitrous oxide anesthesia causes a significant increase in plasma tHcy in children.

METHODS: Twenty-seven children (aged 10–18 years) undergoing elective major spine surgery were enrolled, and serial plasma samples from 0 to 96 hours after induction were obtained. The anesthetic regimen, including the use of nitrous oxide, was at the discretion of the anesthesiologist. Plasma tHcy was measured using standard enzymatic assays.

RESULTS: The median baseline plasma tHcy concentration was 5.1 $\mu\text{mol/L}$ (3.9–8.0 $\mu\text{mol/L}$, interquartile range) and increased in all patients exposed to nitrous oxide ($n = 26$) by an average of +9.4 $\mu\text{mol/L}$ (geometric mean; 95% confidence interval, 7.1–12.5 $\mu\text{mol/L}$) or +228% (mean; 95% confidence interval, 178%–279%). Plasma tHcy peaked between 6 and 8 hours after induction of anesthesia. One patient who did not receive nitrous oxide had no increase in plasma tHcy. Several patients experienced a severalfold increase in plasma tHcy (maximum +567%). The increase in plasma tHcy was strongly correlated with the duration and average concentration of nitrous oxide anesthesia ($r = 0.80$; $P < 0.001$).

CONCLUSIONS: Pediatric patients undergoing nitrous oxide anesthesia develop significantly increased plasma tHcy concentrations. The magnitude of this effect seems to be greater compared with adults; however, the clinical relevance is unknown.

一项随机对照研究：连续股神经阻滞与腰后丛阻滞用于髋关节成形术后镇痛的比较

Continuous Femoral Versus Posterior Lumbar Plexus Nerve Blocks for Analgesia After Hip Arthroplasty: A Randomized, Controlled Study

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背景：髋关节成形术通常需要术后有效的镇痛，经常由椎管内或腰后丛局麻药输注提供。然而，现在美国区域麻醉学会指南推荐在髋关节成形术后经常给予的各种抗凝药围术期给药期间，取消椎管内或腰后丛阻滞。连续股神经阻滞是一种可能的镇痛选择，而这种方式是否能在髋关节成形术后提供与连续腰后丛阻滞同等的镇痛效果仍不明确。因此，我们验证了髋关节成形术后改变导管置入位置（股神经或腰后丛）对于术后镇痛没有影响的假说。

方法：行髋关节成形术的患者术前随机分组，接受股神经或者是腰后丛刺激导管，导管深度分别是通过针尖 5-15cm 或 0-1cm。术后，病人神经周围注射 0.2% 罗哌卡因至少 2 天（背景剂量为 6mL/hr，每次推注为 4mL，锁定时间 30min）。主要研究指标为平均每天的疼痛评分，用数字等级评分量表（0-10）测定，从手术后早晨 07:30 开始记录，记录 24 小时，排除每天两次的物理治疗时间。次要研究指标是包括在物理治疗期间的疼痛评分、走动距离、在同样的 24 小时内镇痛药的追加量以及在住院期间对镇痛的满意度。

结果：接受股神经输注阻滞的患者（n=25）与接受腰后丛输注阻滞的患者（n=22）的疼痛评分平均值（SD）分别为 3.6（1.8）和 3.5（1.8），组间差异为 0.1（95% 可信区间为 -0.9 至 1.2， $P=0.78$ ）。因为可信区间在 -1.6 至 1.6 的范围之内，我们推论两种镇痛方法的效应是相等的。类似地，我们发现次要研究指标在两种处理方式之间无差异，但有一个例外：股神经置管的患者手术后早晨步行距离的平均值（第 10-第 90 百分位数）为 2（0-17）m，而腰后丛神经置管的患者为 11（0-31）m（非参数数据， $P=0.02$ ）。

结论：在髋关节成形术后，应用刺激性神经周围导管行连续股神经阻滞是一种可以接受的替代连续腰后丛神经阻滞的镇痛方式。然而，股神经输注时早期的下床活动能力受影响。

（黄丽娜 译 李士通 马皓琳 校）

BACKGROUND: Hip arthroplasty frequently requires potent postoperative analgesia, often provided with an epidural or posterior lumbar plexus local anesthetic infusion. However, American Society of Regional Anesthesia guidelines now recommend against epidural and continuous posterior lumbar plexus blocks during administration of various perioperative anticoagulants often administered after hip arthroplasty. A continuous femoral nerve block is a possible analgesic alternative, but whether it provides comparable analgesia to a continuous posterior lumbar plexus block after hip arthroplasty remains unclear. We therefore tested the hypothesis that differing the catheter insertion site (femoral versus posterior lumbar plexus) after hip arthroplasty has no impact on postoperative analgesia.

METHODS: Preoperatively, subjects undergoing hip arthroplasty were randomly assigned to receive either a femoral or a posterior lumbar plexus stimulating catheter inserted 5 to 15 cm or 0 to 1 cm past the needle tip, respectively. Postoperatively, patients received perineural ropivacaine, 0.2% (basal 6 mL/hr, bolus 4 mL, 30-minute lockout) for at least 2 days. The primary end point was the average daily pain scores as measured with a numeric rating scale (0–10) recorded in the 24-hour period beginning at 07:30 the morning after surgery, excluding twice-daily physical therapy sessions. Secondary end points included pain during physical therapy, ambulatory distance, and supplemental

analgesic requirements during the same 24-hour period, as well as satisfaction with analgesia during hospitalization.

RESULTS: The mean (SD) pain scores for subjects receiving a femoral infusion ($n = 25$) were 3.6 (1.8) versus 3.5 (1.8) for patients receiving a posterior lumbar plexus infusion ($n = 22$), resulting in a group difference of 0.1 (95% confidence interval -0.9 to 1.2 ; $P = 0.78$). Because the confidence interval was within a prespecified -1.6 to 1.6 range, we conclude that the effect of the 2 analgesic techniques on postoperative pain was equivalent. Similarly, we detected no differences between the 2 treatments with respect to the secondary end points, with one exception: subjects with a femoral catheter ambulated a median (10th–90th percentiles) 2 (0–17) m the morning after surgery, in comparison with 11 (0–31) m for subjects with a posterior lumbar plexus catheter (data nonparametric; $P = 0.02$).

CONCLUSIONS: After hip arthroplasty, a continuous femoral nerve block is an acceptable analgesic alternative to a continuous posterior lumbar plexus block when using a stimulating perineural catheter. However, early ambulatory ability suffers with a femoral infusion.

鞘内注射 Kappa-2 阿片受体激动剂 GR89696 和白介素-10 以协同的相互作用方式减轻骨癌痛

The Intrathecally Administered Kappa-2 Opioid Agonist GR89696 and Interleukin-10 Attenuate Bone Cancer–Induced Pain Through Synergistic Interaction

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背景：虽然骨癌痛是晚期癌症患者中最具破坏性的症状之一，但是患者用药物治疗常常无效；因此，需要更加有效的治疗措施用于骨癌痛。我们在骨癌痛大鼠模型中评估鞘内注射 GR89696（一种 κ_2 阿片受体激动剂）和白介素（IL）-10 的镇痛效能及其相互作用。

方法：采用右侧胫骨髓内注射大鼠乳腺癌细胞法建立大鼠骨癌痛模型，同时行鞘内置管。模型建立后第十天，鞘内注射 GR89696 和 IL-10 后，用以上-下法测定大鼠对 von Frey 纤维丝引起的机械性刺激的缩足阈值。以等辐射分析法评估这 2 种药物间的相互作用。

结果：鞘内注射 GR89696 和 IL-10 以剂量依赖性方式，明显增加癌细胞植入大鼠的缩足阈值，其 50% 有效剂量值（95% 可信区间）分别为 $50.78 \mu\text{g}$ (31.80 – $80.07 \mu\text{g}$) 和 $0.83 \mu\text{g}$ (0.59 – $1.15 \mu\text{g}$)。等辐射分析法显示 GR89696 和 IL-10 之间存在协同作用。

结论：鞘内注射 GR89696 和 IL-10 减轻骨癌痛，这 2 种药物在脊髓中存在协同作用。这些结果提示 κ_2 阿片受体激动剂和 IL-10 非常可能成为治疗骨癌相关疼痛的一种新方法。

(江继宏 译 马皓琳 李士通 校)

BACKGROUND: Although bone cancer-related pain is one of the most disruptive symptoms in patients with advanced cancer, patients are often refractory to pharmacological treatments; thus, more effective treatments for bone cancer pain are needed. We evaluated the analgesic efficacy of and interaction between intrathecal GR89696, a κ_2 -opioid receptor agonist, and interleukin (IL)-10 in a rat model of bone cancer pain.

METHODS: The rat model of bone cancer pain was produced by right tibia intramedullary injection of rat breast cancer cells, and an intrathecal catheterization was performed. Ten days later, a paw-withdrawal threshold to mechanical stimulus by von Frey hairs was measured using the up-down method, after intrathecal administration of GR89696 and IL-10. The interaction between the 2 drugs was also evaluated using an isobolographic analysis.

RESULTS: Intrathecal GR89696 and IL-10 significantly increased the paw withdrawal threshold of the cancer cell-implanted rat, in a dose-dependent manner, with 50% effective dose values (95% confidence interval) of 50.78 μg (31.80–80.07 μg) and 0.83 μg (0.59–1.15 μg), respectively. Isobolographic analysis revealed a synergistic interaction between intrathecal GR89696 and IL-10.

CONCLUSIONS: Intrathecally administered GR89696 and IL-10 attenuated bone cancer-induced pain, and the 2 drugs interacted synergistically in the spinal cord. These results raise the intriguing possibility of κ_2 -opioid receptor agonists and IL-10 as a new therapeutic approach for the management of bone cancer-associated pain.

在超声引导下的斜角肌间沟臂丛神经阻滞中 0.75%罗哌卡因的最小有效麻醉容量 The Minimum Effective Anesthetic Volume of 0.75% Ropivacaine in Ultrasound-Guided Interscalene Brachial Plexus Block

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背景: 应用超声监测进针部位和局麻药的扩散,可减少麻醉周围神经阻滞所需的局麻药容量。本研究旨在研究用斜角肌间沟臂丛神经阻滞完成的手术麻醉所需的最小容量。

方法: 入选 ASA 分级 I-III 级的患者 20 名,年龄 18 到 75 岁,择期在斜角肌间沟臂丛神经阻滞下行肩部手术。用以前已验证的递增/递减法,我们根据先前的阻滞结果决定相邻患者 0.75% 罗哌卡因的注射容量。起始容量为 15mL (分 3 次注射,每个神经干各 5mL);如果阻滞失败,则容量增加 1mL;如果阻滞成功,剂量减少 1mL。当达到次要终止规则时,即连续 10 次以 5ml 的 0.75% 罗哌卡因阻滞成功,则试验终止。臂丛神经阻滞达到的成功的手术麻醉定义为出现足够的运动阻滞

(运动评分 ≤ 2 ，总计 0 到 4 分)，注射 30 分钟内温觉及针刺觉消失，且完成手术无须全麻。由通过询问患者以记录痛觉首次出现的时间评估感觉阻滞的持续时间。

结果：在我们的研究条件下，用 0.75% 罗哌卡因 5mL 或臂丛的三个神经干（上、中、下）各约 1.7mL 均可成功完成肩关节镜手术的麻醉。研究在连续 10 次以 5mL 局麻药成功阻滞终止（100%，95% 可信区间 [CI] 74.1%–100%）。整组的感觉阻滞起效时间中位数（范围）为 5（5–20）分钟，二头肌时间中位数（范围）为 7.5（5–15）分钟，外展运动阻滞的起效时间中位数（范围）为 10（5–15）分钟。阻滞持续时间中位数（范围）为 9.9（5–19）小时，平均（标准差）阻滞实施时间为 8.0 ± 3.2 分钟。平均镇痛持续时间为 9.9 ± 3.7 小时。镇痛持续时间与局麻药的容量无关（ $r = 0.05$, $P = 0.83$ ）。

结论：本研究中所有患者均成功以 5mL 局麻药实施了手术阻滞。然而，可信区间的下限（据一例失败假设计算而得）包含 25% 失败率的可能性；故使用类似的用于剂量大于 5mL 的终止规则的研究，也是正当的。

（陈彬彬译 马皓琳 李士通校）

BACKGROUND: The use of ultrasound to monitor needle placement and spread of local anesthetics (LA) has allowed reductions in the volume of LA required to anesthetize peripheral nerves. In the current study we investigated the minimal volume necessary to accomplish surgical anesthesia with interscalene brachial plexus block.

METHODS: Twenty ASA physical status I–III patients, ages 18 to 75 years and scheduled for shoulder surgery under interscalene brachial plexus block, were enrolled. Using a previously validated step-up/step-down method, we determined the injection volume of 0.75% ropivacaine used for consecutive patients by the outcome of the preceding block. The starting volume was 15 mL (3 injections of 5 mL per each trunk); in the case of block failure, the volume was increased by 1 mL, whereas after successful block, the volume was reduced by 1 mL. The study was stopped upon achieving the secondary stopping rule of 10 consecutive successful interscalene blocks using 5 mL of ropivacaine 0.75%. Successful surgical anesthesia with the brachial plexus block was defined as presence of adequate motor block (motor score of ≤ 2 on 0 to 4 scale), absent sensation to cold and pinprick sensation within 30 minutes of injection, and absence of the need for general anesthesia for completion of surgery. Duration of sensory blockade was assessed by asking the patient to record the time of first pain sensation.

RESULTS: Under our study conditions, successful surgical anesthesia for arthroscopic shoulder surgery can be achieved with 5 mL of 0.75% ropivacaine, or approximately 1.7 mL per each of the 3 trunks of the brachial plexus (superior, middle, and inferior). The study was stopped after 10 consecutive successful blocks with 5 mL of LA (100%, 95% confidence interval [CI]: 74.1%–100%). For the group as a whole, the median (range) sensory block onset time was 5 (5–20) minutes, the median (range) motor block for the biceps was 7.5 (5–15) minutes, and for abduction 10 (5–15) minutes. The median (range) block duration was 9.9 (5–19) hours, and the mean (SD) block performance time was 8.0 ± 3.2 minutes. Mean duration of analgesia was 9.9 ± 3.7 hours. Duration of analgesia was not associated with volume of LA ($r = 0.05$, $P = 0.83$).

CONCLUSIONS: All patients in our study had successful surgical blocks with 5 mL of LA. However, the lower limit of the CI (calculated on the assumption of a single failure) does include the possibility of a 25% failure rate; thus studies using similar stopping rules for doses higher than 5 mL are nonetheless warranted.

