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*Anesthesia & Analgesia. 121(4):1089-1096, October 2015.*
Assessing the Methodology for Calculating Platelet Contribution to Clot Strength (Platelet Component) in Thromboelastometry and Thrombelastography.

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Anesthesia & Analgesia 2015 121 868–878

The viscoelastic properties of blood clot have been studied most commonly using thrombelastography (TEG®) and thromboelastometry (ROTEM®). ROTEM®-based bleeding treatment algorithms recommend administering platelets to patients with low EXTEM clot strength (e.g., clot amplitude at 10 minutes [A10] < 40 mm) once clot strength of the ROTEM® fibrin-based test (FIBTEM) is corrected. Algorithms based on TEG® typically use a low value of maximum amplitude (e.g., <50 mm) as a trigger for administering platelets. However, this parameter reflects the contributions of various blood components to the clot, including platelets and fibrin/fibrinogen. The platelet component of clot strength may provide a more sensitive indication of platelet deficiency than clot amplitude from a whole blood TEG® or ROTEM® assay. The platelet component of the formed clot is derived from the results of TEG®/ROTEM® tests performed with and without platelet inhibition. In this article, we review the basis for why this calculation should be based on clot elasticity (e.g., the E parameter with TEG® and the CE parameter with ROTEM®) as opposed to clot amplitude (e.g., the A parameter with TEG® or ROTEM®). This is because clot elasticity, unlike clot amplitude, reflects the force with which the blood clot resists rotation within the device, and the relationship between clot amplitude (variable X) and clot elasticity (variable Y) is nonlinear. A specific increment of X (ΔX) will be associated with different increments of Y (ΔY), depending on the initial value of X. When calculated correctly, using clot elasticity data, the platelet component of the clot can provide a valuable insight into platelet deficiency in emergency bleeding.

A Recirculatory Model for Pharmacokinetics and the Effects on Bispectral Index After Intravenous Infusion of the Sedative and Anesthetic AZD3043 in Healthy Volunteers

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Anesthesia & Analgesia 2015 121 904–913
背景：AZD3043 是一种 γ-氨基丁酸 A 型受体阳性变构调节剂，具有镇静和麻醉作用。我们描述一个在健康志愿者中动脉 AZD3043 的浓度和药效学效应对脑电双频指数（BIS）的作用的群体药代动力学 (PK) 模型。

方法：在 2 个临床研究 125 名健康志愿者中测量动脉和静脉 AZD3043 血浆浓度和 BIS 值，AZD3043 给予一个 1 分钟的单次剂量 (1-6 毫克/公斤)，一个 30 分钟的输注 (1-81 毫克/公斤/小时)，或 0.8 + 10，1 + 15，3 + 30，4 + 40（毫克/千克单次剂量 + 毫克/公斤/小时 30 分钟输注）。群体药代动力学 /药效学分析，使用 NONMEM。

结果：一个循环模型，包括一系列的 5 个室用于静脉和动脉血浆药物之间的运输，2 个周围分布室，和 1 个为从动脉到静脉血浆药物的非分配运输室，描述了 AZD3043 的药代动力学。全身清除率高 (2.2 升/分钟；95%置信区间，2.12-2.25)，表观分布容积低，导致一个短的消除半衰期。动脉和外周室分布的表观体积随剂量的增加而增加，总的表观体积为最低剂量后的 15 升和最大剂量后的 37 升。乙状结肠最大效应 (Emax)，15.6 克/毫升的 EC50 和 1.7 的 γ 描述了 AZD3043 效应部位浓度 EC50 和 BIS 之间的关系模型。个体间变异的 EC50 为 37%。效应室模型半衰期平衡速率常数 ke0 为 1.1 分钟，描述了有关的动脉血浆浓度效果的延迟。

结论：AZD3043 具有较高的清除和较低的分布容积，导致半衰期减短。而表观体积分布呈剂量依赖性 (P<0.001)，导致半衰期与剂量的增加。效应位置的分布快速且同步于短血浆半衰期导致的快速起效和失效作用。

（黄凫卿 译，李士通 审校）

BACKGROUND: AZD3043 is a positive allosteric modulator of the gamma-aminobutyric acid type A receptor, with sedative and anesthetic properties. We describe a population pharmacokinetic (PK) model of arterial and venous concentrations of AZD3043 and the pharmacodynamic effects on bispectral index (BIS) in healthy volunteers.

METHODS: Arterial and venous plasma concentrations of AZD3043 and BIS were measured in 2 clinical studies in 125 healthy volunteers, where AZD3043 was given as a 1-minute bolus (1-6 mg/kg), a 30-minute infusion (1-81 mg/kg/h), or 0.8 + 10, 1 + 15, 3 + 30, and 4 + 40 (mg/kg bolus + mg/kg/h infusion for 30 minutes). Population PK/pharmacodynamic analysis was performed with NONMEM.

RESULTS: A recirculatory model, comprising a series of 5 compartments for the transit of drug between venous and arterial plasma, 2 peripheral distribution compartments, and 1 compartment for the nondistributive transit of drug from arterial to venous plasma, described the PK of AZD3043. Systemic clearance was high (2.2 L/min; 95% confidence interval, 2.12-2.25), and apparent volumes of distribution were low, leading to a short elimination half-life. The apparent volumes of distribution of the arterial and peripheral compartments increased with increasing administered dose, giving a total apparent volume of distribution of 15 L after the lowest dose and 37 L after the greatest dose. A sigmoid maximum effect (Emax) model with an EC50 of 15.6 g/mL and a gamma of 1.7 described the relationship between AZD3043 effect-site concentrations and BIS. The between-subject variability in EC50 was 37%. An effect compartment model, with a half-life of the equilibration rate constant ke0 of 1.1 min, described the delay in effect in relation to the arterial plasma concentrations.

CONCLUSIONS: AZD3043 had a high clearance and a low apparent volume of distribution, leading to a short half-life. However, the apparent volume of distribution was dose dependent (P < 0.001), leading to an increased half-life with increasing dose. The distribution to the effect site was fast and together with the short plasma half-life led to a fast onset and offset of effects.

对比术中胸骨上及食管多普勒，上腹部大手术改变心脏生物电抗输出读数，NICOM
Major Upper Abdominal Surgery Alters the Calibration of Bioreactance Cardiac Output Readings, the NICOM, When Comparisons Are Made Against Suprasternal and Esophageal Doppler Intraoperatively

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Anesthesia & Analgesia 2015 121 936–945

BACKGROUND: Minimally invasive continuous cardiac output measurements are recommended for use during anesthesia to guide fluid therapy, but such measurements must trend changes reliably. The NICOM Cheetah, a BioReactance monitor, is being recommended for intraoperative use. To validate its use, Doppler methods, suprasternal USCOM and esophageal CardioQ, were used in tandem to provide reliable estimates of changing trends in cardiac output. Preliminary comparisons showed that upper abdominal surgical interventions caused shifts in the calibration of the NICOM. The purpose of this study was to confirm and measure these calibration shifts.

METHODS: Major surgery patients, aged 58 (32–78) years, 12 males and 15 females, were divided into 4 study groups: (a) controls—lower abdominal or peripheral surgery (n = 9); (b) laparoscopy with abdominal insufflation (n = 6); (c) open upper abdominal surgery with large multiblade retractor placement (n = 6) and (d) head-down robotic surgery (n = 6). Simultaneous NICOM and Doppler readings were taken every 15 to 30 minutes. Within-individual time plots were drawn, and regression analysis between NICOM-USCOM and CardioQ-USCOM readings was performed. Bland-Altman and trend (concordance) analyses were also performed.

RESULTS: Three hundred ninety NICOM comparisons were collected. Duration of surgeries was 4 (1 to 11) hours, with 7 to 22 sets of readings per case. Mean (SD) cardiac index from
USCOM readings was 3.5(1.0) L/min/m. Individual time plots showed shifts in NICOM calibration relative to Doppler (USCOM) in cardiac index of ±0.9 (0.6-1.4) L/min/m during the surgical interventions. In 13 of 18 patients (72%), the shift was downward, but upward shifts did occur. Within-individual correlations between CardioQ-USCOM showed good trending R = 0.87 (range, 0.60-0.97). In the control group, NICOM-USCOM also showed good trending R = 0.89 (0.69-0.97). However, trending was poor in the intervention groups, R = 0.43 (0.03-0.71; P < 0.0001). The Bland-Altman percentage error between NICOM-USCOM (57 [54-60%]) was greater than that between CardioQ-USCOM (42 [40-44%]) (P < 0.0001). Concordance rates were 82 (77-88)% from 101 data pairs and 95 (90-99)% from 72 data pairs, respectively.

CONCLUSIONS: Doppler monitoring used in tandem provided valid trend lines of cardiac output changes against which NICOM readings could be compared. Intraoperatively, the NICOM was shown to track changes in cardiac output reliably in most circumstances. However, surgical interventions to the upper abdomen caused shifts in readings by >1 L/min/m, and the direction of the shifts was unpredictable. Anesthesiologists need to be aware of these calibration shifts and anticipate their occurrence, whenever the NICOM is used intraoperatively.

A Multimodal Intervention Improves Postanesthesia Care Unit Handovers

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Anesthesia & Analgesia 2015 121 957–971

BACKGROUND: Failures of communication are a major contributor to perioperative adverse events. Transitions of care may be particularly vulnerable. We sought to improve postoperative handovers.

一种改善麻醉后复苏室交接的多模式干预

A Multimodal Intervention Improves Postanesthesia Care Unit Handovers

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Anesthesia & Analgesia 2015 121 957–971

背景：沟通失败是围术期不良事件的一个主要因素。护理的转变可能特别容易。我们试图改善术后交接。

方法：我们介绍了一种成人及小儿麻醉后复苏室多模式干预以改善麻醉实施者（AP）与麻醉后复苏室注册护士（RN）间的术后交接。干预措施由一个标准化电子交接报表、教学性的网络研讨会、以集中提高跨专业交流的强制模拟训练及培训后绩效反馈组成。利用盲法，培训后的护士采用由8个分量表和一个整体的评分（1-5级）组成的结构式工具对麻醉后复苏室交接进行评分。多因素 logistic 回归分析对交接时整体评分等级≥3所占的比例来评价干预效果。

结果：观察和评估了受过模拟培训的452名临床医生及981次交接。在成人PACU，估算AP与RN之间可接受的交接（整体评分≥3）的比例。AP-RN均未接受模拟训练，该比例在40天为3%（95%的可信区间1%-11%），训练开始后40天为10%（5%-19%），训练一年后（405天）为57%（33%-78%）；而在AP-PN其中至少有一个接受模拟训练者，该比例在40天及405天分别为18%（11%-28%）及68%（57%-76%）。在未经训练的AP-PN组与训练有素的AP-PN组，可接受的交接百分比在405天时均显著高于40天（P<0.001）。在儿童PACU观察到类似的情况。培训三年后，据不精确估计可接受的交接比例在成人PACU及儿童PACU分别约为87%（72%-95%）及56%（40%-72%）。

结论：这一多模式干预显著改善了包括未接受正规模拟训练的临床医生PACU的跨专业交接，3年后显效。

（徐卉红 译，李士通 审校）

BACKGROUND: Failures of communication are a major contributor to perioperative adverse events. Transitions of care may be particularly vulnerable. We sought to improve postoperative handovers.
METHODS: We introduced a multimodal intervention in an adult and a pediatric postanesthesia care unit (PACU) to improve postoperative handovers between anesthesia providers (APs) and PACU registered nurses (RNs). The intervention included a standardized electronic handover report form, a didactic webinar, mandatory simulation training focused on improving interprofessional communication, and post-training performance feedback. Trained, blinded nurse observers scored PACU handovers during 17 months using a structured tool consisting of 8 subscales and a global score (1–5 scale). Multivariate logistic regression assessed the effect of the intervention on the proportion of observed handovers receiving a global effectiveness rating of ≥3.

RESULTS: Four hundred fifty-two clinicians received the simulation-based training, and 981 handovers were observed and rated. In the adult PACU, the estimated percentages of acceptable handovers (global ratings ≥3) among AP-RN pairs, where neither received simulation-based training (untrained dyads), was 3% (95% confidence interval, 1%–11%) at day 0, 10% (5%–19%) at training initiation (day 40), and 57% (33%–78%) at 1-year post-training initiation (day 405). For AP-RN pairs where at least one received the simulation-based training (trained dyads), these percentages were estimated to be 18% (11%–28%) and 68% (57%–76%) on days 40 and 405, respectively. The percentage of acceptable handovers was significantly greater on day 405 than it was on day 40 for both untrained (P < 0.001) and trained dyads (P < 0.001). Similar patterns were observed in the pediatric PACU. Three years later, the unadjusted estimate of the probability of an acceptable handover was 87% (72%–95%) in the adult PACU and 56% (40%–72%) in the pediatric PACU.

CONCLUSIONS: A multimodal intervention substantially improved interprofessional PACU handovers, including those by clinicians who had not undergone formal simulation training. An effect appeared to be present >3 years later.

Several Ryanodine Receptor Type 1 Gene Mutations of p.Arg2508 Are Potential Sources of Malignant Hyperthermia

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RESULTS: Cells transfected with each of the 4 mutants, p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, or p.Arg2508Lys, were more sensitive to caffeine and 4CmC than cells transfected with the wild type (all 4 P ≤ 0.0004). Mean ± SD of EC50 values for caffeine of wild type, p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, and p.Arg2508Lys were 2.53 ± 0.89, 1.72 ± 0.72, 1.73 ± 0.79, 1.69 ± 0.80, and 1.61 ± 0.74 mM, respectively, and those for 4CmC were 125.92 ± 38.11, 70.42 ± 27.09, 79.30 ± 39.04, 73.03 ± 19.20, and 72.81 ± 28.44 mM.

CONCLUSIONS: Any of these 4 mutations in RYR1 may cause important changes related to MH. Studying the effects of changes in amino acids at 2508 in RYR1 on the movement of this large protein may lead to a better understanding of the pathology of MH events.
BACKGROUND: Patients with chronic pain often suffer from affective disorders and cognitive decline, which significantly impairs their quality of life. In addition, many of these patients also experience stress unrelated to their illness, which can aggravate their symptoms. These nociceptive inputs are received by the hippocampus, in which maladaptive neuroplastic changes may occur in the conditions of chronic pain. The hippocampus is a structure involved in emotionality, learning, and memory, and the proliferating cells in the granular layer of the hippocampal dentate gyrus respond to chronic pain by slowing their turnover. However, whether the maturation, survival, and integration of newborn cells in the hippocampus are affected by chronic pain remains unclear. In addition, it is unknown whether an added stress may increase this effect.

METHODS: We have evaluated the proliferation, differentiation, and survival of newborn hippocampal cells in a rat model of neuropathic pain (chronic constriction injury), with or without stress (chronic immobilization), by assessing the incorporation of bromodeoxyuridine into proliferating cells and immunostaining.

RESULTS: The data obtained indicated that there was a decrease in the number of proliferating cells 8 days after nerve injury in animals subjected to neuropathic pain, an effect that was exacerbated by stress. Moreover, 4 weeks after nerve injury, neuropathic pain was associated with a loss of neuroblasts and the reduced survival of new mature neurons in the hippocampal granular layer, phenomena that also were increased by stress. By contrast, the rate of differentiation was not affected in this paradigm.

CONCLUSIONS: Neuropathic pain negatively influences hippocampal neurogenesis (proliferation and survival), and this effect is exacerbated by stress. These neuroplastic changes may account for the affective and cognitive impairment seen in patients with chronic pain.
背景：低镁血症与术后房颤（POAF）发生率增加相关。尽管已有研究提示镁剂治疗的有益效果，但是这些研究均受限于过小的样本量和过低的镁剂剂量。本研究假设大剂量镁剂能减少新发POAF的发生率，选取了一项评估镁剂对心脏手术患者的认知转归影响的前瞻性数据来验证此假设。

方法：总数389名接受心脏手术的患者被纳入了这项双盲、安慰剂对照的实验。研究对象随机接受了50mg/kg镁剂作为负荷剂量，麻醉诱导后即刻给予总量为50mg/kg，持续输注3小时的镁剂（总量100mg/kg），而对照组则给予生理盐水。采用logistic回归法评估镁剂对POAF的治疗效果，并用多中心研究的心脏手术术后房颤的围术期缺血风险指数来校正房颤(AF)风险。

结果：排除术前发生急慢性房颤的病人后，共363名对象纳入分析（安慰剂组n=177，镁剂治疗组n=186）。镁剂治疗组的POAF新发率为42.5%（95%CI，35%–50%），安慰剂组为37.9%（95%CI，31%–45%），两组无统计学差异（P=0.40）。4.6%的绝对风险差异的95%CI为−5.5%到14.7%。两组POAF起始时间也是相同的，在校正AF风险后，用logistic回归法分析镁剂治疗未见显著效果。

结论：术中大剂量镁剂疗法未能降低心脏手术术后新发POAF的概率。

（宣伟 译 陈杰 校）

BACKGROUND: Hypomagnesemia has been associated with an increased risk of postoperative atrial fibrillation (POAF). Although previous studies have suggested a beneficial effect of magnesium (Mg) therapy, almost all of these are limited by small sample size and relatively low Mg dose. We hypothesized that high-dose Mg decreases the occurrence of new-onset POAF, and we tested this hypothesis by using data from a prospective trial that assessed the effect of Mg on cognitive outcomes in patients undergoing cardiac surgery.

METHODS: A total of 389 patients undergoing cardiac surgery were enrolled in this double-blind, placebo-controlled trial. Subjects were randomized to receive Mg as a 50-mg/kg bolus immediately after induction of anesthesia followed by another 50 mg/kg as an infusion given over 3 hours (total dose, 100 mg/kg) or placebo. We tested the effect of Mg therapy on POAF with logistic regression, adjusting for the risk of atrial fibrillation (AF) by using the Multicenter Study of Perioperative Ischemia risk index for Atrial Fibrillation after Cardiac Surgery.

RESULTS: Among the 363 patients analyzed, after we excluded patients with chronic or acute preoperative AF (placebo: n = 177; Mg: n = 186), the incidence of new-onset POAF was 42.5% (95% confidence interval [CI], 35%–50%) in the Mg group compared with 37.9% (95% CI, 31%–45%) in the placebo group (P = 0.40). The 95% CI for this absolute risk difference of 4.6% is −5.5% to 14.7%. The time to onset of POAF also was identical between the groups, and no significant effect of Mg was found in logistic regression analysis after we adjusted for AF risk (odds ratio, 1.09; 95% CI, 0.69–1.72; P = 0.73).

CONCLUSIONS: High-dose intraoperative Mg therapy did not decrease the incidence of new-onset POAF after cardiac surgery.

对健康志愿者单次静脉注射及静注后持续泵注一种研发中的静脉镇静/麻醉药AZD3043的安全性及药效学研究

A Bolus and Bolus Followed by Infusion Study of AZD3043, an Investigational Intravenous Drug for Sedation and Anesthesia: Safety and Pharmacodynamics in Healthy Male and Female Volunteers

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背景: AZD3043(THRX-918661) 是一个研发中的，可被血液和肝脏中的酯酶快速代谢的苯丙烷类镇静/麻醉药。在其首次人体研究中，使用 AZD3043 持续静脉输注 30 min 行麻醉诱导并无重大安全性或耐受性问题，且具有快速复苏的特点。

方法: 这个临床 1 期、单中心、开放性研究（临床试验，编号 NCT00984880）的主要目标是评估单次静脉推注及单次静注后持续泵注 AZD3043 的安全性和耐受性。次要目标包括评估 AZD3043 的药效学特征和疗效。递增剂量队列研究中 8 名 18 岁到 65 岁的健康志愿者分别接受单次 1 min 静脉推注（A 队）或 1 min 静注后持续泵注 30 min（B 队）该药。评估项目包括不良反应、生命体征、血气、实验室检查、镇静/麻醉的临床体征及脑电双频指数。

结果: 72 名志愿者（8 名女性，64 名男性）接受 1 min 静注 1、1.5、2、4、6 mg/kg（A 队）或 0.8、1、3、4 mg/kg 静注后分别泵注 10、15、30、40 mg/kg/h 的 AZD3043 持续 30 min（B 队）。本研究中没有患者脱落。发生超过 1 例的不良反应包括头痛（n = 15；21%）、恶心（n = 7；10%）、呕吐（n = 3；4%）和倦怠（n = 2；3%）。21 名受试者出现至少 1 种不良反应。暂无证据表明药物与不良反应间存在量效关系。呼吸不受影响，但心率按增加剂量相关性。没有注射痛报告。麻醉对象为 32 名受试者，包括 A 队中的最高剂量组和 B 队中 2 个高剂量组的所有对象。麻醉复苏较快，定位和本体感受迅速恢复。除 A 队的 2 mg/kg 组和 B 队的 4 mg/kg 静注 + 40 mg/kg/h 泵注 30 min 组各 1 名受试者外，其他受试者在用药结束 30 min 后的首次评估中均能在没有任何支撑下行走 10 米，另 2 名受试者停药 45 min 后的再次评估中通过行走测试。在高剂量组中可观察到无意识体动伴随肌肉张力增加。

结论: 需要进一步的临床研究来证实 AZD3043 提供快速麻醉复苏并维持正常通气的能力。
dosing. Involuntary movements were observed at higher doses, accompanied by increased muscle tone.

CONCLUSIONS: AZD3043 provided rapid recovery from anesthesia with maintained ventilation. Further studies are warranted in a clinical setting.

快速代谢和超短效氯胺酮类似物的发展

Development of Rapidly Metabolized and Ultra-Short-Acting Ketamine Analogs

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背景：氯胺酮是一种经典的，起效迅速的分离性麻醉药。由于可能出现精神病样症状，临床应用受限，且此药往往需与催眠药物合用。本研究假设，具有超短效消除时间的氯胺酮酯类似物可能显著地降低突发的烦躁现象，即增加一个氯胺酮样的催眠和镇痛效用。本研究寻求对5酯((1-(2-氯苯基)-2-氧代环己基)氨基)戊酸甲酯盐酸盐，即第一个设计目的为快速代谢的氯胺酮类似物，进行药理学研究。

方法：比较5种去甲氯胺酮酯类似物(R1-R5)削弱大鼠翻正反射和产生痛觉钝化的能力。在大鼠中对2种类似物(R1,R5)进行毒性测试并评估50%致命剂量(LD50)。通过高效液相色谱法对兔血浆和全血进行体外代谢稳定性测试。观察兔子的行为和血流动力学影响。最后估计这些类似物在兔子中的药代动力学特征。

结果：在研究的模型中，所有的5种去甲氯胺酮酯都能迅速地使翻正反射消失和踏板撤出减弱，且药物效应能超快速地消除(R1与氯胺酮在大鼠翻正反射恢复时间方面的比较：87秒 [四分位距(IQR) 78-131] vs 996秒 [IQR 840-1304]; P <0.01)。它们与氯胺酮在LD50方面具有可比性(R1 LD50: 50.2mg/kg [95%置信区间，30-63])。所有类似物在水解唯一羧酸衍生物方面从快至慢，依次为体内(R1清除率: L/kg/min [IQR 0.40-2.42])，全血和血浆。相对于其镇静作用，类似物R5表现出更强大的痛觉钝化效应(踏板撤回评分，与R1相比，P <0.001)。

结论：5种去甲氯胺酮酯类似物保留母体药物的催眠特性，并由于超速代谢而消除更快。

（冯迪 译 陈杰 校）

BACKGROUND: Ketamine is a well-established, rapidly acting dissociative anesthetic. Clinical use is limited by prolonged psychotomimetic phenomena on emergence, often requiring the coadministration of additional hypnotic drugs. We hypothesized that the development of ketamine ester analogs with ultrashort offset times might markedly reduce the dysphoric emergence phenomena and, hence, increase the utility of a ketamine-like hypnotic and analgesic.

Here, we describe the results of studies that seek to define the pharmacology of 5 esters of ((1-(2-chlorophenyl)-2-oxocyclohexyl)amino)pentanoate hydrochloride, the first ketamine analogs designed to be susceptible to ultrarapid metabolism.

METHODS: Five norketamine ester analogs (R1–R5) were compared by ability to produce loss of righting and nociceptive blunting in rats. Toxicity testing was performed for 2 analogs (R1, R5) with 50% lethal dose (LD50) estimation in rats. In vitro metabolic stability was tested in rabbit plasma and whole blood by high-performance liquid chromatography. Behavioral and hemodynamic effects were observed in rabbits. We estimated the pharmacokinetics of these analogs in rabbits.

RESULTS: All 5 norketamine esters produced rapid loss of righting reflex and diminished pedal withdrawal with ultrarapid offset in the models studied (return of righting reflex 87 seconds [interquartile range (IQR) 78–131] R1 vs 996 seconds [IQR 840–1304] ketamine in rats; P <
The LD50 was comparable to that of ketamine (LD50 R1 50.2 mg/kg [95% confidence interval, 30–63]). For all analogs, hydrolysis to sole carboxylic acid derivatives was most rapid in vivo (clearance 1.61 L/kg/min R1 [IQR 0.40–2.42]), followed by whole blood and then plasma. Analog R5 demonstrated relatively greater nociceptive blunting than hypnotic effect (P < 0.001; pedal withdrawal score comparison with R1).

CONCLUSIONS: The 5 norketamine ester analogs retain the hypnotic characteristics of the parent compound, yet display rapid offset due to ultrarapid metabolism.

Background: An anesthesia preinduction checklist (APIC) to be performed before anesthesia induction was introduced and evaluated with respect to 5 team-level outcomes, each being a surrogate end point for patient safety: information exchange (the percentage of checklist items exchanged by a team, out of 12 total items); knowledge of critical information (the percentage of critical information items out of 5 total items such as allergies, reported as known by the members of a team); team members’ perceptions of safety (the median scores given by the members of a team on a continuous rating scale); their perception of teamwork (the median scores given by the members of a team on a continuous rating scale); and clinical performance (the percentage of completed items out of 14 required tasks, e.g., suction device checked).

Methods: A prospective interventional study comparing anesthesia teams using the APIC with a control group not using the APIC was performed using a multimethod design. Trained observers rated information exchange and clinical performance during on-site observations of anesthesia teams. Anesthesia Preinduction Checklist to Improve Information Exchange, Knowledge of Critical Information, Perception of Safety, and Possibly Perception of Teamwork in Anesthesia Teams

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anesthesia inductions. After the observations, each team member indicated the critical information items they knew and their perceptions of safety and teamwork.

**RESULTS:** One hundred five teams using the APIC were compared with 100 teams not doing so. The medians of the team-level outcome scores in the APIC group versus the control group were as follows: information exchange: 100% vs 33% (P < 0.001), knowledge of critical information: 100% vs 90% (P < 0.001), perception of safety: 91% vs 84% (P < 0.001), perception of teamwork: 90% vs 86% (P = 0.028), and clinical performance: 93% vs 93% (P = 0.60).

**CONCLUSIONS:** This study provides empirical evidence that the use of a preinduction checklist significantly improves information exchange, knowledge of critical information, and perception of safety in anesthesia teams—all parameters contributing to patient safety. There was a trend indicating improved perception of teamwork.
aggregate serious morbidity rate in women who received general anesthesia secondary to thrombocytopenia was 6.5% (95% confidence interval, 2.1%–14.5%).

CONCLUSIONS: Our work supports the relative maternal safety of neuraxial anesthesia in parturients with mild thrombocytopenia and estimates the maternal complication rate associated with the avoidance of neuraxial anesthesia. Remaining uncertainties at lower platelet counts make a national “low platelet” registry critical to a more accurate assessment of the risk of epidural hematoma and would aid in standardization of anesthesia practice.

Clinical Research Methodology 1: Study Designs and Methodologic Sources of Error
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Clinical research can be categorized by the timing of data collection: retrospective or prospective. Clinical research also can be categorized by study design. In case-control studies, investigators compare previous exposures (including genetic and other personal factors, environmental influences, and medical treatments) among groups distinguished by later disease status (broadly defined to include the development of disease or response to treatment). In cohort studies, investigators compare subsequent incidences of disease among groups distinguished by one or more exposures. Comparative clinical trials are prospective cohort studies that compare treatments assigned to patients by the researchers. Most errors in clinical research findings arise from 5 largely distinguishable classes of methodologic problems: selection bias, confounding, measurement bias, reverse causation, and excessive chance variation.

ContraLateral Hyperalgesia from Injection of Endothelin-1 into the Ipsilateral Paw Requires Efferent Conduction into the Contralateral Paw
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Background: Single-sided injury induces hyperalgesia contralateral to the lesion and is often characterized by central sensitization. Previous studies demonstrated that injection of endothelin-1 (ET-1) into the ipsilateral paw of rats prolonged the mechanical and chemical sensitization of the contralateral paw. The present study investigated the role of efferent conduction on hyperalgesia in the contralateral paw after injection of ET-1 into the ipsilateral paw.

Methods: Rats received a single injection of ET-1 into the ipsilateral paw. The paw withdrawal latency to radiant heat and the paw withdrawal threshold to von Frey hairs were measured. The contralateral paw was treated with a 60-minute topical application of lidocaine. The results were analyzed using two-way ANOVA and post hoc tests.

Results: The mean paw withdrawal latency in the contralateral paw was significantly increased after injection of ET-1 into the ipsilateral paw. The paw withdrawal threshold was also significantly increased in the contralateral paw. The effect was sustained for up to 60 minutes.

Conclusion: Efferent conduction from the ipsilateral paw to the contralateral paw is necessary for the induction of hyperalgesia after ET-1 injection into the ipsilateral paw. This finding provides new insights into the neural mechanisms underlying hyperalgesia.
另一部分在注射 ET-1 前 30min，皮下注射比卡因释放微粒阻滞对侧坐骨神经 6 至 12h。通过在颈部正中线的皮下注射来模拟这些布比卡因制剂的全身作用。

结果:注射 ET-1 后，同侧和对侧后爪的机械阈第 2h 开始下降，24h 降到最低，第 48h 开始恢复直至第 72h 到达注射前的水平。注射 ET-1 前，同侧后爪注射布比卡因可以抑制此超敏反应。对侧后爪注射布比卡因在每个测试时段也都能抑制超敏反应；除了在超敏反应期间第 2h，同侧后爪注射布比卡因组敏感度增加，其余情况类似。当布比卡因释放微粒阻滞对侧坐骨神经时，这种类似变化的模式也会出现。布比卡因制剂的全身作用要相对微弱得多且只有在 ET-1 注射后 24h 才有显著性差异。同侧和对侧后爪在注射 ET-1 后都出现了热超敏，表明对两种对侧麻醉操作的反应模式是相同的。

结论:这些结果表明通过后爪对侧神经支配的传出神经传导对于对侧 ET-1 的敏感性是必要的，提出远端神经末梢释放的物质也涉及其中。释放到外周的物质对对侧 ET-1 的敏感性非常重要，这可能也与手术或神经损伤后，在离原发损伤较远位点的继发性痛觉过敏有关。

（李悦 译 陈杰 校）

BACKGROUND: Contralateral hyperalgesia, occurring after unilateral injury, is usually explained by central sensitization in spinal cord and brain. We previously reported that injection of endothelin-1 (ET-1) into one rat hindpaw induces prolonged mechanical and chemical sensitization of the contralateral hindpaw. Here, we examined the role of contralateral efferent activity in this process.

METHODS: ET-1 (2 nmol, 10 μL) was injected subcutaneously into the plantar surface of right (ipsilateral) hindpaw (ILP), and the thermal response latency and mechanical threshold for nocifensive withdrawal were determined by the use of, respectively, plantar radiant heating and von Frey filaments, for both ILP and contralateral hindpaws (CLP). Either paw was anesthetized for 60 minutes by direct injection of bupivacaine (0.25%, 40 μL), 30 minutes before ET-1. Alternatively, the contralateral sciatic nerve was blocked for 6 to 12 hours by percutaneous injection of bupivacaine-releasing microspheres 30 minutes before injection of ET-1. Systemic actions of these bupivacaine formulations were simulated by subcutaneous injection at the nuchal midline.

RESULTS: After the injection of ET-1, the mechanical threshold of both ILP and CLP decreased by 2 hours, appeared to be lowest around 24 hours, and recovered through 48 hours to preinjection baseline at 72 hours. These hypersensitive responses were suppressed by bupivacaine injected into the ipsilateral paw before ET-1. Injection of the CLP by bupivacaine also suppressed the hypersensitivity of the CLP at all test times, and that of the ILP, except at 2 hours when it increased the sensitivity. This same pattern of change occurred when the contralateral sciatic nerve was blocked by bupivacaine-releasing microspheres. The systemic actions of these bupivacaine formulations were much smaller and only reached significance at 24 hours post–ET-1. Thermal hypersensitivity after ET-1 injection also occurred in both ILP and CLP and showed the same pattern in response to the 2 contralateral anesthetic procedures.

CONCLUSIONS: These results show that efferent transmission through the contralateral innervation into the paw is necessary for contralateral sensitization by ET-1, suggesting that the release of substances by distal nerve endings is involved. The release of substances in the periphery is essential for contralateral sensitization by ET-1 and may also contribute to secondary hyperalgesia, occurring at loci distant from the primary injury, that occurs after surgery or nerve damage.
First Human Study of the Investigational Sedative and Anesthetic Drug AZD3043: A Dose-Escalation Trial to Assess the Safety, Pharmacokinetics, and Efficacy of a 30-Minute Infusion in Healthy Male Volunteers

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BACKGROUND: AZD3043 is a positive allosteric modulator of the gamma-aminobutyric acid type A receptor that is rapidly metabolized to an inactive metabolite by esterases present in blood and liver. Preclinical results suggest that AZD3043 has the potential as a short-acting IV sedative/anesthetic drug with rapid and predictable recovery characteristics and a favorable safety and tolerability profile.

METHODS: Our primary objective in this phase 1, single-center, open-label study was to evaluate the safety and tolerability of AZD3043 after IV infusion and to estimate the maximal tolerated dose. Secondary objectives included the evaluation of AZD3043 pharmacokinetics, pharmacodynamics, and efficacy. Sequential ascending-dose cohorts of 5 or 6 healthy male volunteers aged 18 to 45 years received a single 30-minute IV infusion of AZD3043. Assessments included adverse events, vital signs, blood gases, laboratory values, clinical signs of sedation/anesthesia, and bispectral index.

RESULTS: Fifty-three subjects received AZD3043 in infusion rate cohorts of 1, 3, 6, 12, 18, 27, 36, 54, and 81 mg/kg/h. There were no discontinuations, and dose escalation was stopped on reaching the predefined exposure limit. Adverse events occurring in >1 subject were headache (n = 4), erythema (n = 3), chest discomfort (n = 2), nausea (n = 2), and dyspnea (n = 2). The frequency and character of adverse events appeared unrelated to dose. There were no spontaneous reports of pain on injection and no clinically relevant changes in respiratory rate or arterial blood
pressure. However, heart rate increased dose-dependently at infusion rates >18 mg/kg/h. Occurrence of sedation/anesthesia corresponded with dose; the lowest applied infusion rate to induce anesthesia according to clinical signs of sedation/anesthesia at predefined time points was 12 mg/kg/h (1 of 6 subjects anesthetized), and all subjects in the 3 highest dose groups were anesthetized. The onset of anesthesia ranged from 4 minutes in the highest infusion rate group to 29 minutes in the 12-mg/kg/h infusion rate group. Return of response to oral command occurred at 3 minutes after the end of infusion in the single subject who was anesthetized in the 12-mg/kg/h group and median 25 minutes in the 81-mg/kg/h group. Involuntary movements ranging from minor twitches to extensive movements were accompanied by increased muscle tone.

CONCLUSIONS: AZD3043 was well tolerated in this first human study and seems to exhibit rapid onset and recovery, indicating potential use as a short-acting drug for anesthesia and sedation.

一种新型羟-5α-孕烷二酮的水剂与丙泊酚在效能和安全性上的比较的临床 1c 期药物试验

A Phase 1c Trial Comparing the Efficacy and Safety of a New Aqueous Formulation of Alphaxalone with Propofol

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背景: Phaxan™ (即 PHAX，密西根坎墩化学实验室) 是一种 10 毫克/毫升的羟-5α-孕烷二酮和 13% 7-磺丁基醚-β-环糊精（β-环糊精复合物）的水溶液。在临床前期研究中，PHAX 是一种和异丙酚一样起效快-失效快的静脉麻醉药，但对心血管的抑制更少。本项是其第一次用于人体的药物试验，旨在找到 PHAX 的麻醉剂量以及与等效剂量的丙泊酚比较安全性、效能、麻醉恢复及苏醒质量。

方法: 本研究坚持贯彻 GCP 的规定 (临床试验注册号，actrn12611000343909)。本项研究随机、双盲，研究使用贝叶斯算法来确定 PHAX 和丙泊酚对脑电双频指数 (BIS) 的效应的等效剂量。受试者为男性志愿者，ASA 分级Ⅰ级，知情同意（分为丙泊酚和 PHAX 两组，每组 12 人）。评价参量为药物注射 (单次剂量) 80 分钟后的注射痛、不自主运动、脑电双频指数、血压、是否需要气道支持以及作为苏醒恢复质量的评价指标的 Richmond 躁动镇静量表和数字符号替换测试。动脉血液的抽取用于生化，血液学和补体水平的测定。

结果: PHAX 组的受试者没有一例报告注射痛，而 12 例丙泊酚组的受试者中有 8 例报告了注射痛。达到等效的 BIS 值≤50 的受试者，PHAX 组有 9 例，丙泊酚组有 8 例，分别所需的中位数剂量为 PHAX 组：0.5 (0.5-0.6)mg/kg；丙泊酚组：2.9 (2.4-3.0) mg/kg。组内能达到的最低 BIS 中位数数值都是 27-28，在两组起效的时间和 BIS 值的恢复时间都没有显著的差异。伴随的收缩压和舒张压的中位数值变化，PHAX 组与丙泊酚组相比分别是收缩压-11% vs -19%，舒张压-25% vs -37%。丙泊酚组 12 例受试者中 9 例需要气道支持，PHAX 组受试者均无需要。达到等效的 BIS 值≤50 的受试者中: Richmond 躁动镇静量表和数字符号替换测试达到 0 时，丙泊酚受试者和 PHAX 的中位数起效时间分别为为 5 (IQR，5-10) 分钟和 15 (IQR，10-20) 分钟。丙泊酚组和 PHAX 组受试者的 BIS 值恢复到 90 所需要的时间分别是 21 分钟 (SD，10.1) 和 21 分钟 (SD 9.2)。丙泊酚组和 PHAX 组受试者的数字符号替换测试分数恢复到静脉用药前水平的时间的中位数分别为为 50 (IQR，35-72.5) 分钟和 42.5 (IQR，35-76.3) 分钟。两种药物在注射后 C3 和 C4 补体水平没有增加。

结论: PHAX 能与丙泊酚提供类似的起效快-失效快和短时间麻醉的快速认知恢复，但心血管抑制更少，气道阻塞更少，且无注射痛。
**BACKGROUND:** Phaxan™ (PHAX, Chemic Labs, Canton, MA) is an aqueous solution of 10 mg/mL alphaxalone and 13% 7-sulfobutylether β-cyclodextrin (betadex). In preclinical studies, PHAX is a fast onset-offset IV anesthetic like propofol, but causes less cardiovascular depression. This first-in-man study was designed to find the anesthetic dose of PHAX and to compare it with an equivalent dose of propofol for safety, efficacy, and quality of recovery from anesthesia and sedation.

**METHODS:** The study adhered to compliance with Good Clinical Practices regulations (clinical trials registry number, ACTRN12611000343909). This randomized, double-blind study compared PHAX and propofol using a Bayesian algorithm to determine dose equivalence for effects on the bispectral index (BIS). Male volunteers, ASA physical status I, gave written informed consent (n = 12 per group; PHAX or propofol). Parameters assessed for 80 minutes after drug injection (single bolus dose) were pain on injection, involuntary movement, BIS, blood pressure, need for airway support, and, as measures of recovery from sedation, the Richmond Agitation and Sedation Scale and the Digit Symbol Substitution Test. Arterial blood was withdrawn for biochemistry, hematology, and complement levels.

**RESULTS:** No subject complained of pain on injection with PHAX, whereas 8 of the 12 subjects given propofol did. Nine PHAX and 8 propofol subjects reached BIS values of ≤50: median (interquartile range [IQR]) mg/kg dose = 0.5 (0.5-0.6) for PHAX and 2.9 (2.4-3.0) for propofol. The lowest median BIS reached was 27 to 28 for both agents with no significant differences between them for timing of onset and recovery of BIS. The concomitant median changes in systolic and diastolic blood pressures were -11% vs -19% for systolic and -25% vs -37% for diastolic in PHAX- and propofol-treated subjects, respectively. Nine of the 12 propofol-treated subjects and none of 12 PHAX-treated subjects required airway support. For subjects reaching an equivalent BIS of ≤50: a Richmond Agitation and Sedation Scale score of 0 was reached at a median of 5 (IQR, 5-10) and 15 (IQR, 10-20) minutes after PHAX and propofol, respectively; BIS returned to 90 at a mean of 21 (SD, 10.1) and 21 (SD, 9.2) minutes after PHAX and propofol, respectively; and Digit Symbol Substitution Test scores returned to predrug injection values at median of 50 (IQR, 35-72.5) and 42.5 (IQR, 35-76.3) minutes after PHAX and propofol, respectively. There was no increase in C3 and C4 complement fractions after either drug.

**CONCLUSIONS:** PHAX causes fast-onset, short-duration anesthesia with fast cognitive recovery similar to propofol, but with less cardiovascular depression, or airway obstruction and no pain on injection.

在 Listening to Mothers II 调查中妇女接受脊髓镇痛的分娩体验：一项开放性回答的内容分析

Women’s Experiences with Neuraxial Labor Analgesia in the Listening to Mothers II Survey: A Content Analysis of Open-Ended Responses

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背景：大多数在美国医院进行生产的妇女在分娩时接受脊髓镇痛。在这项分析中，我们在一个全美母亲的样本中调查了脊髓镇痛的体验。

方法：我们的数据来自 Listening to Mothers II 调查，这个全国性的样本包括了 2005 年在美国医院中分娩了单胎的妇女（N=1573）。我们研究的对象是计划剖腹产却进行了自然
分娩并接受脊髓镇痛的妇女（n=914）。我们采用定性内容分析的方法，分析了妇女在分娩过程中与脊髓镇痛相关的最好和最糟糕方面的开放性的回答。

结果：30%的的妇女在他们的开放性回答中提到了脊髓镇痛（n=300）。我们发现能够有效地缓解疼痛是接受了脊髓镇痛的妇女最常提到的积极方面。然而一些妇女提到了在脊髓镇痛中与时效有关的问题，包括在等待进行脊髓镇痛时的疼痛，在分娩过程中太晚进行脊髓镇痛以及镇痛效果消退得太快。另一些接受脊髓镇痛的妇女提到的问题包括知情同意，副作用以及计划和预期的问题。

结论：这项调查结果显示妇女们对于脊髓镇痛在生产过程中缓解疼痛的作用很满意。尽管脊髓镇痛有效地控制了疼痛，但在接受脊髓镇痛的过程中还有另外的影响因素。麻醉师可以和产科医生、护士、分娩指导员以及孕妇和正在分娩的妇女一起合作来减少在时机、交流、脊髓镇痛的实施和效果预期方面的问题来改善妇女的生产体验。

（施芸岑 译 薛张纲 校）

BACKGROUND: Most women who give birth in United States hospitals receive neuraxial analgesia to manage pain during labor. In this analysis, we examined themes of the patient experience of neuraxial analgesia among a national sample of U.S. mothers.

METHODS: Data are from the Listening to Mothers II survey, conducted among a national sample of women who delivered a singleton baby in a U.S. hospital in 2005 (N = 1,573). Our study population consisted of women who experienced labor, did not deliver by planned cesarean, and who reported neuraxial analgesia use (n = 914). We analyzed open-ended responses about the best and worst parts of women's birth experiences for themes related to neuraxial analgesia using qualitative content analysis.

RESULTS: Thirty-three percent of women (n = 300) mentioned neuraxial analgesia in their open-ended responses. We found that effective pain relief was frequently spontaneously mentioned as a key positive theme in women's experiences with neuraxial analgesia. However, some women perceived timing-related challenges with neuraxial analgesia, including waiting in pain for neuraxial analgesia, receiving neuraxial analgesia too late in labor, or feeling that the pain relief from neuraxial analgesia wore off too soon, as negative aspects. Other themes in women's experiences with neuraxial analgesia were information and consent, adverse effects of neuraxial analgesia, and plans and expectations.

CONCLUSIONS: The findings from this analysis underscored the fact that women appreciate the effective pain relief that neuraxial analgesia provides during childbirth. Although pain control was 1 important facet of women's experiences with neuraxial analgesia, their experiences were also influenced by other factors. Anesthesiologists can work with obstetric clinicians, nurses, childbirth educators, and pregnant and laboring patients to help mitigate some of the challenges with timing, communication, neuraxial analgesia administration, or expectations that may have contributed to negative aspects of women's birth experiences.
正手术方法使得硬膜外腔置管更容易，但术后的变化仍可能影响椎管内分娩镇痛的效果。本前瞻性病例对照研究旨在比较矫正手术史产妇与无背部手术史产妇椎管内置管时间和每小时布比卡因需求剂量。

方法：期间研究纳入了所有普伦蒂斯女子医院内既往有脊柱内手术治疗脊柱侧弯矫形史并要求行椎管内分娩镇痛的妇女。对照组选择以麻醉师水平经验作为匹配内容。主要观察指标是椎管内成功置管时间和每小时布比卡因需求剂量。次要观察结果包括补充镇痛要求和椎管内镇痛失败率和并发症。

结果：研究统计并分析了41位脊柱侧凸矫正手术史女性和41位对照组女性的椎管内分娩镇痛数据。两组间产科及人口学特征并无统计学差异。脊柱手术史组中位数每小时布比卡因消费量为15.2毫克（12.5-18.7），对照组为14.2毫克（11.8-16.0），中位数的差异为1毫克（95%置信区间：-1.3至3.0，P = 0.38）。两组间总体布比卡因消耗量、病人自控镇痛次数以及需要高浓度布比卡因的个体数量没有差异。脊柱手术史组镇痛失败5例（12%），较对照组（0例）发生率提高12%（95%置信区间：0.3%至25%，P = 0.06）。脊柱手术史组完成置管所需的平均时间为41%（95%置信区间：7%-108%，P = 0.01）较对照组显著延长。此外，脊柱手术史组还需要更多穿刺针重定向、间隙尝试次数，或更换更有经验的麻醉医生。

结论：本研究的结果表明，既往脊柱侧凸矫正手术不影响椎管内分娩镇痛药物需求量，但椎管内操作难度明显提升。我们认为既往有脊柱侧凸矫正手术史的产妇可以接受椎管内分娩镇痛，但知情同意书中应注明技术困难及镇痛失败的可能。

（俞颖译 薛张纲校）

BACKGROUND: Neuraxial analgesic techniques are the most effective form of labor analgesia. Small studies (9-21 patients), conducted 10 to 20 years ago, demonstrated successful neuraxial labor analgesia in only 50% to 66% of patients with surgical correction for scoliosis. Newer surgical techniques for scoliosis correction make the epidural space more accessible, but postsurgical changes may still alter the efficacy of neuraxial labor analgesia. The purpose of this prospective case-matched study was to compare hourly bupivacaine consumption and time to placement of neuraxial technique in laboring women with spinal instrumentation compared with women without previous back surgery.

METHODS: All women with previous spinal instrumentation surgery for scoliosis correction who requested neuraxial labor analgesia at Prentice Women's Hospital during the study period were approached. Control subjects were matched for anesthesiologist level of experience. The primary outcomes were bupivacaine consumption per hour of labor analgesia and time to placement of the neuraxial technique. Secondary outcomes included supplemental analgesia requirements and neuraxial analgesia failures and complications.

RESULTS: Data from 41 women with surgical correction for scoliosis and 41 control subjects requesting neuraxial labor analgesia were analyzed. Obstetric and demographic characteristics of study participants were not different between groups. Median (interquartile range) hourly bupivacaine consumption was 15.2 mg/h (12.5-18.7) in the spinal instrumentation group and 14.2 mg/h (11.8-16.0) in the control group; the difference in medians was 1 mg/h (95% confidence interval [CI], -1.3 to 3.0; P = 0.38). The total bupivacaine consumption, number of manual reboluses, and number of subjects requiring greater bupivacaine concentrations did not differ between groups. Neuraxial analgesia failure occurred in 5 (12%) of women in the spinal instrumentation group but in none of the control patients (difference [95% CI], 12% [-0.3% to 25%]; P = 0.06). The mean time required to complete the neuraxial technique was 41% (95% CI, 7%-108%; P = 0.01) longer in the spinal instrumentation group than in the control group. The spinal instrumentation group also required a greater number of needle redirections, attempted interspaces, and need to switch to a more experienced provider than matched controls.

CONCLUSIONS: The findings of this investigation suggest that previous surgery for scoliosis repair does not affect neuraxial labor analgesia consumption, but performance of the neuraxial technique is more difficult. Our findings suggest that neuraxial labor analgesia should be offered
Preparing Parents to Be Present for Their Child’s Anesthesia Induction: A Randomized Controlled Trial

Bailey, Kristen M. MSc; Bird, Sally J. MD, FRCPC; McGrath, Patrick J. PhD; Chorney, Jill E. PhD

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让父母参与到自己孩子的麻醉诱导中:一组随机对照试验

Preparing Parents to Be Present for Their Child’s Anesthesia Induction: A Randomized Controlled Trial

Bailey, Kristen M. MSc; Bird, Sally J. MD, FRCPC; McGrath, Patrick J. PhD; Chorney, Jill E. PhD

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让父母参与到自己孩子的麻醉诱导中:一组随机对照试验支持父母的行为以及双亲生产性能可以减少他们孩子的术前焦虑

背景：这项研究的目的是为了将有父母陪伴的具有准备干预的麻醉诱导与标准麻醉诱导产生的效果做比较。

方法：在儿童医院即将行择期手术的年龄为2-10岁之间的93个孩子与他们的父母一起参与了这项研究。父母在他们的孩子麻醉诱导前将会被随机分配到麻醉诱导准备组或者标准麻醉诱导组。被分配到这两组的父母的孩子将会在以下四方面做比较：术前焦虑程度，诱导中的配合度，有无谵妄，术后疼痛。父母将会被比较他们在手术室中的焦虑程度以及自我角色重要程度。

结果：在稳定阶段，父母陪伴这个干预因素对于减少孩子术前焦虑的效果并不明显。（P=0.15, Wilcoxon Mann Whitney校验，[WMWodds; 95%置信区间{CI}] = 1.41 [0.75–3.10]），家庭离开等候区的时间点（P = 0.39, WMWodds [95% CI] = 1.18 [0.60–2.45]），他们进入手术室的时间点（P = 0.28, WMWodds [95% CI] = 1.23 [0.65–2.67]），或者孩子扣上加压面罩的时间点（P = 1.3, WMWodds [95% CI] = 1.23 [0.64–2.63]）。然而，麻醉诱导准备组的父母相对于麻醉诱导标准组的父母，他们更倾向于认为自己在手术室中的自我效能高（P = 0.03, WMWodds [95% CI] = 1.69 [1.07–2.87]）。

结论：一项利用父母在孩子麻醉诱导时的陪伴来减少其术前焦虑的基于视频的简要干预研究并不成功。但是，在此研究中的父母是否按照干预中的指示去表现自己以减少孩子的焦虑这件事还有待商榷。将来的研究应监督父母的行为以及双亲生产性能来减少他们孩子的术前焦虑。

（王洁 译 薛张纲 校）

Preparing Parents to Be Present for Their Child’s Anesthesia Induction: A Randomized Controlled Trial parent behavior and support parental performance to reduce their children’s preoperative anxiety.

BACKGROUND: The purpose of this study is to compare the effectiveness of a brief preparation intervention for parental presence during induction of anesthesia (PPIA preparation) with a PPIA with standard preparation (PPIA standard).

METHODS: Ninety-three children, aged 2 to 10 years, undergoing elective surgery at a children’s hospital participated together with their parents. Parents were randomly assigned to receive either PPIA preparation or PPIA standard before their children’s induction of anesthesia. Children of parents assigned to each group were compared on measures of preoperative anxiety, cooperation at induction, emergence delirium, and postoperative pain. Parents were compared on measures of state anxiety and self-efficacy about their role in the operating room (OR).

RESULTS: The effectiveness of parental presence in reducing children’s preoperative anxiety was not improved by the intervention at the holding stage (P = 0.15, Wilcoxon Mann-Whitney odds [WMWodds; 95% confidence interval {CI}] = 1.41 [0.75–3.10]), the point at which the
family left the holding area (P = 0.39, WMWodds [95% CI] = 1.18 [0.60–2.45]), the point that they entered the OR (P = 0.28, WMWodds [95% CI] = 1.23 [0.65–2.67]), or the point at which the anesthesia mask was introduced (P = 1.3, WMWodds [95% CI] = 1.23 [0.64–2.63]). However, parents who received PPIA preparation trended toward greater self-efficacy about their role in the OR than those who received PPIA standard (P = 0.03, WMWodds [95% CI] = 1.69 [1.07–2.87]).

CONCLUSIONS: A brief, video-based intervention aimed at preparing parents to be present for their child’s anesthesia induction was not successful in reducing the children’s preoperative anxiety. However, it is unclear whether parents included in this study actually performed as instructed in the intervention to reduce their children’s anxiety. Future research should monitor parent behavior and support parental performance to reduce their children’s preoperative anxiety.

Clinical Research Methodology 3: Randomized Controlled Trials
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临床研究方法3：随机对照试验

随机分配可以排除反向因果关系和选择偏倚，并且研究足够大时可以有效地防止混杂偏倚。实施盲法可以防止测量偏倚。包括以上保护措施的研究被称为随机盲法临床试验。当有足够的患者，该方法可以提供最有效的结果。虽然以上概念简单明确，但在设计临床试验时需要在各个相互矛盾的方案中仔细权衡。所选择的方案会影响招募患者的数量、招募时间、内部和外部有效性、评估治疗之间的相互作用和成本。

（邬其玮译 薛张纲校）

Randomized assignment of treatment excludes reverse causation and selection bias and, in sufficiently large studies, effectively prevents confounding. Well-implemented blinding prevents measurement bias. Studies that include these protections are called randomized, blinded clinical trials and, when conducted with sufficient numbers of patients, provide the most valid results. Although conceptually straightforward, design of clinical trials requires thoughtful trade-offs among competing approaches—all of which influence the number of patients required, enrollment time, internal and external validity, ability to evaluate interactions among treatments, and cost.

Conventional Landmark-Guided Midline Versus Preprocedure Ultrasound-Guided Paramedian Techniques in Spinal Anesthesia
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背景：多次脊髓重复穿刺麻醉会增加腰麻后头痛、感觉异常、脊髓血肿的发生率。我们假设常规使用超声引导蛛网膜下腔阻滞旁正中方法，相比传统的标志引导的正中入路，可以降低重复穿刺的次数。

方法：100 名签署知情同意计划进行全关节（髋关节或膝关节）置换的患者被随机分成 C 组（传统组）和 P 组（操作前超声引导旁正中方法组），每组 50 人。患者不知道自己被分到哪个研究组。所有的蛛网膜下腔阻滞都是由高年资麻醉医生实施。在 C 组，蛛网膜
BACKGROUND: Multiple passes and attempts while administering spinal anesthesia are associated with a greater incidence of postdural puncture headache, paraesthesia, and spinal hematoma. We hypothesized that the routine use of a preprocedural ultrasound-guided paramedian technique for spinal anesthesia would reduce the number of passes required to achieve entry into the subarachnoid space when compared with the conventional landmark-guided midline approach.

METHODS: One hundred consenting patients scheduled for elective total joint replacements (hip and knee) were randomized into group C (conventional) and group P (preprocedural ultrasound-guided paramedian technique) with 50 in each group. The patients were blinded to the study group. All spinal anesthetics were administered by a consultant anesthesiologist. In group C, spinal anesthetic was done via the midline approach using clinically palpated landmarks. In group P, a preprocedural ultrasound scan was used to mark the paramedian insertion site, and spinal anesthetic was performed via the paramedian approach.

RESULTS: The average number of passes (defined as the number of forward advancements of the spinal needle in a given interspinous space, i.e., withdrawal and redirection of spinal needle without exiting the skin) in group P was approximately 0.34 times that in group C, a difference that was statistically significant (P = 0.01). Similarly, the average number of attempts (defined as the number of times the spinal needle was withdrawn from the skin and reinserted) in group P was approximately 0.25 times that of group C (P = 0.0021). In group P, on an average, it took 81.5 (99% confidence interval, 68.4–97 seconds) seconds longer to identify the landmarks than in group C (P = 0.0002). All other parameters, including grading of palpated landmarks, time taken for spinal anesthetic injection, periprocedural pain scores, periprocedural patient discomfort visual analog scale score, conversion to general anesthetic, paresthesia, and radicular pain during needle insertion, were similar between the 2 groups.

CONCLUSIONS: Routine use of paramedian spinal anesthesia in the orthopedic patient population undergoing joint replacement surgery, guided by preprocedure ultrasound examination, significantly decreases the number of passes and attempts needed to enter the subarachnoid space.