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Positioning an Intraaortic Balloon Pump Using Intraoperative Transesophageal Echocardiogram Guidance
Matthew A. Klopman, MD*, Edward P. Chen, MD† and Roman M. Sniecinski, MD, FASE*
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A 72-year-old man with an ejection fraction of 25% is scheduled to undergo elective coronary artery bypass graft using cardiopulmonary bypass. Because of the high-risk nature of the operation, the surgeon wants to insert an intraaortic balloon pump (IABP) before initiating cardiopulmonary bypass. An intraoperative transesophageal echocardiogram (TEE) is requested to ensure correct placement.

A Comparison of Desflurane Versus Propofol: The Effects on Early Postoperative Lung Function in Overweight Patients
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A 72-year-old man with an ejection fraction of 25% is scheduled to undergo elective coronary artery bypass graft using cardiopulmonary bypass. Because of the high-risk nature of the operation, the surgeon wants to insert an intraaortic balloon pump (IABP) before initiating cardiopulmonary bypass. An intraoperative transesophageal echocardiogram (TEE) is requested to ensure correct placement.

Background: In this study, we evaluated and compared the effects of propofol and desflurane on lung function and arterial oxygen saturation in overweight patients.

Methods: We prospectively studied 134 overweight patients with an ejection fraction of 25% to 35 kg/m² who were undergoing thoracic surgery. Patients were randomly assigned to receive propofol (total intravenous anesthesia) or inhalational desflurane, with end-tidal carbon dioxide maintained between 30 and 40 mmHg. Preoperative medication, supplemental drugs, and ventilator settings were standardized. Oxygen saturation and lung function were measured before induction, 10 minutes after extubation, and at 0.5, 2, and 24 hours. All values were compared to baseline values.

A Comparison of Desflurane Versus Propofol: The Effects on Early Postoperative Lung Function in Overweight Patients
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Anesth Analg July 2011 113:63-69
In this study, we evaluated the influence of propofol versus desflurane anesthesia in overweight patients on postoperative lung function and pulse oximetry values.

**METHODS:** We prospectively studied 134 patients with body mass indices of 25 to 35 kg/m² undergoing minor peripheral surgery lasting 40 to 120 minutes. Patients were randomly assigned to receive propofol (total IV anesthesia) or desflurane anesthesia via a tracheal tube targeting bispectral index values of 40 to 60. Premedication, adjuvant drug usage, and ventilation were standardized. We measured oxyhemoglobin saturation and lung function preoperatively (baseline), and at 10 minutes, 0.5 hour, 2 hours, and 24 hours after tracheal extubation. All values were measured with the patient supine, in a 30° head-up position. Changes from preoperative baseline values were first analyzed for the impact of body mass index and type of anesthesia using univariate methods, followed by linear regression and multivariate analysis of variance.

**RESULTS:** Within the first 2 hours after surgery, the propofol group displayed lower oxyhemoglobin saturation (at 2 hours, mean ± SD, 93.8% ± 2.0% vs 94.6% ± 2.1%; P < 0.007) and lung function (forced vital capacity, forced expiratory volume exhaled in 1 second [FEV₁], peak expiratory flow, midexpiratory flow [MEF], forced inspiratory vital capacity, and peak inspiratory flow; between 11% and 20% larger reduction from baseline in the propofol group, all P < 0.001) compared with the desflurane group. Even 24 hours after surgery, FEV₁, peak expiratory flow, MEF, forced inspiratory vital capacity, and peak inspiratory flow were reduced more in the propofol group (all P < 0.01). At 2 hours after extubation, increasing obesity was associated with decreasing FEV₁ and MEF in patients anesthetized with propofol but not desflurane (P < 0.01).

**CONCLUSION:** We conclude that, for superficial surgical procedures of up to 120 minutes, maintenance of anesthesia with propofol impairs early postoperative lung function and pulse oximetry values more than with desflurane. Furthermore, increasing obesity decreases pulmonary function at 2 hours after propofol anesthesia but not after desflurane anesthesia.

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**短缺前準備程式的疏漏步驟**

Missed Steps in the Preanesthetic Set-Up
Samuel Demaria Jr., MD, Kimberly Blasius, MD and Steven M. Neustein, MD
BACKGROUND: Anesthesiologists accomplish many tasks rapidly during induction of an anesthetic. Key preparation for induction is needed to maximize patient safety. Given the intense environment of the operating room, preparatory steps may be missed either unintentionally or possibly even intentionally to save time. We conducted this study to determine the incidence of missed steps in the operating room immediately before induction.

METHODS: In this study, 200 surgical procedures were randomly checked for missed steps before induction of anesthesia using a “Revised Preanesthetic Set-Up.” Additionally, multiple other operating room/case variables were recorded to determine whether there was correlation between the missed steps and certain variables such as room case load and regional versus general anesthesia.

RESULTS: Twenty-three missed steps were discovered. Manual resuscitation device availability and a working suction set-up were the most frequently missed steps. A higher percentage of missed steps was found in cases in which regional was the planned anesthesia technique, in rooms with higher case loads (≥5 cases scheduled), and in rooms that attending anesthesiologists completed the set-up.

CONCLUSIONS: Missed steps do occur at a significant and measurable rate. Measures need to be taken to decrease the number of missed steps to improve patient safety.
The sniffing position (SP) has traditionally been considered the optimal head position for direct laryngoscopy (DL). Its superiority over other head positions, however, has been questioned during the last decade. We reviewed the scarce literature on the subject to examine the evidence either in favor or against the routine use of the SP. A standard definition for the position should be used (e.g., 35° neck flexion and 15° head extension) to avoid confusion about what constitutes a proper SP and to compare the results from different studies. Although several theories were proposed to explain the superiority of the SP, the three axes alignment theory is still considered a valid anatomical explanation. Although head elevation is needed to achieve the desired neck flexion, the elevation height may vary from one patient to another depending on head and neck anatomy and size of the chest. In infants and small children, for example, no head elevation is needed because the size and shape of the head allow axes approximation in the head-flat position. Horizontal alignment of the external auditory meatus with the sternum, in both obese and non-obese patients, indicates, and can be used as a marker for, proper positioning. Analysis of the available literature supports the use of the SP for DL. To achieve a proper SP in obese patients, the “ramped” (or the back-up) position should be used. The SP does not guarantee adequate exposure in all patients, because many other anatomical factors control the final degree of visualization. However, it should be the starting head position for DL because it provides the best chance at adequate exposure. Attention to details during positioning and avoidance of minor technical errors are essential to achieve the proper position. DL should be a dynamic procedure and position adjustment should be instituted in case poor visualization is encountered in the SP.
BACKGROUND: Our aim in this multinational, multicenter, randomized, blinded trial was to determine the optimum of 3 volumes of autologous blood for an epidural blood patch.

METHODS: Obstetric patients requiring epidural blood patch after unintentional dural puncture during epidural catheter insertion were allocated to receive 15, 20, or 30 mL of blood, stratified for the timing of epidural blood patch and center. Participants were followed for 5 days. The primary study end point was a composite of permanent or partial relief of headache, and secondary end points included permanent relief, partial relief, persisting headache severity, and low back pain during or after the procedure.

RESULTS: One hundred twenty-one women completed the study. The median (interquartile range) volume administered was 15 (15–15), 20 (20–20), and 30 (22–30) mL, with 98%, 81%, and 54% of groups 15, 20, and 30 receiving the allocated volume. Among groups 15, 20, and 30, respectively, the incidence of permanent or partial relief of headache was 61%, 73%, and 67% and that of complete relief of headache was 10%, 32%, and 26%. The 0- to 48-hour area under the curve of headache score versus time was highest in group 15. The incidence of low back pain during or after the epidural blood patch was similar among groups and was of low intensity, although group 15 had the highest postprocedural back pain scores. Serious morbidity was not reported.

CONCLUSIONS: Although the optimum volume of blood remains to be determined, we believe these findings support an attempt to administer 20 mL of autologous blood when
treating postdural puncture headache in obstetric patients after unintentional dural puncture.

**Reactive Oxygen Species Scavenger Inhibits STAT3 Activation After Transient Focal Cerebral Ischemia–Reperfusion Injury in Rats**

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BACKGROUND: Signal transducer and activator of transcription 3 (STAT3) activation in ischemic brain has been verified. However, the mechanism and the role of STAT3 activation after cerebral ischemia–reperfusion are poorly elucidated. In the present study, we sought to test the hypothesis that STAT3 activation after cerebral ischemia–reperfusion was related to reactive oxygen species (ROS) production.

METHODS: Adult male Sprague–Dawley rats were subjected to focal cerebral ischemia induced by middle cerebral artery occlusion. STAT3 activation was evaluated by immunohistochemistry and Western blotting. Rats were subjected to permanent ischemia or ischemia–reperfusion to clarify the temporal profile of STAT3 activation. The role of ROS in inducing STAT3 activation was assessed by administration of the ROS scavenger dimethylthiourea (DMTU). The effects of DMTU and the STAT3 activation inhibitor AG490 administration on brain ischemic injuries were evaluated by neurologic behavior scores and brain infarct volumes.

RESULTS: The activation of STAT3 after middle cerebral artery occlusion was significantly increased within peri-ischemia neurons and astrocytes. STAT3 activation mainly occurred in the reperfusion phase rather than in the ischemia phase. In addition,
DMTU suppressed STAT3 activation in a dose-dependent manner, indicating that STAT3 activation may be a subsequent event after ROS production. DMTU and AG490 significantly reduced infarct sizes and improved neurologic outcomes.

**CONCLUSION:** In comparison with ischemia, reperfusion is a more powerful stimulus for STAT3 activation. ROS scavenging is closely correlated with an inhibition of STAT3 activation. Neuroprotective effects are achieved through ROS scavenging and down-regulation of STAT3 activation.

**美金剛對大鼠浸潤性皮膚鎮痛的局部麻醉作用**

**The Local Anesthetic Effect of Memantine on Infiltrative Cutaneous Analgesia in the Rat**

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**BACKGROUND:** Memantine blocks N-methyl-D-aspartate receptors and the Na+ current, one principal mechanism of local anesthesia. Until now, no study mentioned that memantine had a local anesthetic effect, and therefore we investigated the local anesthetic effect of memantine.
METHODS: After blockade of cutaneous trunci muscle reflex with subcutaneous injections, we evaluated the cutaneous analgesic effect of memantine, lidocaine, and dizocilpine (MK-801) in rats. The dose-dependent response of memantine on cutaneous analgesia was compared with lidocaine and MK-801 in rats. The duration of action for each drug was evaluated and compared on an equipotent basis (20% effective dose \([ED_{20}]\), \([ED_{50}]\), and \([ED_{80}]\)). Lidocaine, a frequently used local anesthetic, was used as control.

RESULTS: We demonstrated that memantine, lidocaine, and MK-801 produced dose-dependent local anesthetic effects as infiltrative cutaneous analgesia. The relative potency was MK-801 (10.4 [9.7–11.1]) > memantine (17.6 [15.2–20.4]) > lidocaine (25.9 [23.8–28.1]) \((P < 0.01)\). On an equipotent basis, memantine showed longer duration than lidocaine \((P = 0.012)\) and MK-801 \((P = 0.008)\). Coadministration of memantine (13.3 \(\mu\)mol/kg) and MK-801 (1.3 \(\mu\)mol/kg) produced greater blockade and duration than memantine (13.3 \(\mu\)mol/kg) or MK-801 (1.3 \(\mu\)mol/kg) alone. Neither local injection of saline nor intraperitoneal administration of a large dose of memantine, lidocaine, or MK-801 produced cutaneous analgesia (data not shown).

CONCLUSIONS: This study indicated that memantine is less potent than MK-801, and that memantine elicits longer analgesic duration than both lidocaine and MK-801. When combined with MK-801, memantine demonstrates a synergetic effect of cutaneous analgesia. We conclude that memantine produces better local analgesia than lidocaine and that \(N\)-methyl-D-aspartate receptors also contribute to the analgesic effect of memantine.

Does Perioperative Systolic Blood Pressure Variability Predict Mortality After Cardiac Surgery? An Exploratory Analysis of the ECLIPSE trials

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背景：對圍術期血壓穩定性與手術預後關係進行探討的相關報導較罕見。本研究驗證接受心臟手術患者收縮壓（SBP）變異性與術後30天死亡率相關的假設。

方法：評估 ECLIPSE 試驗中隨機選取的 1512 名圍術期高血壓患者的圍術期血壓變異性。使用偏離設定收縮壓範圍所產生的壓力幅度×持續時間（曲線下面積）來評估圍術期血壓變異性。
BACKGROUND: Few studies describe an association of perioperative blood pressure stability with postoperative outcome. We tested the hypothesis that systolic blood pressure (SBP) variability in patients undergoing cardiac surgery is associated with 30-day mortality.

METHODS: Perioperative blood pressure variability was evaluated in the 1512 patients who were randomized and had perioperative hypertension in the ECLIPSE trials. Blood pressure variability was assessed as the product of magnitude × duration of SBP excursions outside defined SBP ranges (area under the curve). SBP ranges were analyzed from 65 to 135 mm Hg intraoperatively and 75 to 145 mm Hg pre- or postoperatively, up to 105 to 135 mm Hg intraoperatively and 115 to 145 mm Hg pre- or postoperatively, with the narrower ranges defined by progressively increasing the lower SBP limit by 10 mm Hg increments. Multiple logistic regression was used to assess the association of blood pressure variability with 30-day mortality obtained from the primary ECLIPSE trial results.

RESULTS: Increased SBP variability outside a range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively is significantly associated with 30-day mortality. The odds ratio was 1.16 (95% confidence interval, 1.04–1.30) for 30-day mortality risk per incremental SBP excursion of 60 mm Hg × min/h. The predicted probability of 30-day mortality increased for low-risk patients from 0.2% to 0.5%, and for high-risk patients from 42.4% to 60.7% if the area under the curve increased from 0 to 300 mm Hg × min/h.

CONCLUSIONS: Perioperative blood pressure variability is associated with 30-day mortality in cardiac surgical patients, proportionate to the extent of SBP excursions outside the range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively. Predicted mortality was greater for high-risk patients than for low-risk patients.
BACKGROUND: An influence of polymorphic cytochromes P450 (CYP) 2D6 genetic variants on antiemetic efficacy of ondansetron has been suggested. However, the role of CYP3A in ondansetron metabolism and efficacy has been unclear. In this study, we evaluated the hypothesis that genotype-dependent CYP2D6 and CYP3A activity selectively influences plasma concentrations of ondansetron enantiomers. Additionally, the effects of doubling the ondansetron dose on genotype-dependent plasma concentrations were investigated.

METHODS: Patients received IV ondansetron 4 or 8 mg for emesis prophylaxis before emergence from anesthesia. The CYP2D6-dependent activity score representing no, decreased, normal, or increased CYP2D6 enzyme activity as well as CYP3A low (CYP3A5*3/*3) and high expressor status (CYP3A5 wt/wt or wt/*3) were determined. Plasma concentrations of R- and S-ondansetron enantiomers were measured by liquid
chromatography–tandem mass spectrometry. Area under the plasma concentration-time curves (AUCs) of R- and S-ondansetron were associated with CYP2D6 and CYP3A5 genotype-dependent enzyme activity.

**RESULTS:** Complete data of 141 subjects were analyzed. Concentrations of S-ondansetron differed between CYP2D6 activity groups ($P = 0.01$) with highest values in patients with no CYP2D6 activity (mean [95% confidence interval]: 362.5 [238.3/486.7] h · ng/mL) and lowest values in those with increased activity (149.6 [114.5/184.8] h · ng/mL) compared with subjects displaying genotypes resulting in reduced or normal CYP2D6 activity (263.6 [228.8/298.8], 255.4 [228.2/282.7] h · ng/mL). AUC of R-ondansetron was 2 times higher in CYP3A5 low expressors compared with high expressors (281.5 [248.6/314.3] vs 142.5 [92.4/192.7] h · ng/mL; $P = 0.003$). Doubling the ondansetron dose increased plasma concentrations only in individuals with low CYP3A activity, but not in individuals with high enzyme activity ($P < 0.001$).

**CONCLUSIONS:** The metabolism of ondansetron seems to be enantioselective. In this postoperative setting, CYP2D6 activity scores correlated with concentrations of S-ondansetron, whereas CYP3A5 expressor status mainly influenced concentrations of R-ondansetron. Genetically and environmentally determined CYP2D6 and CYP3A enzyme activity might have implications for antiemetic efficacy.

**通過七氟醚濃度和腦電雙頻指數間滯後效應的測量證實肥胖不影響七氟起效和失效時間**

**Obesity Does Not Influence the Onset and Offset of Sevoflurane Effect as Measured by the Hysteresis Between Sevoflurane Concentration and Bispectral Index**

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**背景**：在肥胖患者中，可能因患者的呼吸變化和氣體交換改變而推遲麻醉氣體的起效和失效的時間。這項研究評估了肥胖對於七氟醚顯效滯後現象的影響。七氟醚的顯效是通過腦電雙頻指數（BIS）測量來證實。由於呼氣末正壓（PEEP）可改善肥胖病人氣體交換能力，作者還評估了 PEEP 對於滯後現象的影響。

**方法**：本研究對15名肥胖和15名體重正常，ASA 分級 I 級和 II 級，20 至 50 歲，接受全身麻醉的選期腹腔鏡手術的患者進行前瞻性研究。使用異丙酚進行麻醉誘導，七氟醚和芬太尼進行麻醉維持。在手術結束後並使 BIS 值穩定在 60 至 65，增加七氟醚吸入濃度至 5%維持 5 分鐘後或直到 BIS 值<40 時降低吸入濃度。此項七氟醚的轉換過程在體重正常的受試者（無 PEEP）進行一次，在肥胖患者中進行兩次（PEEP 爲 0 和 8cmH2O）。使用 NONMEM 6 建立人群藥代學/藥效動力學（PK / PD）相關的抑制 Emax 模型。應用此模型描述在轉換過程中七氟醚呼氣末濃
Degree and BIS values between the lag effects. The intravenous concentration of sevoflurane and its effect as measured by BIS (P > 0.05) did not influence the effect-site elimination rate constant. Neither obesity nor PEEP showed any influence on the PK/PD descriptors.

**CONCLUSIONS:** Our results do not support the hypothesis that obesity prolongs induction or recovery times when sevoflurane, a poorly soluble anesthetic, is used to maintain anesthesia from 90 to 120 minutes.
BACKGROUND: Aspiration pneumonia remains a serious anesthetic-related complication. A reliable diagnostic tool to assess gastric volume is currently lacking. We recently demonstrated that gastric sonography can provide reliable qualitative and quantitative information about gastric content and volume in healthy volunteers. In the current study, we performed a prospective qualitative and quantitative analysis of the gastric antrum in 200 fasted patients undergoing elective surgery.

METHODS: A standardized gastric scanning protocol was applied before anesthetic induction. Patients were classified following a 3-point grading system based solely on qualitative sonographic assessment of the antrum in the supine and right lateral decubitus positions.

RESULTS: Eighty-six patients were classified as grade 0 (empty antrum); 107 patients as grade 1 (minimal fluid volume detected only in the right lateral decubitus position); and 7 patients were classified as grade 2 (antrum clearly distended with fluid visible in both supine and lateral positions). The 3-point grading system correlated with total gastric fluid volume as predicted by a previously reported mathematical model. Essentially grade 0 corresponds to a completely empty stomach, grade 1 corresponds to negligible fluid volumes (16 ± 36 mL) within normal ranges expected for fasted patients, and grade 2 correlates with significantly higher predicted gastric fluid volumes (180 ± 83 mL) beyond previously reported “safe” limits. One patient with a grade 2 antrum had an episode of significant regurgitation of gastric contents on emergence from anesthesia.

CONCLUSION: We propose a 3-point grading system based exclusively on qualitative sonographic assessment of the gastric antrum that correlates well with predicted gastric volume. This grading system could be a promising “biomarker” to assess perioperative aspiration risk. Before it can be applied widely to clinical practice, this diagnostic tool needs to be further validated and characterized.
Hydroxyethyl Starch (130 kD) Inhibits Toll-Like Receptor 4 Signaling Pathways in Rat Lungs Challenged with Lipopolysaccharide

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BACKGROUND: A number of studies have shown that hydroxyethyl starch (HES) solutions are able to down-regulate the expression of inflammatory mediators and inhibit neutrophil-mediated tissue injuries when they are used in patients with sepsis or other diseases with severe inflammatory responses. However, our knowledge about the underlying mechanisms is limited. Toll-like receptor 4 (TLR4) signaling has a pivotal role in inflammatory processes. In this study, we examined the possible involvement of TLR4 signaling in the antiinflammatory effects of HES.

METHODS: Male Sprague-Dawley rats were exposed to lipopolysaccharide (LPS) (10 mg/kg, IV) and received IV saline (30 mL/kg) or HES 130/0.4 (15 or 30 mL/kg). Six hours after LPS challenge, rats were killed and their lungs harvested. Lung injury was examined by hematoxylin-staining (伊紅染色). TLR4 mRNA expression, p38 mitogen-activated protein kinase (MAPK) and extracellular signal-regulated kinases 1/2 MAPK activation, and activator protein 1 (AP-1) activity in the lungs were detected.
with quantitative polymerase chain reaction, Western blotting, and electrophoretic mobility shift assay, respectively.

RESULTS: Compared with saline, HES profoundly attenuated the histological changes induced by LPS in the lungs at both dose levels. Molecular analysis showed that both 15 and 30 mL/kg HES significantly decreased TLR4 mRNA levels and inhibited activation of p38 MAPK and AP-1 in rats challenged with LPS, whereas activation of extracellular signal-regulated kinases 1/2 MAPK was not affected by either dose of HES.

CONCLUSIONS: These findings indicate that the beneficial effects of HES 130/0.4 on inflammation are mediated at least in part by inhibiting the TLR4/p38 MAPK/AP-1 pathway in lungs from rats challenged with LPS.

Allergic Reactions to Propofol in Egg-Allergic Children

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BACKGROUND: Egg and/or soy allergy are often cited as contraindications to propofol administration. Our aim was to determine whether children with an immunoglobulin (Ig)E-mediated egg and/or soy allergy had an allergic reaction after propofol use.
METHODS: We performed a retrospective case review over an 11-year period (1999–2010) of children with IgE-mediated egg and/or soy allergy who had propofol administered to them at the Children's Hospital Westmead, Sydney.

RESULTS: Twenty-eight egg-allergic patients with 43 propofol administrations were identified. No child with a soy allergy who had propofol was identified. Twenty-one children (75%) were male, the median age at anesthesia was 2.4 years (range, 1–15 years), and the presence of other atopic disease was common (eczema 61%, asthma 32%, peanut allergy 43%). Most children (n = 19, 68%) had a history of an IgE-mediated clinical reaction to egg with evidence of a significantly positive egg white skin prick test (SPT) reaction (≥7 mm). Two of these had a history of egg anaphylaxis. The remaining children (n = 9, 32%) had never ingested egg because of significantly positive SPT (≥7 mm). All SPTs to egg were performed within 12 months of propofol administration. There was one nonanaphylactic immediate allergic reaction (n = 1 of 43, 2%) that occurred 15 minutes after propofol administration in a 7-year-old boy with a history of egg anaphylaxis and multiple other IgE-mediated food allergies (cow's milk, nut, and sesame). SPT to propofol was positive at 3 mm. No other egg-allergic child reacted to propofol.

CONCLUSIONS: Despite current Australian labeling warnings, propofol was frequently administered to egg-allergic children. Propofol is likely to be safe in the majority of egg-allergic children who do not have a history of egg anaphylaxis.

神經肽通過調節角質細胞白介素-1β的產生導致周圍神經痛覺過敏
Neuropeptides Contribute to Peripheral Nociceptive Sensitization by Regulating Interleukin-1β Production in Keratinocytes
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肽都會劑量依賴性提高角質細胞內白介素-1β和蛋白的表達。此外，P物質能時間和劑量依賴性地上調角質細胞內NALP-1和蛋白酶1的mRNA和蛋白水準。相比之下，降鈣素基因相關肽時間和劑量依賴性地增加角質細胞內NALP-1和蛋白-1的mRNA水準，但NALPNALP-1和蛋白酶1的蛋白水準並沒有顯著改變。應用蛋白酶1選擇性抑制劑Ac-YVAD-CHO可減少P物質和降鈣素基因相關肽（效應較弱）引起的角質細胞內IL-1β產生增加。選擇性組織蛋白酶B抑制劑CA-74Me也抑制角質細胞內神經肽刺激白介素1β的產生。

**結論**: 結果表明，神經肽通過增加角質細胞白介素-1β的產生誘發痛覺過敏。神經肽的增加角質細胞白介素-1β的產生是依賴蛋白酶-1和組織蛋白酶。神經皮膚信號包括天然免疫神經肽的啟動可能導致了複雜性區域疼痛綜合症患者的疼痛。

（黃丹 譯 陳傑 校）

**BACKGROUND:** It is increasingly evident that there is a close connection between the generation of cutaneous inflammatory cytokines and elevated neuropeptide signaling in complex regional pain syndrome (CRPS) patients. Previously, we observed in the rat tibia fracture model of CRPS that activation of caspase-1 containing NALP1 inflammasomes was required for interleukin (IL)-1β production in keratinocytes, and that administration of an IL-1 receptor antagonist (anakinra) reduced the fracture-induced hindpaw mechanical allodynia. We therefore hypothesized that neuropeptides lead to nociceptive sensitization through activation of the skin's innate immune system by enhancing inflammasome expression and caspase-1 activity.

**METHODS:** We determined whether the neuropeptides substance P (SP) and calcitonin gene-related peptide (CGRP) require IL-1β to support nociceptive sensitization when injected into mouse hindpaw skin by testing mechanical allodynia. We then investigated whether these neuropeptides could stimulate production of IL-1β in a keratinocyte cell line (REKs), and could increase the expression of inflammasome component proteins including NALP1 and caspase-1. Finally, we determined whether neuropeptide-stimulated IL-1β production required activation of caspase-1 and cathepsin.

**RESULTS:** Intraplantar injections of SP and CGRP lead to allodynia in mouse hindpaws but CGRP was approximately 10-fold less potent in causing this response. Moreover, systemic administration of the IL-1 receptor (IL-1R) antagonist anakinra prevented sensitization after neuropeptide injection. Also, mouse skin keratinocytes express IL-1R, which is up-regulated after local neuropeptide application. In vitro data demonstrated that both SP and CGRP increased IL-1β gene and protein expression in REKs in a dose-dependent manner. Furthermore, SP time- and dose-dependently up-regulated NALP1 and caspase-1 mRNA and protein levels in REKs. In contrast, CGRP time- and dose-dependently enhanced NALP1 and caspase-1 mRNA levels without causing a significant change in NALP1 or caspase-1 protein expression in REKs. Inhibition of caspase-1 activity using the selective inhibitor Ac-YVAD-CHO reduced SP and, less effectively, CGRP induced increases in IL-1β production in REK cells. The selective cathepsin B inhibitor CA-74Me inhibited neuropeptide induced IL-1β production in REKs as well.

**CONCLUSIONS:** Collectively, these results demonstrate that neuropeptides induce nociceptive sensitization by enhancing IL-1β production in keratinocytes. Neuropeptides rely on both caspase-1 and cathepsin B for this enhanced production. Neurocutaneous signaling involving neuropeptide activation of the innate immunity may contribute to pain in CRPS patients.
Brief Reports: An Assessment of Subarachnoid Block: A Survey of 175 Articles and Recommendations for Improvement
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BACKGROUND: Assessment of subarachnoid block, particularly the sensory component, may be incomplete and influence the conclusions of studies involving subarachnoid anesthesia, as well as their application in routine clinical practice.

METHODS: We manually searched 175 articles concerning subarachnoid block published from 2006 to 2009 in 8 anesthesia journals to determine the components of the subarachnoid anesthetic procedure recorded as well as the extent of sympathetic and motor block.

RESULTS: The level of subarachnoid injection was reported in 86% of the articles, baricity in 84%, concentration of local anesthetic in 77%, patient's position in 75%, needle size in 77%, and needle type in 71%. The stimulus used for assessing sensory block was reported in 69% of the articles; 17% described the block as unilateral or bilateral, and 11% described the lines along which the stimulus was applied. Motor and sympathetic block were assessed in 40% and 18% of studies, respectively.

CONCLUSIONS: These results suggest incomplete description of tools and assessment of sensory block in studies involving subarachnoid anesthesia. We propose a checklist to facilitate a more standardized evaluation of the extent of subarachnoid anesthesia.

多重電極全血血小板聚集試驗、血小板功能分析儀-100 及體內出血時間在阿司匹林介導的血小板功能障礙患者術前重點照護評估中的作用
Multiple Electrode Whole Blood Aggregometry, PFA-100, and In Vivo Bleeding Time for the Point-of-Care Assessment of Aspirin-Induced Platelet Dysfunction in the Preoperative Setting.
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Background: Acquired platelet dysfunction due to aspirin ingestion may increase bleeding tendency during surgery. Thus, we examined the diagnostic accuracy of in vivo bleeding time (BT) and 2 platelet function assays for the preoperative assessment of a residual antiplatelet effect in patients treated with aspirin.

Methods: Consecutive patients scheduled for surgery were prospectively enrolled in this study. The patients' last aspirin ingestion had occurred within the previous 48 hours.
before blood sampling in the "full aspirin effect" group, between 48 and 96 hours before in the "variable aspirin effect" group, and >96 hours before in the "recovered aspirin effect" group. The control group had not taken any aspirin. Multiple electrode aggregometry, platelet function analyzer (PFA)-100, and in vivo BT were performed to assess the effects of aspirin. One-way analysis of variance on ranks with a post hoc multiple-comparison procedure (Dunn) was used to detect differences among the groups. Categorical data were compared using the z test. Receiver operating characteristic (ROC) curves were created to determine the diagnostic accuracy of the platelet function assays investigated. The area under the ROC curve (AUC), sensitivity, and specificity of the assays were calculated. The level of statistical significance was set at P < 0.05.

**Results:** Three hundred ninety-four patients were included in the analysis (133 control and 261 aspirin-treated patients). All 3 methods were able to detect the antiplatelet effect of aspirin in the full aspirin effect group. Furthermore, no difference in the measurement values between the recovered aspirin effect and control group was found, irrespective of the assay performed. Measurement values in the variable aspirin effect group were different from those of the control group in the ASPItest using multiple electrode aggregometry and COL-EPI using PFA-100 but not in BT. ROC analysis showed the highest diagnostic accuracy in excluding the residual aspirin effect in the ASPItest (AUC 0.81, P < 0.001), followed by COL-EPI (AUC 0.78, P < 0.001) and BT (AUC 0.56, P = 0.05). The cutoff value of 53 U in the ASPItest excluded the effect of aspirin with a sensitivity of 88% and specificity of 71%.

**Conclusions:** The full therapeutic antiplatelet effects of aspirin can be expected within 48 hours of the patient's last aspirin ingestion. Platelet function recovered in our study if aspirin cessation occurred >96 hours (4 days) before; thus, in these patients, preoperative platelet function testing is not useful. To quantify any residual aspirin effect in patients who ceased their intake of aspirin between 48 and 96 hours before surgery, the ASPItest might have the highest diagnostic accuracy.
Background: The unique anesthetic risks associated with the morbidly obese (MO) population have been documented. Pharmacologic management of these patients may be altered because of the physiologic and anthropometric changes associated with obesity. Unfortunately, studies examining the effects of extreme obesity on the pharmacology of anesthetics have been sparse. Although propofol is the induction drug most frequently used in these patients, the appropriate induction dosing scalar for propofol remains controversial in MO subjects. Therefore, we compared different weight-based scalars for dosing propofol for anesthetic induction in MO subjects.

Methods: Sixty MO subjects (body mass index ≥40 kg/m²) were randomized to receive a propofol infusion (100 mg·kg⁻¹·h⁻¹) for induction of anesthesia based on total body weight (TBW) or lean body weight (LBW). Thirty control subjects (body mass index ≤25 kg/m²) received a propofol infusion (100 mg·kg⁻¹·h⁻¹) based on TBW. Syringe drop was used as the marker for loss of consciousness (LOC), at which point the propofol infusion was stopped. The propofol dose required for syringe drop and time to LOC were recorded.

Results: Total propofol dose (mg/kg) required for syringe drop and time to LOC were similar between control subjects and MO subjects given propofol based on LBW. MO subjects receiving a propofol infusion based on TBW had a significantly larger propofol dose and significantly shorter time to LOC. There was a strong relationship between LBW and total propofol dose received in all 3 groups.

Conclusion: LBW is a more appropriate weight-based scalar for propofol infusion for induction of general anesthesia in MO subjects.
是交感神經阻斷對於光學體積描記圖不同元件的影響。方法：在10名健康志願者中，進行單側腋路臂叢神經阻滯，從而使得交感神經阻斷，血管擴張。未進行臂叢神經阻滯的一側做為對照。使用光學體積描記法連續測量雙側的手指血容量和手指的溫度。將手指的光學體積描記圖像分離出AC和DC組分。並且計算AC與DC的比值(AC/DC)。所有資料從臂叢神經阻滯完成開始連續記錄30分鐘。使用鄧尼特檢驗法重複測量分析各個變數以確定臂叢神經阻滯對手指光學體積描記圖和手指溫度的影響。

結果：臂叢神經阻滯後2.7分鐘開始，被阻滯的手臂血管擴張，手指光學體積描記圖的DC部分明顯減少(P<0.0001)。阻滯後30分鐘，DC減少的平均值為51%±19%(95%可信區間為-61%---42%)。光學體積描記圖的其他組分與基線值相比，無明顯變化。臂叢神經阻滯後5.7分鐘開始手指溫度明顯上升(P<0.0001)。阻滯後30分鐘，溫度上升的平均值為7.1°C±3.8°C (95%可信區間為5.1°C-9.0°C)。光學體積描記圖中的DC組分對於預測神經阻滯的效果敏感性和特異性均為最優。

結論：本研究闡明了交感神經阻斷所引起的手指光學體積描記圖中AC和DC組分的變化情況。本次試驗模型中，我們發現DC組分對於監測外周血管擴張情況最為敏感。

（黃劍譯 薛張綱校）

BACKGROUND: Photoplethysmography uses light transmission to measure changes in tissue volume. The resulting photoplethysmogram is composed of AC and DC components. Limited data are available on the effects of vasodilation on the AC and the DC components of the photoplethysmograph signal. The aims of our study were (1) to investigate the effects of sympathectomy on different components of the photoplethysmogram, and (2) to compare sympathectomy-induced changes in the photoplethysmogram with changes in peripheral temperature.

METHODS: In 10 healthy subjects, sympathetic-induced peripheral vasodilation was achieved using an axillary brachial plexus block. The nonblocked arm served as control. We obtained measurements of bilateral continuous measurements of finger blood volume (by photoplethysmography) and finger temperature. We separated the finger photoplethysmogram into its AC and DC components. In addition, we calculated the ratio of AC to DC (AC/DC). All data were recorded until 30 minutes after the end of brachial plexus block. Repeated-measures analysis of variance followed by the Dunnett post hoc test determined the effect of brachial plexus block on the finger photoplethysmogram and finger temperature.

RESULTS: The DC component of the finger photoplethysmogram decreased (vasodilation) significantly (P < 0.0001) after brachial plexus block in the blocked arm starting 2.7 minutes after the block. Average decrease in DC values was -51% ± 19% (95% confidence interval: -61% to -42%) at 30 minutes after the block. None of the other photoplethysmogram components changed significantly from preblock baseline values. On average, the finger temperature increased significantly (P < 0.0001) starting 5.7 minutes after brachial plexus block in the blocked arm. Average increase in temperature was 7.1°C ± 3.8°C (95% confidence interval: 5.1°C-9.0°C) 30 minutes after the block. The DC component of the photoplethysmogram had the highest sensitivity and specificity to predict a successful block.
CONCLUSIONS: This study characterizes sympathectomy-induced changes in the AC and DC components of the finger photoplethysmogram. In this experimental model, we found the DC component to be most sensitive in detecting peripheral vasodilation.

BACKGROUND: Klippel-Trenaunay syndrome (KTS) is a rare congenital malformation characterized by the triad of varicose veins or venous malformations, capillary malformations that may involve neurovascular structures, and bony or soft tissue hypertrophy in affected limbs. Areas such as the trunk, bowel, bladder, and spinal cord may be involved as well. KTS should not be confused with Klippel-Feil syndrome, which involves abnormalities of the cervical vertebrae. Anesthetic management for patients with KTS has only been described in limited case reports that caution about potential airway difficulty but do not report surgical hemorrhage requiring transfusion.

METHODS: We performed an electronic search of the Mayo Clinic medical record database to identify patients who had undergone an anesthetic for surgery related to KTS. Review of medical records was performed for type of surgery, anesthetic technique, airway management and difficulty, medications used, intraoperative fluid administration, transfusion requirements, vascular access used, and postoperative complications.
RESULTS: Eighty-two unique patients were identified who underwent 134 general anesthetics and 2 lumbar neuraxial anesthetics for surgeries related to KTS. Preoperatively, 27% of patients had a history of recurrent bleeding, 24% recurrent cellulitis, 9% deep vein thrombosis, and 2% pulmonary embolism. The mean age at time of surgery was 21 ± 15 years. The majority of surgical procedures involved laser coagulation or varicose vein sclerotherapy or stripping. All of the 74 direct laryngoscopies and tracheal intubations were performed on the first attempt without difficulty. Mask ventilation was possible in all 131 patients for whom this was attempted, with only 1 requiring an oral airway. Documented estimated blood loss ranged from 20 to 18,000 mL, with a mean of 740 ± 2739 mL. Use of a tourniquet did not obviate the possibility of substantial blood loss. The only significant postoperative complication involved a calf hematoma after vein stripping and avulsion that required return to the operating room for evacuation.

CONCLUSIONS: Patients with KTS have multiple associated comorbidities relevant to perioperative management. In contrast to previous reports, difficulty with airway management was not encountered. Surgery related to severe KTS may be associated with massive hemorrhage despite tourniquet use, and the anesthesiologist should anticipate the need for appropriate fluid resuscitation. Neuraxial techniques may be considered only if the possibility of trauma to neurovascular malformations has been excluded with recent spine imaging.

Capillary refill time (CRT) is widely used by health care workers as part of the rapid, structured cardiopulmonary assessment of critically ill patients. Measurement involves the visual inspection of blood returning to distal capillaries after they have been emptied by pressure. It is hypothesized that CRT is a simple measure of alterations in peripheral perfusion. Evidence for the use of CRT in anesthesia is lacking and further research is required, but understanding may be gained from evidence in other fields. In this report,
we examine this evidence and factors affecting CRT measurement. Novel approaches to the assessment of CRT are under investigation. In the future, CRT measurement may be achieved using new technologies such as digital videography or modified oxygen saturation probes; these new methods would remove the limitations associated with clinical CRT measurement and may even be able to provide an automated CRT measurement.

The Potential Dual Effects of Anesthetic Isoflurane on Hypoxia-Induced Caspase-3 Activation and Increases in (beta)-Site Amyloid Precursor Protein-Cleaving Enzyme Levels.

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背景：β澱粉樣蛋白(Aβ)積聚、含半胱氨酸的天冬氨酸蛋白水解酶3啓動和β位澱粉樣前體蛋白裂解酶增加潛在的雙重作用

方法：人類H4神經膠質瘤細胞由單純缺氧(3% O2)、不同濃度異氟醚(0.5%和2%)和缺氧聯合0.5%或2%異氟醚處理。我們通過蛋白印跡分析測量含半胱氨酸的天冬氨酸蛋白水解酶3裂解啓動、β位澱粉樣前體蛋白裂解酶和B細胞淋巴瘤-2基因水準。

結果：結果顯示初次處理後0.5%異氟醚處理8小時減弱了缺氧誘導的含半胱氨酸的天冬氨酸蛋白水解酶3啓動和β位澱粉樣前體蛋白裂解酶水準增加作用，而2%異氟醚處理8小時可增強這種作用。2%異氟醚處理也促進了缺氧誘導的B細胞淋巴瘤-2基因水準降低。
BACKGROUND: β-Amyloid protein (Aβ) accumulation, caspase activation, apoptosis, and hypoxia-induced neurotoxicity have been suggested to be involved in Alzheimer disease neuropathogenesis. Aβ is produced from amyloid precursor protein through proteolytic processing by the aspartyl protease β-site amyloid precursor protein-cleaving enzyme (BACE) and γ-secretase. Inhaled anesthetics have long been considered to protect against neurotoxicity. However, recent studies have suggested that the inhaled anesthetic isoflurane may promote neurotoxicity by inducing caspase activation and apoptosis, and by increasing levels of BACE and Aβ. We therefore sought to determine whether isoflurane can induce concentration-dependent dual effectson hypoxia-induced caspase-3 activation and increases in BACE levels: protection versus promotion.

METHODS: H4 human neuroglioma cells were treated with hypoxia (3% O(2)) alone, different concentrations of isoflurane (0.5% and 2%), and the combination of hypoxia and 0.5% or 2% isoflurane. The levels of caspase-3 cleavage (activation), BACE, and Bcl-2 were determined by Western blot analysis.

RESULTS: We show for the first time that treatment with 0.5% isoflurane for 8 hours attenuated, whereas treatment with 2% isoflurane for 8 hours enhanced, hypoxia-induced caspase-3 activation and increases in BACE levels. The 2% isoflurane treatment also enhanced a hypoxia-induced decrease in Bcl-2 levels.

CONCLUSIONS: These results suggest a potential concept that isoflurane has dual effects (protection versus promotion) on hypoxia-induced toxicity, which may act through Bcl-2 family proteins. These findings could lead to more systematic studies to determine the potential dual effects of anesthetics on Alzheimer disease-associated neurotoxicity.
**METHODS**: Male Wistar rats were implanted with 2 intrathecal (IT) catheters, and 1 IT catheter was connected to a mini-osmotic pump, used for either morphine infusion (15 μg/h) or saline (1 μL/h) infusion for 5 days. On day 5, either etanercept (50 μg) or saline (10 μL) was injected after discontinued morphine infusion. Three hours later, acute morphine (15 μg/10 μL, IT) treatment was given and all rats received a nociceptive tail-flick test.

**RESULTS**: The results showed that acute etanercept (50 μg) treatment caused a significant antinociceptive effect of morphine in morphine-tolerant rats. Western blotting indicated that etanercept attenuated the downregulation of membrane glutamate transporters GLT-1 and GLAST in morphine-tolerant rats. Etanercept also inhibited the upregulation of surface AMPA-receptor and N-methyl-d-aspartate–receptor subunits, including GluR1/GluR2 and NR1/NR2A.

**CONCLUSIONS**: These results demonstrate that etanercept partially restores the antinociceptive effect of morphine in morphine tolerance after a morphine challenge. Etanercept has potential for use in the clinical management of pain, particularly in patients who require long-term opioid treatment, and the effectiveness of which can be hampered by tolerance.
The combined effects of anesthesia, motor blockade, and chemically induced sympathectomy after brachial plexus blockade can have a beneficial impact, when applied in selected, isolated diseased states of the upper limb. With the aim of using the prolonged effects of brachial plexus blockade for a future therapeutic application, we demonstrated a dependable methodology of venous blood gas monitoring and confirmed an improved oxygen balance of the blocked versus nonblocked upper extremity in a controlled, prospective study in healthy patients undergoing elective hand surgery.