

ABSTRACTS

Evoked EEG patterns during burst suppression with propofol

A.-M. Huotari, M. Koskinen, K. Suominen, S. Alahuhta, R. Remes, K. M. Hartikainen and V. Jäntti

Results. The EEG response to a painful stimulus had four successive components:

(i) N20 and P22 potentials, reflecting activation of fast somatosensory pathways; (ii) a high-amplitude negative wave, possibly reflecting activation of the somatosensory Cortex SII bilaterally; (iii) a burst (i.e. A negative slow wave with superimposed 10 Hz activity, probably reflecting an arousal mechanism); and (iv) a 1315 Hz spindle, probably originating from the thalamus, similar to sleep spindles. These could be seen separately and in different combinations. Bursts and spindles during burst suppression were also seen without stimulation. In deepening propofol anaesthesia, spindles were seen in the continuous EEG before burst suppression was achieved. In deep anaesthesia, spindles were seen when bursts had ceased, and painful stimuli evoked sharp waves without subsequent bursts.

Conclusion. In addition to SSEP (somatosensory evoked potentials), three different evoked responses are noted that could be useful for clinical monitoring.

Br J Anaesth 2004; 92: 1824

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Effects of ephedrine, dobutamine and dopexamine on cerebral haemodynamics: transcranial Doppler studies in healthy volunteers

I. K. Moppett, M. J. Wild, R. W. Sherman, J. A. Latter, K. Miller and R. P. Mahajan

Results. There was no significant change in the strength of autoregulation (from (mean (SD)) 1.07 (0.16) to 1.07 (0.18); from 1.07 (0.16) to 1.03 (0.19); from 1.04 (0.12) to 1.04 (0.25)), reactivity to carbon dioxide (from 40% (8) to 36 (10); from 37 (12) to 37 (11); from 45 (12) to 43 (11)) with ephedrine, dobutamine, or dopexamine, respectively. Despite a clinically significant increase in MAP with ephedrine and dobutamine and a clinically significant increase in cardiac index with dopexamine, the estimated cerebral perfusion pressure did not change significantly (from 81 (38) to 60 (16) mm Hg with ephedrine; from 67 (22) to 63 (11) mm Hg with dobutamine; from 87 (27) to 79 (17) mm Hg with dopexamine). The ZFP increased significantly with ephedrine (from 29 (10) to 44 (11) mm Hg) and dobutamine (from 35 (14) to 43 (10) mm Hg) but not dopexamine (from 3 (23) to 11 (22) mm Hg).

Conclusions. Sympathomimetic agents do not significantly change cerebrovascular homeostasis as assessed by the transient hyperaemic response test, reactivity to carbon dioxide and estimated cerebral perfusion pressure.

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Strong ions, weak acids and base excess: a simplified FencIStewart approach to clinical acidbase disorders

D. A. Story, H. Morimatsu and R. Bellomo

Methods. We reduced two complex equations for the sodiumchloride effect on base excess to one simple equation: sodiumchloride effect (meq litre⁻¹) = [Na⁺][Cl]³⁸. We simplified the equation of the albumin effect on base excess to an equation with two constants: albumin effect (meq litre⁻¹) = 0.25 × (42[albumin]g litre⁻¹). Using 300 blood samples from critically ill patients, we examined the agreement between the more complex FencIStewart equations and our simplified versions with BlandAltman analyses.

Results. The estimates of the sodiumchloride effect on base excess agreed well, with no bias and limits of agreement of 0.5 to 0.5 meq litre⁻¹. The albumin effect estimates required log transformation. The simplified estimate was, on average, 90% of the FencIStewart

estimate. The limits of agreement for this percentage were 8298%. **Conclusions.** The simplified equations agree well with the previous, more complex equations. Our findings suggest a useful, simple way to use the FencIStewart approach to analyse acidbase disorders in clinical practice.

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Preoperative saline versus gelatin for hip fracture patients; a randomized trial of 396 patients

M. J. Parker, R. Griffiths and A. Boyle

Results. There was no statistically significant difference between groups for mortality (30-day mortality 9/198 for saline group vs 19/198 for colloid group, 95% confidence intervals 0.211.02), length of hospital stay (22.5 days vs 17.3 days, 95% CI 10.78 to 0.38), or occurrence of postoperative complications.

Conclusions. The inclusion of 500 ml of colloid solution to the i.v. fluid regime before hip fracture surgery does not improve outcome.

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Outcome of ASA III patients undergoing day case surgery

G. L. Ansell and J. E. Montgomery

Background. Day case surgery is becoming more acceptable, even for patients with complex medical conditions. Current recommendations suggest that patients who are graded as American Society of Anaesthesiologists physical status (ASA) III may be suitable for this approach. There is only a small amount of published data available to support this. We present a retrospective review of ASA III patients who had undergone day surgical procedures in our unit.

Methods. We carried out a retrospective case controlled review of 896 ASA III patients who had undergone day case procedures between January 1998 and June 2002 using the existing computerized patient information system. The system records admission rates, unplanned contact with healthcare services and post-operative complications in the first 24 h after discharge.

Results. We demonstrated no significant differences in unplanned admission rates, unplanned contact with health care services, or post-operative complications in the first 24 h after discharge between ASA III and ASA I or II patients.

Conclusion. With good pre-assessment and adequate preparation ASA III patients can be treated safely in the day surgery setting.

Br J Anaesth 2004; 92: 714

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Applied anatomy of the superior vena cava the carina as a landmark to guide central venous catheter placement

K. Albrecht, H. Nave, D. Breitmeier, B. Panning and H. D. Tröger

Background. The FencIStewart approach to acidbase disorders uses five equations of varying complexity to estimate the base excess effects of the important components: the strong ion difference (sodium and chloride), the total weak acid concentration (albumin) and unmeasured ions. Although this approach is straightforward, most people would need a calculator to use the equations. We proposed four simpler equations that require only mental arithmetic and tested the hypothesis that these simpler equations would have good agreement with more complex FencIStewart equations.

Methods. We reduced two complex equations for the sodiumchloride effect on base excess to one simple equation: sodiumchloride effect (meq litre⁻¹) = [Na⁺][Cl]³⁸. We simplified the equation of the albumin effect on base excess to an equation with two constants: albumin effect (meq litre⁻¹) = 0.25 × (42[albumin]g litre⁻¹). Using 300 blood samples from critically ill patients, we

examined the agreement between the more complex FencIStewart equations and our simplified versions with BlandAltman analyses.

Results. The estimates of the sodiumchloride effect on base excess agreed well, with no bias and limits of agreement of 0.5 to 0.5 meq litre⁻¹. The albumin effect estimates required log transformation. The simplified estimate was, on average, 90% of the FencIStewart estimate. The limits of agreement for this percentage were 8298%.

Conclusions. The simplified equations agree well with the previous, more complex equations. Our findings suggest a useful, simple way to use the FencIStewart approach to analyse acidbase disorders in clinical practice.

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Shortcomings of cuffed paediatric tracheal tubes

M. Weiss, A. Dullenkopf, C. Gysin,
C. M. Dillier and A. C. Gerber

Background. Cardiac tamponade is a serious complication of central venous catheter (CVC) insertion. Current guidelines strongly advise that the CVC tip should be located in the superior vena cava (SVC) and outside the pericardial sac. This may be difficult to verify as the exact location of the pericardium cannot be seen on a normal chest x-ray. The carina is an alternative radiographic marker for correct CVC placement, suggested on the basis of studies of embalmed cadavers.

Methods. We set out to confirm this radiographic landmark in 39 fresh cadavers (age 58.4 (3.4) (mean and SE) yr) and to compare the results with those from ethanolformalin-fixed cadavers.

Results. We found that the carina was 0.8 (0.05) cm above the pericardial sac as it transverses the SVC. In no case was the carina inferior to the pericardial reflection and our study confirmed the previous findings. All the measured distances were significantly greater in fresh cadavers.

Conclusions. We confirm that the carina is a reliable, simple anatomical landmark that can be identified *in vivo* for the correct placement of CVCs outside the boundaries of the pericardial sac.

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Shortcomings of cuffed paediatric tracheal tubes

M. Weiss, A. Dullenkopf, C. Gysin,
C. M. Dillier and A. C. Gerber

Background. The goal of this investigation was to evaluate adequacy of the design of readily available paediatric cuffed tracheal tubes (CPTT).

Methods. In 15 series of cuffed (11) and uncuffed (four) paediatric tracheal tubes (ID: 2.57.0 mm) from four different manufacturers the following dimensions were measured: outer diameter of the tube, position and largest diameter of the tube cuff inflated at 20 cm H₂O and position of depth markings and compared with age-related dimensions.

Results. Outer diameters for tubes with similar IDs varied markedly between manufacturers and between cuffed and uncuffed tracheal tubes from the same manufacturer. Cuff diameters at 20 cm H₂O cuff pressure and cross-sectional cuff area at 20 cm H₂O cuff pressure did not always cover maximal internal age-related tracheal diameters and cross-sectional areas. Placing the tube tip in the mid-trachea, the cuffs of cuffed tubes with ID 3.0, 4.0, or 5.0 mm would become positioned within the larynx. If the cuffs were placed 1 cm below the cricoid level, many of the tube tips would be dangerously deep within the trachea. Only five of the 11 cuffed tubes had a depth marking. In many of these tubes the distances from depth marking to tube tip were greater than the age-related minimal tracheal length.

Conclusion. Most cuffed paediatric tracheal tubes are poorly designed, in particular the smaller sizes. A better design of cuffed tubes with a short high-volume, low-pressure cuff, cuff-free subglottic space and adequately placed depth markings are urgently needed.

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Comparison of the role of endothelin, vasopressin and angiotensin in arterial pressure regulation during sevoflurane anaesthesia in dogs

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and T. W. L. Scheeren

Background. In this study we aimed to clarify the role of endothelin in arterial pressure regulation during anaesthesia with increasing concentrations of sevoflurane (13 MAC) and compare it with those of vasopressin and angiotensin.

Methods. After an awake control period, on different days, six dogs underwent each of the following four interventions: sevoflurane anaesthesia alone (13 MAC), sevoflurane after block of either endothelin receptors using tezosentan (3 mg kg⁻¹ followed by 3 mg kg⁻¹ h⁻¹), vasopressin V_{1a} receptors using [d(CH₂)₅Tyr(Me²)]AVP (40 µg kg⁻¹) or angiotensin receptors using losartan (6 mg kg⁻¹ h⁻¹). Plasma concentrations of endothelin, big endothelin, vasopressin and renin were measured. Effects of sevoflurane in the presence and absence of the respective receptor block were analysed and compared using analysis of variance for repeated measures (ANOVA followed by Fisher's PLSD (protected least significant difference) (*P*<0.05)).

Results. Mean arterial pressure decreased in a dose-dependent manner with sevoflurane during all interventions. At 1 MAC, this decrease was greatest during angiotensin receptor block (mean (SEM), 41 (3) mm Hg), intermediate during vasopressin and endothelin receptor block (31 (4) and 30 (2) mm Hg respectively), and least during sevoflurane alone (24 (3) mm Hg). The course of systemic vascular resistance mirrored the course of arterial pressure, while cardiac output did not differ between groups. Plasma concentrations of endothelin, big endothelin and renin did not change during any intervention, whereas vasopressin concentration increased from 0.5 to 40 ng litre⁻¹ at 3 MAC as arterial pressure decreased in all groups.

Conclusions. At 1 MAC, angiotensin attenuated the decrease in arterial pressure during sevoflurane anaesthesia more than endothelin and vasopressin. However, at higher MAC only vasopressin was specifically activated to partly compensate for the arterial pressure decrease.

Br J Anaesth 2004; 92: 1028



Obstetric epidurals and chronic adhesive arachnoiditis

I. Rice, M. Y. K. Wee and K. Thomson

It has been suggested that obstetric epidurals lead to chronic adhesive arachnoiditis (CAA). CAA is a nebulous disease entity with much confusion over its symptomatology. This review outlines the pathological, clinical, and radiological features of the disease. The proposed diagnostic criteria for CAA are: back pain that increases on exertion, with or without leg pain; neurological abnormality on examination; and characteristic MRI findings. Using these criteria, there is evidence to show that epidural or subarachnoid placement of some contrast media, preservatives and possibly vasoconstrictors, may lead to CAA. No evidence was found that the preservative-free, low concentration bupivacaine with opioid mixtures or plain bupivacaine currently used in labour lead to CAA.

Br J Anaesth 2004; 92: 10920



Methicillin resistant *Staphylococcus aureus* in the critically ill

K. J. Hardy, P. M. Hawkey, F. Gao
and B. A. Oppenheim

Methicillin resistant *Staphylococcus aureus* (MRSA) is endemic within many hospitals worldwide. Critically ill patients on intensive care units have increased risk factors making them especially prone to nosocomially acquired infections. This review addresses the current situation regarding the evolution of MRSA and the techniques for identifying and epidemiologically typing it. It discusses specific risk factors, the morbidity and mortality associated with critically ill patients, and possibilities for future antibiotic treatments.

Br J Anaesth 2004; 92: 12130

Use of a ProSeal™ laryngeal mask airway for airway maintenance during emergency Caesarean section after failed tracheal intubation
R. Awan, J. P. Nolan and T. M. Cook

We report the use of the ProSeal™ laryngeal mask airway to establish and maintain the airway during emergency Caesarean section when tracheal intubation had failed with conventional laryngoscopy and mask ventilation was difficult. The ProSeal™ laryngeal mask allowed controlled ventilation without gas leak and facilitated drainage of the stomach.
Br J Anaesth 2004; 92: 1446

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Ketamine Improves the Management of Exaggerated Postoperative Pain Observed in Perioperative Fentanyl-treated Rats.

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Abstract:

Background: Although opioids are unsurpassed analgesics, experimental and clinical studies suggest that opioids activate N-methyl-d-aspartate pronociceptive systems leading to pain hypersensitivity and short-term tolerance. Because it is difficult in humans to differentiate pain from hyperalgesia during the postoperative period, the authors performed experimental studies with fentanyl using the rat incisional pain model for evaluating relations between hyperalgesia and short-term tolerance. Because N-methyl-d-aspartate receptor antagonists oppose both pain hypersensitivity and tolerance induced by opioids, the authors examined the capability of ketamine for improving exaggerated postoperative pain management.

Methods: During halothane anesthesia, a hind paw plantar incision was performed in rats receiving four fentanyl subcutaneous injections (100 [μg]/kg per injection, every 15 min). In some groups, three subcutaneous ketamine injections (10 mg/kg per injection, every 5 h) were performed in saline- or fentanyl-treated rats. One day after surgery, the analgesic effect of morphine (2 mg/kg subcutaneous) was tested. Analgesia, mechanical hyperalgesia, tactile allodynia, and pain score were assessed for several days using the paw pressure vocalization test, the von Frey application test, and the postural disequilibrium test.

Results: Fentanyl induced analgesia but also produced exaggerated postoperative pain as indicated by the enhancement of hyperalgesia, allodynia, and weight-bearing decrease after hind paw plantar incision. Ketamine pretreatment prevented such a fentanyl-induced enhancement of postoperative pain and improved its management by morphine.

Conclusions: By opposing postoperative pain hypersensitivity and subsequent short-term tolerance induced by perioperative opioid use, ketamine not only improves exaggerated postoperative pain management but also provides better postoperative rehabilitation.

Anesthesiology. 102(2):421-428, February 2005.

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Continuous Infusion of Ropivacaine for Pain Relief after Iliac Crest Bone Grafting for Shoulder Surgery.

Stephan Blumenthal, M.D.; Alexander Dullenkopf, M.D.; Katharina Rentsch, M.D.; Alain Borgeat, M.D.

Abstract:

Background: The aim of the study was to compare the efficacy of either ropivacaine or placebo through an iliac crest (IC) catheter after Bankart repair with IC bone grafting.

Methods: With approval of the local ethics committee and after written informed consent was obtained, 36 patients had an interscalene catheter placed preoperatively. Intraoperatively, the surgeon placed a catheter at the IC donor site. At the end of surgery, 30 ml ropivacaine, 0.5% (ropivacaine group), or 30 ml NaCl, 0.9%

(placebo group), was administered. Ropivacaine, 0.2%, was started 6 h after the initial block through the interscalene catheter for 48 h (t48) in all patients. At t0, the patient received either 5 ml/h ropivacaine, 0.2% (ropivacaine group), or 5 ml/h NaCl, 0.9% (placebo group), for 48 h through the IC catheter. All patients received an intravenous morphine patient-controlled analgesia device. Pain scores at the shoulder and at the IC donor site were assessed at rest and during motion every 8 h for 48 h and after 3 months. Plasma concentrations of total and unbound ropivacaine, morphine consumption, and patient satisfaction were assessed.

Results: At the IC donor site, pain was significantly lower in the ropivacaine group compared with the placebo group at rest and during motion at any time. Total and unbound plasma concentrations of ropivacaine were below the toxic threshold in both groups. Morphine consumption was significantly lower in the ropivacaine group after 24 and 48 h. Patient satisfaction was significantly higher in the ropivacaine group. At 3 months, pain at the IC during motion was significantly lower in the ropivacaine group.

Conclusions: Continuous application of 0.2% ropivacaine through an IC catheter after Bankart repair with IC bone grafting is an effective method for pain relief for the first 48 h, with few adverse effects and high patient satisfaction. The benefit of this technique is still present after 3 months.

Anesthesiology. 102(2):392-397, February 2005.

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Action of Isoflurane on the Substantia Gelatinosa Neurons of the Adult Rat Spinal Cord.

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Abstract:

Background: Although isoflurane, a volatile anesthetic, can block the motor response to noxious stimulation (immobility and analgesia) and suppress autonomic responsiveness, how it exerts these effects at the neuronal level in the spinal cord is not fully understood.

Methods: The effects of a clinically relevant concentration (1 rat minimum alveolar concentration [MAC]) of isoflurane on electrically evoked and spontaneous excitatory/inhibitory transmission and on the response to exogenous administration of the [gamma]-aminobutyric acid type A receptor agonist muscimol were examined in lamina II neurons of adult rat spinal cord slices using the whole cell patch clamp technique. The effect of isoflurane on the action potential-generating membrane property was also examined.

Results: Bath-applied isoflurane (1.5%, 1 rat MAC) diminished dorsal root-evoked polysynaptic but not monosynaptic excitatory postsynaptic currents. Glutamatergic miniature excitatory postsynaptic currents were also unaffected by isoflurane. In contrast, isoflurane prolonged the decay phase of evoked and miniature [gamma]-aminobutyric acid type A receptor-mediated inhibitory postsynaptic currents and increased the amplitude of the muscimol-induced current. Isoflurane had little effect on action potential discharge activity.

Conclusions: Isoflurane augments [gamma]-aminobutyric acid-mediated inhibitory transmission, leading to a decrease in the excitability of spinal dorsal horn neurons. This may be a possible mechanism for the antinociceptive effect of isoflurane in the spinal cord.

Anesthesiology. 102(2):379-386, February 2005.

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Human Kidneys Play an Important Role in the Elimination of Propofol.

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Abstract:

Background: Extrahepatic clearance of propofol has been suggested because its total body clearance exceeds hepatic blood flow. However, it remains uncertain which organs are involved in the extrahepatic clearance of propofol. In vitro studies suggest that the

kidneys contribute to the clearance of this drug. The purpose of this study was to confirm whether human kidneys participate in propofol disposition in vivo.

Methods: Ten patients scheduled to undergo nephrectomy were enrolled in this study. Renal blood flow was measured using para-aminohippurate. Anesthesia was induced with vecuronium (0.1 mg/kg) and propofol (2 mg/kg) and then maintained with nitrous oxide (60%), sevoflurane (1~2%) in oxygen, and an infusion of propofol (2 mg [middle dot] kg⁻¹ [middle dot] h⁻¹). Radial arterial blood for propofol and para-aminohippurate analysis was collected from a cannula inserted in the radial artery. The renal venous sample and the radial arterial sample were obtained at the same time after the steady state of propofol was established.

Results: The renal extraction ratio of propofol was 0.58 +/- 0.15 (mean +/- SD). The renal clearance of propofol was 0.41 +/- 0.15 l/min (mean +/- SD), or 27 +/- 9.9% (mean +/- SD) of total body clearance.

Conclusion: Human kidneys play an important role in the elimination of propofol.

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Type 2 Diabetes Mellitus and the Catabolic Response to Surgery.

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Abstract:

Background: The authors tested the hypothesis that the catabolic responses to colorectal surgery are amplified in the presence of type 2 diabetes mellitus.

Methods: Seven nondiabetic and seven diabetic patients underwent a 6-h stable isotope infusion study (3 h fasted, 3-h glucose infusion at 4 mg [middle dot] kg⁻¹ [middle dot] min⁻¹) on the second postoperative day. Leucine rate of appearance (Ra), leucine oxidation, nonoxidative leucine disposal, and glucose Ra were assessed by L-[1-¹³C]leucine and [6,6-²H₂]glucose. Circulating concentrations of glucose, lactate, insulin, glucagon, and cortisol also were determined.

Results: Diabetic patients had a higher leucine oxidation than nondiabetic patients (P = 0.0003), whereas leucine Ra and nonoxidative leucine disposal were not different. Administration of glucose did not affect leucine kinetics regardless of whether patients were diabetic. In diabetic patients, glucose Ra was greater than in the nondiabetic group (P = 0.0032). Glucose infusion suppressed the endogenous glucose Ra to a lesser extent in diabetic than in nondiabetic patients (P = 0.0048). Plasma glucose concentrations were higher in diabetic than in nondiabetic patients (P = 0.0203), both in the postabsorptive and the fed state. Circulating concentrations of glucagon were higher (P = 0.0065) and concentrations of insulin were lower (P = 0.0146) in the presence of diabetes, resulting in a lower insulin/glucagon ratio (P = 0.0002). In diabetic patients, the insulin/glucagon ratio increased during glucose infusion to a lesser extent than in the nondiabetic group (P = 0.0014).

Conclusion: Protein catabolism after colorectal surgery is increased in patients with type 2 diabetes mellitus as reflected by an increased oxidative protein loss.

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Cricoid Pressure Does Not Increase the Rate of Failed Intubation by Direct Laryngoscopy in Adults.

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Trépanier, M.D., F.R.C.P.C.; Sylvie Marcoux, M.D., Ph.D.; Martin R. Lessard, M.D., F.R.C.P.C.

Abstract:

Background: Cricoid pressure (CP) is applied during induction of

anesthesia to prevent regurgitation of gastric content and pulmonary aspiration. However, it has been suggested that CP makes tracheal intubation more difficult. This double-blind randomized study evaluated the effect of CP on orotracheal intubation by direct laryngoscopy in adults.

Methods: Seven hundred adult patients undergoing general anesthesia for elective surgery were randomly assigned to have a standardized CP (n = 344) or a sham CP (n = 356) during laryngoscopy and intubation. After anesthesia induction and complete muscle relaxation, a 30-s period was allowed to complete intubation with a Macintosh No. 3 laryngoscope blade. The primary endpoint was the rate of failed intubation at 30 s. The secondary endpoints included the intubation time, the Cormack and Lehane grade of laryngoscopic view, and the Intubation Difficulty Scale score.

Results: Groups were similar for demographic data and risk factors for difficult intubation. The rates of failed intubation at 30 s were comparable for the two groups: 15 of 344 (4.4%) and 13 of 356 (3.7%) in the CP and sham CP groups, respectively (P = 0.70). The grades of laryngoscopic view and the Intubation Difficulty Scale score were also comparable. Median intubation time was slightly longer in the CP group than in the sham CP group (11.3 and 10.4 s, respectively, P = 0.001).

Conclusions: CP applied by trained personnel does not increase the rate of failed intubation. Hence CP should not be avoided for fear of increasing the difficulty of intubation when its use is indicated.

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Hemodynamic Changes after Protamine Administration: Association with Mortality after Coronary Artery Bypass Surgery.

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Abstract:

Background: Protamine sulfate is standard therapy to reverse heparin anticoagulation. Hemodynamic responses to protamine are common, ranging from minor perturbations to cardiovascular collapse. Although severe fatal reactions occur, the relation of less extreme responses with postoperative mortality is unknown. Therefore, the authors tested the hypothesis that hemodynamic "protamine reactions" (systemic hypotension and pulmonary hypertension) are associated with mortality after cardiac surgery.

Methods: In a university hospital setting, the authors studied 6,921 coronary bypass patients using automated anesthesia record-keeping data and quality assurance databases. Degree/duration integrals of systemic hypotension (< 100 mmHg) and pulmonary hypertension (> 30 mmHg) for the 30-min after protamine administration were assessed for linear associations with mortality using multiple logistic regression models adjusting for risk factors.

Results: Overall mortality was 2%; greater hemodynamic responses were associated with increased mortality by odds ratios of 1.28 (systemic hypotension: 95% confidence interval, 1.14-1.43; P < 0.001) and 1.27 (pulmonary hypertension: 95% confidence interval, 1.06-1.48; P < 0.001) per 150- mmHg [middle dot] min increment. Proximity of the response to protamine administration strengthened the relation, which persisted after exclusion of major hemodynamic disturbances. Tests for linearity confirmed an association even at the lowest range of values for both pressure effects.

Conclusions: Hemodynamic perturbations after protamine administration are independently related to in-hospital mortality after primary coronary artery bypass surgery; the relation is present even in the lowest observed range of values for both systemic hypotension and pulmonary hypertension. Although randomized trials are necessary to address causality, this evidence suggests that strategies that avoid or attenuate these reactions may improve patient care.

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