

Abstracts

A Randomized Trial of Dural Puncture Epidural Technique Compared With The Standard Epidural Technique For Labor Analgesia

Eric Cappiello, Nollag O'Rourke, Scott Segal, MD, and Lawrence C.

BACKGROUND: We designed this prospective, double-blind, randomized study to examine whether a dural puncture without intrathecal drug administration immediately before epidural drug administration would improve labor analgesia when compared to a traditional epidural technique without prior dural puncture.

METHODS: Eighty nulliparous parturients with cervical dilation less than 5 cm were randomly assigned to receive a standardized epidural technique, with or without a single dural puncture with a 25-gauge (G) Whitacre spinal needle. After successful placement of the needle(s) and the epidural catheter, 12 mL of bupivacaine 2.5 mg/mL was administered through the epidural catheter and a patient-controlled epidural infusion of bupivacaine 1.25 mg/mL + fentanyl 2 µg/mL was initiated. The presence of sacral analgesia (S1) and pain scores were compared between groups.

RESULTS: In demographically similar groups, parturients with prior dural puncture had more frequent blockade of the S1 dermatome, more frequent visual analog scale scores <10/100 at 20 min and reduced one-sided analgesia. The highest median sensory level (T10) was no different between groups.

CONCLUSIONS: Dural puncture with a 25-G spinal needle immediately before the initiation of epidural analgesia improves the sacral spread, onset, and bilateral pain relief produced by analgesic concentrations of bupivacaine with fentanyl in laboring nulliparous patients. (*Anesth Analg* 2008; 107:1646-1651) Acupuncture in patients with headache Jena, S; Witt, CM1; Brinkhaus, B1; Wegscheider, K2; Willich, SN We aimed to investigate the effectiveness of acupuncture in addition to routine care in patients with primary headache (>12months, two or more headaches/month) compared with treatment with routine care alone and whether the effects of acupuncture differ in randomized and non-randomized patients. In a randomized controlled trial plus non-randomized cohort, patients with headache were allocated to receive up to 15 acupuncture sessions over 3months or to a control group receiving no acupuncture during the first 3months. Patients who did not consent to randomization received acupuncture treatment immediately. All subjects were allowed usual medical care in addition to study treatment. Number of days with headache, intensity of pain and health-related quality of life (SF-36) were assessed at baseline, and after 3 and 6months using standardized questionnaires. of 15056 headache patients (mean age 44.1±12.8years, 77% female), 1613 were randomized to acupuncture and 1569 to

control, and 11874 included in the non-randomized acupuncture group. At 3months, the number of days with headache decreased from 8.4±7.2 (estimated mean ±s.e.) to 4.7±5.6 in the acupuncture group and from 8.1±6.8 to 7.5±6.3 in the control group (P<0.001). Similarly, intensity of pain and quality of life improvements were more pronounced in the acupuncture vs. control group (P<0.001). Treatment success was maintained through 6months. The outcome changes in non-randomized patients were similar to those in randomized patients. Acupuncture plus routine care in patients with headache was associated with marked clinical improvements compared with routine care alone. (*Cephalalgia*, Volume 28, Number 9, September 2008, pp. 969-979(11))

Complementary Therapies for Neuropathic and Neuralgic Pain: Systematic Review.

Pittler, Max H., Ernst, Edzard

To assess the evidence from rigorous clinical trials, systematic reviews, and meta-analyses of complementary and alternative therapies for treating neuropathic and neuralgic pain, data on the following complementary and alternative medicine treatments were identified: acupuncture, electrostimulation, herbal medicine, magnets, dietary supplements, imagery, and spiritual healing. On the basis of our findings, the evidence is not fully convincing for most complementary and alternative medicine modalities in relieving neuropathic or neuralgic pain. However, for topically applied capsaicin there is evidence of effectiveness beyond placebo. The evidence can be classified as encouraging and warrants further study for cannabis extract, magnets, carnitine, and electrostimulation. (*Clinical Journal of Pain*. 24(8):731-733, October 2008.)

Desmopressin Reduces Transfusion Needs after Surgery: A Meta-analysis of Randomized Clinical Trials.

Crescenzi G, Landoni G, Biondi-Zoccai G, et al.

Background: Perioperative pathologic microvascular bleeding is associated with increased morbidity and mortality and could be reduced by hemostatic drugs. At the same time, safety concerns regarding existing hemostatic agents include excess mortality. Numerous trials investigating desmopressin have lacked power to detect a beneficial effect on transfusion of blood products. The authors performed a meta-analysis of 38 randomized, placebo-controlled trials (2,488 patients) investigating desmopressin in surgery and indicating at least perioperative blood loss or transfusion of blood products.

Methods: Pertinent studies were searched in BioMed Central, CENTRAL, and PubMed (updated May 1, 2008). Further hand

or computerized searches involved recent (2003-2008) conference proceedings.

Results: In most of the included studies, 0.3 [μ]g/kg desmopressin was used prophylactically over a 15- to 30-min period. In comparison with placebo, desmopressin was associated with reduced requirements of blood product transfusion (standardized mean difference = -0.29 [-0.52 to -0.06] units per patient; $P = 0.01$), which were more pronounced in the subgroup of noncardiac surgery and were without a statistically significant increase in thromboembolic adverse events (57/1,002 = 5.7% in the desmopressin group vs. 45/979 = 4.6% in the placebo group; $P = 0.3$).

Conclusions: Desmopressin slightly reduced blood loss (almost 80 ml per patient) and transfusion requirements (almost 0.3 units per patient) in surgical patients, without reduction in the proportion of patients who received transfusions. This meta-analysis suggests the importance of further large, randomized controlled studies using desmopressin in patients with or at risk of perioperative pathologic microvascular bleeding. (*Anesthesiology*. 109(6):1063-1076, December 2008.)

Gabapentin Acts within the Locus Coeruleus to Alleviate Neuropathic Pain.

Hayashida, Ken-ichiro ; Obata, Hideaki ; Nakajima, Kunie ; Eisenach, James C.

Background: Gabapentin recruits descending inhibition to produce analgesia after nerve injury, but whether this is a local action in the brainstem is unknown. The authors hypothesized that gabapentin activates noradrenergic neurons in the locus coeruleus (LC) by a local action.

Methods: Male rats underwent L5-L6 spinal nerve ligation (SNL) and received drugs by intra-LC or systemic routes for behavior testing, immunohistochemistry in the LC, and microdialysis in the spinal dorsal horn. In other studies, brainstem slices from normal and SNL animals were used for immunohistochemistry.

Results: SNL increased phosphorylated cyclic adenosine monophosphate response element binding protein (pCREB)-expressing nuclei bilaterally in the LC, and increased noradrenaline release in the spinal dorsal horn. Gabapentin, whether in isolated brainstem slices or in conscious or anesthetized animals, increased pCREB-expressing nuclei in the LC. The net increase in pCREB expression by gabapentin did not differ between normal and SNL conditions. This gabapentin-induced pCREB activation in LC neurons was abolished by an AMPA receptor antagonist, 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX). Intra-LC-injected gabapentin reduced hypersensitivity in SNL rats in a dose-dependent manner. Both intra-LC coadministration of CNQX

and intrathecal administration of the [α]2-adrenoceptor antagonist idazoxan blocked antihypersensitivity by intra-LC gabapentin. Intravenous gabapentin induced noradrenaline release in the spinal dorsal horn. The net amount of noradrenaline release by gabapentin is larger in SNL rats compared with the normal condition, although the percentage increases from the baseline were the same.

Conclusions: These results suggest that gabapentin acts directly in the brainstem via a glutamate-dependent mechanism to stimulate descending inhibition to produce antihypersensitivity after peripheral nerve injury. (*Anesthesiology*. 109(6):1077-1084, December 2008.)

Phase 2, Double-blind, Placebo-controlled, Dose-Response Trial of Intravenous Adenosine for Perioperative Analgesia.

Habib, Ashraf S. ; Minkowitz, Harold ; Osborn, Timothy ; Ogunnaike, Babatunde et al.

Background: Adenosine regulates pain transmission by actions at spinal, supraspinal, and peripheral sites. A few studies have suggested that administration of adenosine might be associated with anesthetic- and analgesic-sparing effects. The primary aim of this multicenter study was to determine the dose-response profile of adenosine with respect to perioperative analgesia.

Methods: Women undergoing major gynecologic surgery were enrolled. Subjects were randomly assigned to receive one of four doses of adenosine (25, 50, 100, or 200 [μ]g [\cdot] kg⁻¹ [\cdot] min⁻¹) or matching placebo. A dose-escalation cohort approach was followed. Study drug administration was started in the operating room at the time of skin incision and discontinued at the end of surgery. The anesthetic technique was standardized. Postoperative analgesia was provided with a standardized morphine patient-controlled analgesia system. Data were collected in the hospital and after discharge daily through postoperative day 7.

Results: A total of 166 subjects received treatment with study drug: 125 received adenosine and 41 received placebo. Except for height, there were no differences between treatment groups with respect to demographic or baseline characteristics. Cumulative opioid use during the initial 24-h period after extubation was not significantly different between treatment groups. There were also no differences between treatment groups with respect to cumulative anesthetic use, intraoperative opioid requirements, pain scores, sedation, time to readiness for discharge from the postanesthesia care unit, time to readiness for discharge from the hospital, opioid-related symptom distress scores, patient satisfaction with pain control, and occurrence of adverse events.

Conclusions: There were no differences between placebo and

adenosine with respect to efficacy and safety for perioperative analgesia. (*Anesthesiology*. 109(6):1085-1091, December 2008.)

Thoracic Epidural Analgesia with Low Concentration of Bupivacaine Induces Thoracic and Lumbar Sympathetic Block: A Randomized, Double-blind Clinical Trial.

Freise, Hendrik; Meissner, Andreas; Lauer, Stefan et al.

Background: Clinical benefits of thoracic epidural anesthesia (TEA) are partly ascribed to thoracic sympathetic block. However, data regarding sympathetic activity during TEA are scarce and contradictory. This prospective, randomized, double-blind study evaluated the segmental propagation of sympathetic block after low-concentration, high-volume TEA using digital thermography.

Methods: Twenty-four patients were included in the study. Thoracic epidural catheters were placed at a median insertion level of T8-T9. Patients were accommodated for 20 min to the room temperature of 23[degrees] +/- 0.3[degrees]C. Skin temperature was recorded by digital thermography. After baseline measurement of heart rate, arterial pressure, and core body and skin temperature, 10 ml saline (control group) or 10 ml bupivacaine, 0.25% (TEA group), respectively, was administered epidurally. Five minutes (t5) and 20 min (t20) after baseline measurements, hemodynamic parameters and core body temperature were again measured, and sensory block was identified by loss of cold-warm discrimination. In the thumb, the toe, and each thoracic dermatome, difference from baseline temperature was calculated at t5 and t20. Data were analyzed by Mann-Whitney U test.

Results: Baseline characteristics did not differ among groups. Median spread of sensory block at t20 was T5-L5. At both t5 and t20, skin temperature decreased more in the control group than in the TEA group in all thoracic dermatomes ($P < 0.05$). Toe temperature increased in the TEA group compared with the control group ($P < 0.05$), whereas thumb temperature remained unchanged.

Conclusion: TEA with 10 ml bupivacaine, 0.25%, induced thoracic and lumbar sympathetic block that precedes and exceeds sensory block. Caudal limit of sympathetic block could not be demonstrated in this study. (*Anesthesiology*. 109(6):1107-1112, December 2008.)

Sympathetic Nervous System: Evaluation and Importance for Clinical General Anesthesia.

Neukirchen M.; Kienbaum P.

For more than 100 yr, scientists have studied the sympathetic nervous system and its cardiovascular control mechanisms. Muscle sympathetic activity is the most important direct and rapidly responding variable for evaluation of sympathetic neural

outflow. Because of its significance in response to environmental challenges and its role in cardiovascular control, great attention has been paid to the sympathetic nervous system in both health and disease and, more recently, also during general anesthesia. In fact, general anesthesia can also be considered as an investigational tool to assess mechanisms of cardiovascular regulation. This review evaluates different methods for determination of sympathetic nervous system activity and describes its role in human neurohumoral circulatory control. Furthermore, the effects of general anesthesia on sympathetic nervous system activity and their relevance for clinical anesthesia are discussed. (*Anesthesiology*. 109(6):1113-1131, December 2008.)

Anesthetic Technique for Radical Prostatectomy Surgery Affects Cancer Recurrence: A Retrospective Analysis.

Biki B, Mascha E, Moriarty DC, et al.

Men undergoing radical prostatectomy to treat prostate cancer are less likely to experience biochemical recurrence if they receive regional analgesia with anesthesia, rather than post-operative analgesia, research suggests.

Both general anesthesia and post-operative opioids suppress various immune functions, potentially shifting the balance toward disease recurrence.

Buggy et al found that, over the next 4 years, patients given epidural anesthesia and analgesia were 57% less likely than those given opioids to suffer biochemical recurrence, defined as a rise in prostate-specific antigen (PSA) level that prompted adjuvant therapy. The researchers found a similar association when they propensity-matched epidural analgesia patients with opioid patients, with epidural analgesia associated with a 49% reduction in recurrence risk.

Other independent predictors of recurrence were Gleason score and pre-operative PSA level.

"Regional anesthesia and analgesia may help to preserve immune function by attenuating the surgical stress response, decreasing anesthetic requirement, and diminishing the need for opioids," the team concludes. (*Anesthesiology* 2008; 109: 180187.)'

Acute pain trajectories in postoperative and emergency medicine patients.

Chapman CR, Donaldson GW, Davis J, et al.

Acute pain trajectories improve evaluation of patient discomfort. US researchers have found that considering pain as a function of time can help physicians better gauge the level of acute pain that patients experience in the immediate postoperative or emergency period. The study used an 11-point numerical rating scale, which gauged the worst pain possible as a

score of 10 and no pain as a score of zero.

For their investigation, the researchers studied 502 patients who had undergone surgical procedures and 513 patients who been admitted for emergency room treatment, asking them to rate their level of pain on a daily basis for a period of 6 days.

"For modeling purposes, we construe change in pain over time as an underlying latent process, or linear growth curve," said the researchers. This assumes that each individual has two quantifiable features, an intercept or initial pain level, and a slope, or rate of pain resolution. Using the model, distinct patterns of acute pain were observed among the patient populations. Indeed, 15% of emergency department patients and 24% of postoperative patients did not have reduced levels of pain over the course of the study, as evidenced by "zero or positive slopes" over the 6 days.

Patients admitted to emergency departments were found to suffer more acute pain on average than patients who had undergone surgical procedures that would normally require pain management. They also found that women were more likely than men to initially report higher levels of pain.

"It is possible to improve the precision and quality of measurement [of acute pain] by characterizing acute pain as a trajectory, that is, a change over time."

Analgesic Effects of Sazetidine-A, a New Nicotinic Cholinergic Drug.

Cucchiaro G; Xiao Y; Gonzalez-Sulser A; Kellar, Kenneth J.

Background: The use of nicotinic agonists for analgesia is limited by their unacceptable side effects. Sazetidine-A is a new partial agonist nicotinic ligand that has very high selectivity for [beta]2-containing nicotinic acetylcholine receptors. It potently and selectively desensitizes [alpha]4[beta]2 nicotinic acetylcholine receptors without measurable effects on [alpha]3[beta]4 receptors. The authors investigated the analgesic effects of Sazetidine-A using the formalin model of chronic inflammatory pain.

Methods: The formalin test was conducted after rats received intraperitoneal saline, Sazetidine-A (0.125, 0.25, 0.5, 1, 2 mg/kg), or subcutaneous epibatidine (2.5-5-10 [mu]g/kg). In other experiments, Sazetidine-A was preceded by naloxone (0.5 mg/kg) or mecamylamine (10 mg). Effects of Sazetidine-A and epibatidine on locomotor were tested in an open field, and

seizure activity was measured using the Racine scale. Locus coeruleus neuron extracellular single-unit spontaneous discharge was recorded in anesthetized animals after Sazetidine-A and epibatidine.

Results: Higher doses of Sazetidine-A (0.5, 1, or 2 mg/kg) induced analgesia, with pain scores significantly lower than those seen after saline, lower doses of Sazetidine-A, and epibatidine ($P < 0.001$). Naloxone did not antagonize the effects of Sazetidine-A, and mecamylamine had partial, dose-dependent antagonistic effects. Epibatidine excited locus coeruleus neurons, whereas Sazetidine-A had no effect on these neurons. Epibatidine and Sazetidine-A affected animals' locomotor activity for the initial 20 min. While analgesic doses of epibatidine caused seizures, no seizure activity or other neurologic complications were seen in animals that received as much as four times the minimum analgesic dose of Sazetidine-A.

Conclusions: Sazetidine-A seems to be a potent analgesic without causing neurologic side effects. (*Anesthesiology*. 109(3):512-519, September 2008.)

Radiofrequency Applications to Dorsal Root Ganglia: A Literature Review.

Malik K; Benzon H.

Application of radiofrequency currents to the dorsal root ganglia, in the treatment of various pain syndromes, has been clinically practiced for more than 30 yr. The clinical efficacy and the safety of this technique, however, remain poorly understood. The authors reviewed the literature on this modality of pain relief to determine its clinical efficacy, safety, and mechanisms of action. The two modalities in common clinical use were pulsed and continuous mode radiofrequency. These techniques were generally found to be safe, and the majority of the observational studies reported their clinical efficacy. Five randomized controlled trials evaluated their clinical use; these trials were relatively short-termed and small in size, and their results were variable. The mechanism of action of these techniques was unclear. Larger controlled clinical trials evaluating the long-term effects of these techniques and basic science research to determine their precise mode of action are needed. (*Anesthesiology*. 109(3):527-542, September 2008.)