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Efficacy of Nalmefene for the Treatment of Intrathecal Opioid Induced Pruritus

NN Naughton MD, LS Polley MD, MO Columb FRCA, DM Dorantes MD, DS Wagner PharmD.

University of Michigan Health System, Ann Arbor MI 48109 USA

Introduction: Pruritus is the most common side effect following administration of intrathecal (i.t.) opioids and may adversely effect analgesia quality and maternal satisfaction. Mu opioid antagonists appear to be the most reliable therapeutic agents. However, naloxone is short acting and clinical reports on reversal of analgesia are controversial.(1,2) Nalmefene, a long acting mu opioid antagonist, has recently been shown to effectively antagonize i.t. morphine induced itch in an animal model.(3) The aim of this study was to determine the efficacy of nalmefene for the clinical treatment of i.t. morphine induced itch and assess its effects on antinociception.

Methods: ASA 1 or 2 patients scheduled for primary or repeat cesarean section who selected spinal anesthesia with i.t. morphine for postoperative analgesia were enrolled in this double-blinded, up-down, sequential allocation study. All patients received 11.25 mg hyperbaric bupivacaine with 0.25 mg morphine for surgical anesthesia. Patients reporting moderate/severe itch and requesting treatment for pruritus received i.v. nalmefene. The dose was determined by the response of the previous patient to a higher or lower dose. Anti-pruritic efficacy and analgesia were assessed hourly using a verbal (none, mild, moderate, or severe) and numeric (0-100mm) pruritic scale (PS) and 100 mm visual analogue pain scale (VAPS). Efficacy was defined as a verbal PS of none/mild for 6 hours following i.v. nalmefene. The effective doses in 50% and 95% of subjects (ED50, ED95) were determined using the up-down method of independent pairs.

Results:

	Point Estimate	95% Confidence Interval
ED50	0.41 µg/kg	0.05, 0.76
ED95	0.88 µg/kg	0.19, 1.57

There was no significant difference in pre and post nalmefene VAPS for 6 hours using paired Student's *t* test.

Conclusions: The ED50 for nalmefene was estimated at 0.41 µg/kg with ED95 at 0.88 µg/kg. Effective doses of nalmefene over the six hour observation period did not appear to reverse analgesia. Nalmefene may be an option for the management of i.t. opioid induced pruritus.

References: 1) Anesth Analg 1992; 75:747; 2) Anesth Analg 1994; 78:1110 3) Anesthesiology 1999; April:S(A20)

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Potency And Sterility Of Anesthetic Drugs In An Obstetrical Setting
D.S. Wagner, PharmD; N.N. Naughton, MD; C.L. Pierson, PhD; T. Michel, MD; M. Sikorsky, MD, Anes. Dept., Univ. Of Michigan Hospitals, Ann Arbor, MI.

The goal of this study was to evaluate the sterility and potency over time of commonly used anesthetic drugs in an obstetrical practice area. Current practice involves the daily preparation of medications drawn up into syringes and dated with a 24-hour expiration date. Multiple studies have examined sterility issues independent of potency.¹ Cost implications arise not only with the cost of labor preparation time, but also of wastage.

Syringes were collected on a daily basis over a 30-day period in our obstetric anesthesia area. The medications evaluated in this study were succinyl choline, atropine, lidocaine, and ephedrine. A total of 86 syringes prepared by various personnel utilizing a variety of techniques were collected and stored at room temperature conditions. Random samples were taken of each of the four medications from each week during a 30-day period. Sterility of the samples was assessed for both aerobic and anaerobic growth. Samples were passed through a Falcon disposable filtration unit fitted with a 0.45micron membrane filter and washed with PF sodium chloride solution. The filters were divided into two equal parts. One half was placed on to the surface of commercially prepared standard trypticase soy agar plates supplemented with 5% sheep blood and incubated aerobically in 5% CO2 for 5 days followed by 3 days at room temperature. The other half was placed onto laboratory prepared laked blood agar plates which uses a brain-heart infusion agar base supplemented with 6% laked sheep Rbc's, yeast extract, trypticase peptone, vit K1, and hemin, and incubated in an anaerobic chamber at 35° C for 7 days. No visible growth was observed on any of the filter surfaces for the 30 day time period. Potency was quantified utilizing an HPLC assay comparing a sterile solution of each medication product to one of each sample medication that was 30 days old. Only a 30-day sample was analyzed due to the cost of running multiple samples.

These preliminary results indicate that in general practice, succinyl choline, atropine, ephedrine, and lidocaine are stable for long periods of time without evidence of bacterial growth. This suggests that extension of the generally excepted 24-hour expiration dating of extemporaneously prepared medications could be translated into health care dollar savings. If one could assure accurate labeling practices, as to date and time of medication preparation, a long range cost savings system could be established in a variety of practice areas.

References: 1) Driver RP, etal: Anesth Analg 1998;86:994-7

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Does a test dose increase the likelihood of identifying intrathecal placement of epidural catheters during labor analgesia?

KM Kuczowski MD, DJ Birnbach MD, DA O'Gorman MD FFARCSI, DJ Stein MD, AC Santos MD, MPH. Department of Anesthesiology St. Luke's-Roosevelt Hospital Center, College of Physicians and Surgeons of Columbia University, NY.

Introduction: Unintentional intravascular (IV) or intrathecal (IT) catheter migration may occur during administration of epidural analgesia for labor. Catheter aspiration (ASP) and test doses (TD) have been used to establish correct placement. Recently, controversy has developed regarding the efficacy of TD for intravascular catheters¹. However, the efficacy of TD to detect IT migration has not been addressed. The purpose of this investigation was to compare the accuracy of both tests in identifying IT multi-orificed epidural catheters.

Methods: Anesthetic management was prospectively standardized. Multi-orifice epidural catheters were inserted 5 cm into the epidural space and were followed by aspiration and administration of a 3 cc test dose of lidocaine 1.5% plus epinephrine. Incidence of IT catheter placement as detected by ASP and TD was obtained from the computerized quality assurance database and anesthesia records for 1998. Since TD and ASP were performed on the same population of patients, McNemar chi square was used to compare the ability of these tests to detect IT catheter placement.

Results: Of the 2020 epidurals performed, 10 catheters were detected as being IT by TD, whereas only 5 of these 10 catheters had been detected by positive aspiration. As diagnostic imaging (the "gold standard") was deemed inappropriate in these patients, sensitivity and specificity for these tests were not applicable. When TD and ASP were compared, TD was found to have detected more IT catheters than ASP alone (p<0.05).

Discussion: Our results indicated that a test dose is advantageous in detecting IT catheters that may be missed by aspiration alone. It has been suggested that patients receiving dilute epidural infusions of local anesthetic plus opioid solution will gradually develop a high sensory and motor block, and thus detection of the IT catheter is not problematic. However, laboring women frequently receive a bolus of higher concentrations of local anesthetics when operative delivery ensues. Although IT catheter migration occurs less frequently than IV migration, this occurrence can be just as serious should the unidentified IT catheter be subsequently used for cesarean section.

1. Anesth Analg 1999;88:1073-6.

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Local Anesthetics Given Epidurally Can Inhibit Growth of *Staphylococcus aureus* at Clinically Significant Concentrations

E.J. Goodman, MD; M.R. Jacobs, MD; S. Bajaksouzian, MS; A.R. Windau, MT
Departments of Anesthesiology and Pathology, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, OH

Introduction: Local anesthetics have been shown to have antibacterial effects, especially at high concentrations.^{1,2} Fortunately, *Staphylococcus aureus*, a common cause of epidural abscess, is sensitive to these agents. This study clarifies which concentrations of local anesthetics would be expected to inhibit the growth of *Staphylococcus aureus*.

Methods: After IRB approval, serial dilutions were made of 0.75% and 0.5% bupivacaine, 2% and 5% lidocaine and 3% chloroprocaine. The 0.75% bupivacaine and 5% lidocaine were hyperbaric spinal medications that included 8.25% and 7.5% dextrose, respectively. To each concentration of local anesthetic solution, an equal volume was added of a mixture of Mueller Hinton broth medium with an inoculum of *Staphylococcus aureus* at a concentration of 5 x10⁵ organisms/ml. The resulting solutions were incubated and then observed for growth 24 and 48 hrs later.

Results: After 24 hrs, inhibition of growth was seen with 0.19% and 0.38% bupivacaine starting with the 0.75% solution, and 0.25% with the 0.5% solution. Lidocaine inhibited growth at 1.25% and 2.5% starting with the 5% solution, and at 1% with the 2% solution. Chloroprocaine could inhibit growth at as low a concentration as 0.75%. The 0.19% concentration of bupivacaine and the 1% concentration of lidocaine showed late growth at the 48hr checks. Therefore, the minimum inhibitory concentrations of the local anesthetics were assumed to be 0.25% bupivacaine, 1.25% lidocaine and 0.75% chloroprocaine.

Conclusion: Local anesthetics can protect against epidural abscess formation if they are used at high enough concentrations. This effect may help explain the very low reported incidence of epidural abscess.

References: 1. Reg Anesth 1994;19:43-47.
2. Reg Anesth 1996;21:239-242.