TITLE: DOSE-RESPONSE STUDY OF CONTINUOUS INFUSION EPIDURAL FENTANYL-EPINEPHRINE FOR POSTCESAREAN ANALGESIA

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Introduction. Epidural narcotic infusion for postoperative analgesia is increasingly popular, with widely divergent dosing regimens described. We have compared analgesia and side effects of three different doses in an effort to identify a preferred regimen in postcesarean patients. We used a dilute fentanyl solution containing epinephrine, seeking thereby to exploit the interaction of opiate and adrenergic agonist at the spinal level and minimize dosage and side effects.[1,2]

Methods. ASA Class I and II women having elective cesarean section and no recent narcotic exposure nor history of substance abuse consented to this IRB approved study. Surgical anesthesia via epidural catheter inserted at L_{2-3} or L_{3-4} included 50 mcg fentanyl in local anesthetic. At close of surgery a portable pump (Pharmacia-Deltec 5800) was set to deliver, in randomized, double-blind fashion, a solution containing 4 mcg fentanyl and 1.6 mcg epinephrine per ml at 10, 15 or 20 ml/h (groups A, B and C, respectively). Patients were permitted to self-administer a dose of 4 ml after a 10 min lock-out period up to 3 times per hour. Meperidine 50 mg IM prn was provided for supplemental analgesia. Naloxone 0.1 mg SQ prn was provided for treatment of pruritus, nausea and vomiting. On admission to recovery and 4, 24 and 48 hours thereafter patients marked a 10 cm visual analog pain intensity scale (VAS), and meperidine, naloxone and self-administered epidural fentanyl doses were recorded. Vital signs and side effects were recorded q4h. A blood sample was obtained for fentanyl analysis after 16-28 hours of infusion. Statistical evaluation was by analysis of variance and Mann-Whitney U-test.

Results. Forty-two patients (fourteen per group) have been studied thusfar. Groups did not differ by age, height or weight. Mean VAS scores (1.4, 1.5 and 1.2 for A, B and C, respectively) and total 48 hour self-administered epidural fentanyl doses (432, 284 and 292) were similar between groups. However, over the same interval total meperidine doses (15, 4 and 1) diverged with time, rising in group A. Conversely, total naloxone doses (6, 8 and 28) rose in group C; need for naloxone was generally apparent within 4 postoperative hours. One group C patient required recatheterization for urinary retention. Vital signs did not differ between groups, and the lowest observed respiratory rate was 16 breaths per min. Plasma fentanyl analyses are being completed.

Conclusions. These data suggest that infusion at 15 ml/h (60 mcg fentanyl/h) provides satisfactory postcesarean analgesia. At the present sample size, it appears the 15 ml/h dose may be associated with less meperidine supplementation *and* fewer side effects requiring naloxone treatment compared to the other doses ($p=.21$, Mann-Whitney U-test). At this infusion rate, mean fentanyl requirement (including self-administered doses) was 0.78 mcg/kg/h. Thus, addition of epinephrine decreased by about half the requirement of 1.52 mcg/kg/h fentanyl *without* epinephrine reported in another study of postcesarean analgesia.[3] Further investigation of epinephrine effect at this fentanyl dose is warranted.

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Title: INTRATHECAL SUFENTANIL FOR LABOR ANALGESIA: RESULTS OF A PILOT STUDY

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Introduction: Intrathecal and epidural morphine, fentanyl and sufentanil have been increasingly used as a supplement to the local anesthetic during spinal and epidural anesthesia for labor and Cesarean section.[1,2] Spinal morphine is associated with a moderately high incidence of side effects presumably due to rostral spread in the cerebrospinal fluid. Sufentanil possesses high lipid solubility which should limit its rostral spread, thus providing a more segmental effect and less side effects. The addition of fentanyl or sufentanil to local anesthetic solutions for labor and delivery has allowed for reductions in the concentrations of local anesthetic used; and consequently, reductions in common side effects of local anesthesia, mostly namely hypotension and motor blockade.[3] Intrathecal morphine alone, ie.; without any local anesthetic, has been shown to provide effective analgesia for labor.[4] This pilot study was performed to assess the effectiveness, onset, duration, and side effects of the lipid soluble agent sufentanil, administered intrathecally for labor analgesia.

Methods: IRB approval and informed consent were obtained. To date two different doses of intrathecal sufentanil (10 and 15 µg) have been evaluated in a total of 15 patients for the relief of labor pain. Group 1 (n=8) received sufentanil 10µg and group 2(n=7) received sufentanil 15µg. All doses were diluted to 1 ml with sterile preservative-free normal saline and administered in the lateral position at L_{2-3} or L_{3-4} interspaces via a 26 gauge spinal needle. The Student's t-test was utilized for statistical analysis with a p-value ≤ 0.05 considered significant.

Results: Results indicate that both doses of intrathecal sufentanil are extremely effective for pain relief for the first stage of labor. Onset of analgesia was statistically faster in the 15 µg group. Mean onset was 159.1 ± 18.0 and 125.0 ± 29.5(seconds, mean±S.D) in groups 1 and 2, respectively. Mean duration of analgesia, however, was similar: 194.0 ± 31.3, and 184.0 ± 28.2 (minutes, mean±S.D.) in groups 1 and 2, respectively. All patients in both groups reported their pain relief as excellent. No significant change in blood pressure, pulse, respiratory status or fetal heart tracing was noted at any time in any patient. No patient in either group requested treatment for any of the usual side effects(ie., pruritus or nausea/vomiting) associated with intrathecal narcotics. One patient complained of a postlumbar puncture headache which eventually required an epidural blood patch for total resolution.

Discussion: Our preliminary results suggest that intrathecal sufentanil is a very effective means for providing analgesia for the first stage of labor, the onset of which is extremely rapid, the duration is moderate, side effects appear to be very minimal, and risk of motor blockade or hypotension appears absent. To date our incidence of postlumbar puncture headache is 6.5%. This may, however, merely be a consequence of the few number of patients studied thus far; or it may be related to the use of intrathecal narcotics as previously suggested.[5] As a single bolus, the duration would appear to be most suitable for: multiparous patients, especially those in which a prolonged labor is not anticipated; primiparous patients who are well into active labor; in patients who desire analgesia without "the feeling of numbness" or motor blockade; or in patients who cannot tolerate the sympathetic blockade associated with epidural analgesia. Additionally, we are currently evaluating the use of intrathecal sufentanil for labor analgesia administered via an indwelling intrathecal catheter as a continuous infusion and as repeated boluses, as a PCA technique, and in conjunction with a small amount of local anesthetic; all of which have potential for significantly broadening the applicability of this technique.

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