TITLE: PHARMACOKINETIC PROFILES OF EPIDURAL ALFENTANIL AND FENTANYL: BOLUS FOLLOWED BY CONTINUOUS INFUSION TECHNIQUE

AUTHORS: AO Wilhite, M.D., C Moore, M.S.N., JT Christmas, M.D., N Frank, B.S.N.

AFFILIATION: Departments of Anesthesiology and Ob/Gyn, Medical College of Virginia, Richmond, VA 23298

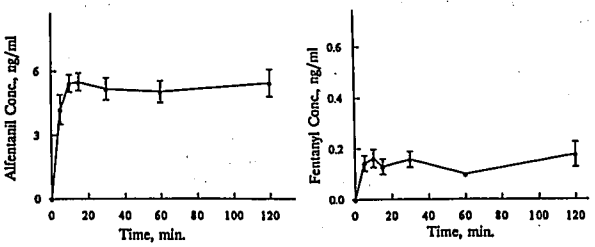
The technique of a bolus followed immediately by continuous epidural infusion of a narcotic/bupivacaine mixture has been described(1), although no pharmacokinetic data for this technique exists.

Institutional approval and patient informed consent was obtained. Healthy term pregnant patients who requested epidural analgesia for labor and delivery were studied. Patients were randomized in a double-blinded manner to receive epidural alfentanil 500 μg in 10ml 0.125% bupivacaine(B) (n=12) or fentanyl 50 μg in 10ml 0.125% B (n=12) as a bolus dose, followed within 10 minutes by continuous infusions of alfentanil 20 μg/ml in 0.125% B or fentanyl 2 μg/ml in 0.125% B, respectively. Mean infusion rate was 10ml/hr. Blood samples were collected at time 0,5,10,15,20,30,60 minutes after injection and hourly through an indwelling 14g IV catheter. Plasma drug levels were analyzed by radioimmunoassay with a sensitivity of 1ng/ml for alfentanil, and 0.2ng/ml for fentanyl. Fetal heart rate(FHR) tracings were retrospectively reviewed by a perinatologist.

T-test and chi square analysis of demographic data showed no significant differences between groups. Drug levels for each group were examined using repeated measures analysis of covariance, which demonstrated stability in drug levels over time. Correlation coefficients for drug concentration vs. body weight were -0.537 for fentanyl and 0.277 for alfentanil. No significant changes in FHR variability data for either group were demonstrated using repeated measures analysis of variance.

We conclude that an initial epidural bolus with continuous infusion technique generates steady state plasma concentrations of alfentanil and fentanyl, achieving drug levels which have not been associated with respiratory depression. However, additional boluses of narcotic during this technique may result in unpredictably high maternal plasma levels with greater potential for placental transfer and side effects.

References: Anesth Analg 67:462-465, 1988



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TITLE: PRURITUS CONTROL FOLLOWING EPIDURAL OPIATES THROUGH CONTINUOUS INFUSION PLUS SELF ADMINISTRATION OF MU ANTAGONISTS VERSUS MIXED AGONIST-ANTAGONISTS IN THE POST CESAREAN SECTION POPULATION

AUTHOR: Will D. Kendrick, M.D., Robert F.H. Birch, M.D., Andrew M. Woods, M.D.

AFFILIATION: Department of Anesthesiology, University of Virginia Health Sciences Center, Charlottesville, VA 22908

Epidural morphine after cesarean section provides excellent analgesia but is often associated with pruritus which may be distressing to patients.[1] Such patients in our institution have been empirically treated with constant infusions of naloxone at 100 ug/hr, although there has been a wide variation in response to this therapy. It has been suggested that use of a mixed agonist-antagonist, such as nalbuphine, may reverse pruritus without compromising analgesia. [2, 3] Therefore, we compared naloxone to nalbuphine in a double-blinded manner using low-dose continuous infusions supplemented with patient self-administered (PSA) boluses using a Bard PCA Pump®.

With institutional approval and patient consent, we studied 51 women undergoing elective cesarean section under epidural anesthesia and receiving Duramorph® (5 mg) following delivery. Patients were randomly assigned to one of three groups. Group A received a nalbuphine infusion at 2.5 mg/hr supplemented with PSA doses of up to 1 mg every 5 minutes. Group B received a naloxone infusion at 50 ug/hr with a sham supplement of PSA saline. Group C received a naloxone infusion at 50 ug/hr supplemented with PSA doses of up to 40 ug every 5 minutes.

The degree of pruritus and pain was assessed every 8 hours for 24 hours by patient self scoring using a 10 cm visual analog scale. Statistical comparison of the change in itch (Δ I) and pain scores (ΔP) during each 8 hour period employed Student's t test, with $P < 0.05$ taken to be significant.

The increase in itch scores was significantly greater in groups B and C (ΔI = 2.4) compared to group A (ΔI = 0.5) at the end of 8 hours. Itch scores in all groups declined during the next two observation periods, but the differences among groups were not significant. The only patients who required treatment for unrelieved pruritus were in groups B and C.

There were no differences in pain scores among the groups during any time period.

This study suggests that nalbuphine may be superior to naloxone in alleviating pruritus associated with epidural morphine. However, this mixed agent appeared to offer no benefit in terms of analgesia. Of note was that the naloxone infusion (group B) was as efficacious as naloxone infusion plus supplemental boluses of naloxone (group C) in treating pruritus. This novel use of the PCA pump to treat the side effects of epidural morphine offers the advantages of enhanced patient control and potentially decreased need for hospital staff intervention.

REFERENCES:
1. Anesth Analg 62:666-672, 1983
2. Anesth Review 15(2):21-27, 1988
3. Anesthesiology 63(3A):A255, 1985