Title: CONTINUOUS NALOXONE INFUSION FOLLOWING EPIDURAL MORPHINE: A DOSE-RESPONSE STUDY

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We administered varying doses of naloxone as a continuous infusion to postoperative cesarean section patients who had received epidural morphine. There is controversy over the efficacy of naloxone in reversing the side effects of epidural morphine in this setting, as well as concern over the possible reversal of analgesia.

Methods. This study was approved by the institutional Human Investigation Committee. Forty healthy parturients undergoing cesarean section with lumbar epidural anesthesia using pH-adjusted lidocaine with epinephrine 1:200,000 received epidural morphine after delivery of the infant. Patients were randomized to receive 0, .05, .1, or .2 mg of naloxone per hour by continuous intravenous infusion starting two hours postoperatively. This was accomplished by the addition of 0, 1, 2, or 4 ampules (0.4 mg) of naloxone to each liter of intravenous fluid which was infused at 125 cc/hr for 24 hours. In addition, a control group included ten parturients who received general anesthesia for cesarean section and were managed with parenteral narcotics in the postoperative period. A blinded observer interviewed all patients at the end of 24 hours. Patients were asked to rate any pain and itching using a visual analog scale (0-10), and were also asked about the presence of nausea. Nursing records were reviewed to determine whether additional analgesic or antipruritic medications were administered during the study period. Groups were evaluated using a nonparametric test (Kruskal-Wallis) for analysis of variance among the groups.

Results. All groups receiving epidural morphine reported significantly less pain ($p<0.02$) than patients in the control group, who were managed with parenteral narcotics (Figure 1). There were no statistical intergroup differences in pain scores or requests for supplemental analgesia in the four groups receiving epidural morphine, and naloxone infusion was not found to reduce the duration of analgesia.

Naloxone infusion was clinically effective in decreasing the subjective symptoms of pruritis. The group receiving epidural morphine and the largest dose of naloxone (0.2 mg/hr) reported significantly less itching than the group receiving epidural morphine and no naloxone ($p<0.02$). The intermediate dosage groups (.05 and .1 mg/hr) displayed no statistically significant differences in pruritis from any other dosage group. However, reference to figure 1 discloses an apparent trend as the dosage is increased, and the lack of statistical significance most likely reflects the small sample size as well as a fairly large intragroup variation. The naloxone infusion was also effective in reducing nausea after epidural morphine in a similar dose-related fashion.

Discussion. There are reports questioning the efficacy of naloxone in reversing the side effects of epidural morphine,[1] as well as the effects of naloxone upon the duration of analgesia.[2] In a similar patient population, Ramanathan et al. found that naloxone infusion (.1 mg/hr) was ineffective in decreasing the severity of itching. However, the group in our study receiving this dose of naloxone had almost identical itching scores as reported by Ramanathan. The difference occurred between the groups receiving no naloxone; in our study, this group had a mean itching score that was twice that of the other study. This may reflect differences in other variables, such as the addition of epinephrine to the epidural anesthetic solution used for surgery.

Our data indicate a wide variation among patients receiving epidural morphine in the severity of itching. For this reason, it is our policy to begin prophylactic antipruritic therapy with a low dose of naloxone (.05 to .1 mg/hr), and increase it if symptoms warrant. It is our belief that this dose also provides additional protection against the unlikely possibility of respiratory depression, since 0.1 mg of naloxone has been used to successfully reverse respiratory depression in this patient population.

Shortening of the duration of epidural morphine analgesia by naloxone infusion has been reported in a nonobstetric population, but only at a dose 3.5 times the largest dose used in our study.[2]

References.

1. Ramanathan S, Horn R, Parker F: Naloxone infusion is ineffective in preventing the side effects of epidural morphine in post-cesarean section patients. Anesthesiology 65:A367, 1986

2. Rawal N, Schott U, Dahlstrom B, et al: Influence of naloxone infusion on analgesia and respiratory depression following epidural morphine. Anesthesiology 64:194-201,1986

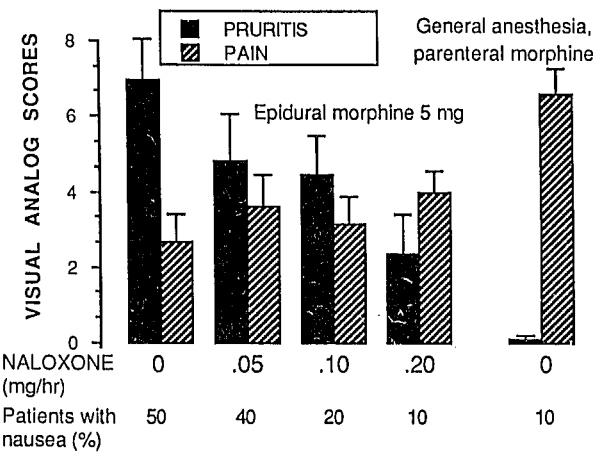

Figure 1. Effects of increasing dosages of naloxone upon pruritis, nausea, and pain in obstetrical patients receiving epidural morphine.