Title: EPIDURAL BUTORPHANOL/FENTANYL FOR POST-CESAREAN DELIVERY ANALGESIA

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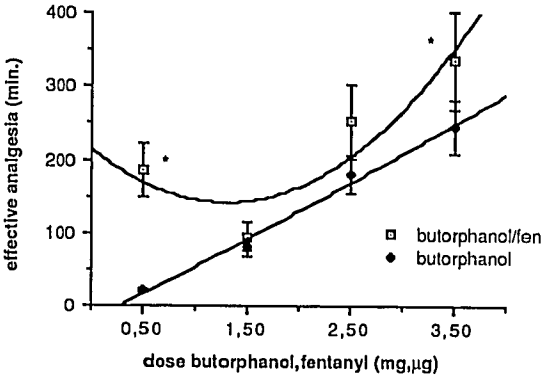
Introduction. Both epidural fentanyl and butorphanol have been shown to provide effective analgesia following cesarean delivery.[1,2] Fentanyl is a μ-opiate receptor agonist, and butorphanol is a μ receptor antagonist and K receptor agonist. A combination of these two drugs might provide prolonged analgesia via stimulation of both spinal cord opiate receptor types, and decrease the incidence of side effects of μ receptor stimulation (pruritus, urinary retention, and respiratory depression). We therefore have performed a double-blind, randomized, dose response study of varying doses of butorphanol and fentanyl.

Methods. The protocol was approved by the hospital's Committee for the Protection of Human Subjects from Research Risks, and written informed consent was obtained. We have studied 25 ASA class I patients scheduled for elective cesarean delivery under epidural anesthesia. After delivery, pain scores (10 cm visual analog pain scale), motor block, sensory levels, vital signs, and the presence or absence of nausea, shivering, somnolence and pruritus were recorded. When the patient reported a pain score of 3 or greater, varying doses of butorphanol and fentanyl in normal saline to a total volume of 10 ml was injected via the epidural catheter. The amount of study drug injected was unknown to the anesthesiologist injecting the medication and evaluating the patients responses. After injection, the above parameters were recorded at frequent intervals until the patient complained of pain. The presence or absence of side effects and the amount of parenteral narcotic drugs administered for the first 24 hours potpartum were recorded. The data were analyzed for statistical significance using analysis of variance for parametric data and Fischer's Exact Test for non-parametric data.

Results. Fig. 1 shows the duration of effective analgesia (time to first narcotic) with butorphanol alone and in combination with fentanyl. It appears that the analgesic effects of fentanyl are completely reversed with low doses of butorphanol (μ antagonism), and then replaced by butorphanol analgesia (K agonism) at higher doses of butorphanol. The analgesia produced by 50 μg fentanyl alone is significantly greater than control (no fentanyl or butorphanol), and that produced by 3 mg butorphanol and 50 μg fentanyl is significantly greater than that produced by 3 mg butorphanol alone, suggesting a synergism at higher doses of butorphanol. Mu side effects, e.g. pruritis, were completely abolished by the addition of butorphanol (Fig. 2). Somnolence, the primary side effect of epidural butorphanol, was not observed with the doses used in this study.

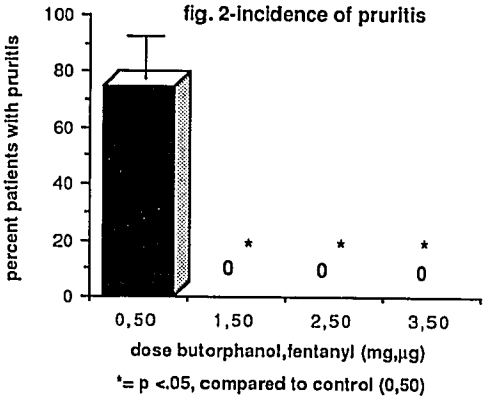
Discussion. The combination of a μ opiate agonist fentanyl) and high doses of a μ antagonist/K agonist (butorphanol) is capable of producing analgesia with a decreased incidence of μ mediated side effects. This interaction may be useful as a method of decreasing the incidence of severe μ side effects associated with drugs like morphine.

fig. 1- duration of effective analgesia



*=p<.05, compared to butorphanol alone

fig. 2-incidence of pruritis



*= p <.05, compared to control (0,50)

References.

1. Naulty JS, Datta S, Ostheimer GW, et al: Epidural fentanyl for postcesarean delivery pain management. Anesthesiology 63:694-698, 1985.
2. Naulty JS, Weintraub S, McMahon J, et al: Epidural Butorphanol for post-cesarean delivery pain management. Anesthesiology 61:A415, 1984.