Title: **Prolongation of Postoperative Sufentanil Analgesia with Epinephrine**

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Introduction: Sufentanil citrate is a highly lipid soluble potent narcotic agent which has recently been shown to be efficacious in providing post Cesarean section analgesia when given via the epidural route. Rapid onset and low potential for delayed respiratory depression have been attributed to its high lipid solubility, both of which appear to be distinct advantages over the more water soluble morphine. However, the duration of action of epidural sufentanil is only 4 to 6 hours compared to the approximate 24 hour duration of epidural morphine.[1] It is fairly well established that the addition of epinephrine to local anesthetic solutions will significantly prolong their duration.[2,5] Therefore, to determine whether epinephrine prolongs the duration of epidural sufentanil analgesia after Cesarean section, we prospectively studied two groups of ten patients each, in a randomized, double blind fashion. Group I received epidural sufentanil 50 mcg and group II received epidural sufentanil 50 mcg plus epinephrine 300 mcg.

Methods: The study received institutional approval and written informed consent was obtained from each patient. Anesthesia for Cesarean section was provided with bupivacaine 0.5% injected via a lumbar epidural catheter after premedication with only a clear antacid. Epinephrine given during the course of the anesthetic was limited to the 15 mcg included in a standard 3 ml test dose. Upon requesting analgesia in the recovery room, the patients were administered the epidural test solution diluted to a total of 10 ml with preservative-free normal saline through the indwelling epidural catheter. Intensity of pain was assessed using a 100 mm visual analog scale immediately prior to the administration of epidural opioid solution, 2.5 minutes after its administration, and then every five minutes until analgesia was adequate. The duration of analgesia was measured as the time interval from the onset of adequate analgesia to first request for additional pain medication. All patients were observed for at least 12 hours after epidural sufentanil injection for the appearance of side effects such as nausea, pruritis, and respiratory depression. The subsequent analgesia requirement over the first 72 postoperative, in terms of morphine equivalents, was recorded for each patient. Time required from onset to 50% and 90% pain relief, duration of effective analgesia and postoperative analgesia requirement were compared using the Student's *t* test. The incidence of side effects was analyzed using Chi-square analysis. A p value of less than 0.05 was considered significant.

Results: Epidural sufentanil provided complete analgesia in all patients. Onset (mean ± SD) to 50% pain relief was 6.2 ± 2.7 minutes in group I and 9.5± 6.3 minutes in Group II. Onset to 90% pain relief required 12.0 ± 4.8 minutes in Group I and 13.5 ± 7.8 minutes in Group II. These differences in onset did not reach statistical significance. Duration of analgesia (mean ± SD) was significantly prolonged in Group II compared to Group I, 348 ± 79 minutes versus 267 ± 80 minutes, respectively. There was no significant difference between the two groups with regard to subsequent analgesia requirement over the first 72 postoperative hours, however. The incidence of nausea and pruritis was similar in the two groups, but there was a significantly higher incidence of these side effects which required treatment in group II. No significant alteration of respiratory rate or effort, blood pressure or pulse was noted in any patient during the study.

Discussion: Our results indicate that the duration of postoperative analgesia with epidural sufentanil is statistically prolonged with the addition of epinephrine. The mechanism for this prolongation of analgesia by the addition of epinephrine is unclear. As is the case with the addition of epinephrine to local anesthetics administered in the subarachnoid space, decreased vascular uptake may not necessarily be the mechanism of prolongation.[3] Epinephrine may act directly on the spinal cord as a modulator of neurotransmission of pain information[4] and, therefore, work independent of vasoconstrictive action. The rather large dose of epinephrine (300 mcg) was selected to demonstrate an unequivocal effect, if one existed, upon the duration of action of epidural sufentanil. This same dose has been shown to be effective in prolonging spinal anesthesia with local anesthetics.[2,5] The use of epinephrine to prolong epidural sufentanil has been preliminary studied with inconclusive results. In studying a total of six patients, Parker et al[6] found the addition of 50 mcg of epinephrine added to 10 mcg of sufentanil did not prolong the duration of analgesia but did increase the incidence of side effects. However, fewer patients were studied and doses of both drugs were much less than in the present study. Tan, et al[7] investigated sufentanil for analgesia after Cesarean section, comparing intravenous sufentanil to epidural sufentanil, with and without epinephrine. They found the duration tended to be longest in the epidural sufentanil with epinephrine group, but did not reach statistical significance, possibly because of the small numbers in each group. A recent study[8] which compared sufentanil and morphine administered epidurally demonstrated better quality analgesia with sufentanil. This finding of better quality analgesia combined with the theoretical safety and fewer side effects of the more lipid soluble drug, would appear to make this statistically significant prolongation of epidural sufentanil by epinephrine clinically relevant as well. In addition to the use of epinephrine, other means for prolonging the duration of epidural sufentanil include utilizing a continuous infusion or intermittent bolus technique. More study is suggested in this regard.

References:

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