Title: ANALGESIC EFFECT OF EPIDURAL CLONIDINE AND NALBUPHINE IN COMBINED USE

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Introduction. Epidural nalbuphine has been shown to produce efficacious analgesia with less side effects than epidural morphine but its duration of action is much shorter than that of epidural morphine[1]. Clonidine, an alpha2-adrenoceptor agonist has been reported to potentiate spinal morphine analgesia when the two drugs are given intrathecally[2] or epidurally[3]. The present study was undertaken to evaluate the synergistic interaction of epidural administration of nalbuphine and clonidine.

Method. The study was conducted after institutional approval and informed consents were obtained from all the patients prior to their entry into the study. Forty-five adult patients scheduled for elective upper abdominal surgeries were enrolled in this study. On the day of surgery, prior to induction of anesthesia, an indwelling #18 gauge epidural catheter was inserted through the L_{1-2} or L_{2-3} lumbar vertebral interspaces and taped securely in place. All the patients were then given general anesthesia with either halothane or enflurane in N_2O-O_2 without any narcotic analgesic. In the post-op period, when the patients fully recovered from the effect of anesthesia and complained of severe pain, they were divided into 3 equal groups of 15 patients each in a randomized, double-blind fashion and received epidural administration of clonidine 75 mcg (group 1), nalbuphine 10 mg (group 2) and clonidine 75 mcg plus nalbuphine 10 mg (group 3) respectively. All medications were prepared in 10 ml normal saline. All patients were observed for pain relief (by visual analogue scores), vital signs, arterial blood gas studies and adverse effects for 24 hrs. "Rescue" analgesics of meperidine 50-75 mg IM were given whenever patients complained of recurrence of severe pain.

Results. The demographic distribution and initial pain intensities were similar for all 3 groups. Onset of pain relief with epidural clonidine was quite slow (about 1 hr.) and the duration of action lasted about 5 hrs. On the other hand, onset of analgesia with epidural nalbuphine appeared at 10 min., peaked at 30 min. with a duration of action about 6 hrs. Epidural nalbuphine produced significantly better pain relief than that of epidural clonidine at all observation points up to 6 hrs. ($p < 0.05$). The combination of clonidine and nalbuphine provided pain relief at 5 min., peaked at 30 min. and analgesic duration lasted about 7 hrs. The combination group showed superior analgesic effect than the nalbuphine group only at the 5-30 min. period with $p < 0.01$ (Fig.) Incidence of adverse effects were quite similar among the 3 groups (Table 1). A statistically significant drop in systolic and diastolic blood pressures at 30-180 min. post drug was observed in both groups (group 1 & 3) with epidural clonidine administration. No significant bradycardia or respiratory depression was observed in any of the patients.

Discussion. Epidural clonidine at dose employed in our study (75 mcg) produced mediocre pain relief which is significantly inferior to that produced by epidural nalbuphine in patients with postoperative pain. The addition of clonidine to epidural nalbuphine appears to hasten the onset but does not significantly alter the magnitude of pain relief nor does it cause appreciable changes in the side effect profile. Our finding diverges from that reported by Nalda and Gonzalez who showed a significant synergistic effect with combination of epidural morphine 2 mg and clonidine 75 mcg[3]. Tamsen and Gordh, on the other hand, reported that epidural clonidine 75 mcg produced analgesia indistinguishable from that of pethidine 25 mg and the combination of both drugs did not achieve any better or more prolonged analgesia[4]. Similarly our study demonstrated no clear advantage in using clonidine in combination with nalbuphine than nalbuphine alone. Furthermore, clonidine, when administered epidurally, produced reduction of blood pressures lasting 2-3 hrs; therefore caution must be exercised when this agent is used.

References.

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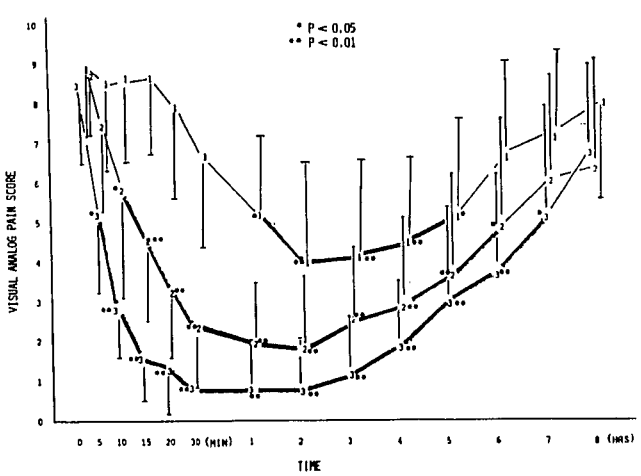

TABLE I: SIDE EFFECTS

	Group I	Group 2	Group 3
NAUSEA	3/15	3/15	4/15
VOMITING	2/15	2/15	2/15
DRY MOUTH	4/15	3/15	5/15
PRURITIS	0	0	0
RESP. DEPRESSION	0	0	0