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A COMPARATIVE STUDY BETWEEN EPIDURAL BUPRENORPHINE AND EPIDURAL NALBUPHINE IN MAJOR GYNAECOLOGICAL SURGERIES

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ABSTRACT Epidural anaesthesia is an effective method of anaesthesia and postoperative analgesia. This randomized control trial compares block characteristics and post operative duration of analgesia of a single dose of two opioids with partial agonist-antagonist properties (buprenorphine 0.3 mg and nalbuphine 10 mg, equivalent to morphine 10 mg) added to 15 ml of epidural levo-bupivacaine.

50 randomised patients received either epidural buprenorphine or nalbuphine adjuvants as group B or Group N of 25 patients each. The demographic profile, operation type and surgical duration were similar between the groups as well as the onset of both the sensory and motor blockade. The incidences of side-effects were similar between the two groups. However, the duration of analgesia of buprenorphine group was significantly greater compared to the nalbuphine group (16.26±2.4 vs 6.46±1.4 hour; $p<0.01$). To conclude, buprenorphine has significantly greater analgesic property as compared to nalbuphine when used as an adjuvant for epidural anaesthesia. (150 words)

KEYWORDS : Epidural anaesthesia, buprenorphine, nalbuphine

Introduction

Immediate postoperative pain is the most annoying and unpleasant experience after recovery from a successful anaesthesia and cause a multitude of physiological insults which are further detrimental to the well being of the patient. Epidural anaesthesia provides a safe, cheap and physiologically beneficial method of pain relief and addition of adjuvants increases the effectiveness of local anaesthetic drugs and decrease side effects of local anaesthetics.

Opioids are the most common choice as adjutants to local anaesthetics[1]. With the exception of morphine, opioids having pure mu receptor agonists (e.g. fentanyl or sufentanil) have a shorter duration of action and are ineffective after a few hours of postoperative analgesia. Morphine on the other hand is associated with a multitude of side effects like delayed respiratory depression, excessive sedation, bradycardia and nausea and vomiting[1]. However, opioids having partial agonist antagonist property have a more prolonged duration with a much lesser chance of development of respiratory depression[1-3].

This study compares two preservative-free preparations of partial agonist agonist opioids – buprenorphine and nalbuphine as adjuvant to epidural bupivacaine and evaluates their relative efficacy in patients undergoing major gynaecological surgeries. Very few studies till date have compared these two drugs in a head-on clinical scenarios[4,5]. No studies previously have compared buprenorphine or nalbuphine as an epidural adjuvant or had used levo-bupivacaine for epidural anesthesia in conjunction with either.

Material and Methods

After approval of the Institutional Ethics Committee, the present double-blind prospective randomized trial was performed on 50 consenting adult patients (aged 18 to 65 years) of American Society of Anesthesiologists (ASA) status 1 and 2, posted for major gynaecological surgeries at Eden OT complex of Medical College and Hospital. Patients having any major co-morbidity, sepsis, bleeding abnormalities, anatomical abnormalities of the spine, history of allergy to any study drugs and those already on analgesic drugs prior to surgery were excluded from the study.

The patients were randomly allocated to two groups using random number table and sealed envelope technique and study drugs were prepared in unmarked identical 20 ml syringes just before procedure by a post graduate trainee, and given by an experienced anaesthesiologist not connected with the study or operative procedure of the particular patient. The various intra and post operative study parameters were noted and recorded in pre-formulated study proforma by post graduate trainees. Apart from collection of data no postgraduate students took no further part in the study.

All patients were fasted for at least 8 hours for solid foods and were allowed water per mouth till two hours before operation. After entering the OT monitors (pulse oximetry and non-invasive blood pressure) were attached and the baseline values were noted and all patients were co-loaded with Ringer's lactate solution 10 ml/kg, while lumbar epidural anaesthesia was initiated such that **Group B (25 patients)** received 15 ml of 0.5% isobaric levo-bupivacaine and 0.3 mg of buprenorhine (1 ml), while **Group N (25 patients)** received 15 ml of 0.5% isobaric levo-bupivacaine and 10 mg of nalbuphine (1 ml). The total volume of drugs given epidurally was 16 ml. All patients had epidural catheters left in place aseptically for postoperative pain relief.

The dose of buprenorphine and nalbuphine as epidural adjuvant i.e. 0.3 mg and 10 mg respectively were chosen based on their equianalgesic potency to 10 mg of morphine[1]. The sample size was calculated to be 22 subjects in each groups based on two-segment regression time, minimum difference in means being 7.1, and assuming alpha value of 0.05, power of 0.8. For study purpose 25 subjects were taken in each group.

The patients were assessed every 3 minutes to evaluate the onset of motor and sensory block along with mean arterial blood pressure. The operation was allowed to progress only after the patient had a block height of T8 and was unable to move the toes of their foot. The mean arterial pressure (MAP) was assessed every 3 minutes for the first 30 minutes, and every 5 minutes thereafter throughout the operation. In the post operative period the pulse oximetry were recorded continuously and MAP were recorded every 10 minutes for first 2 hours and hourly thereafter for the next 16 hours. Any fall in MAP of 20% or more from baseline was defined as a hypotensive episode and treated with inj. phenylephrine 200 mcg intranenously. Similarly a pulse rate of 50/min or less was defined as bradycardia and treated with inj. atropine 0.6 mg intranenously.

The duration of analgesia was calculated as the time from onset of sensory block till the time the patient first complained of pain. Thereafter, patient received a dose of Injection levo-bupivacaine 0.25% 10 ml epidurally along with diclofenac 100 mg suppository per rectally for pain relief. The duration of motor blockade and time to 2 segment block height reduction from maximum sensory block height were also noted. Apart from epidural block characteristics the patients were also observed for various side effects like nausea and vomiting, pruritus, and respiratory depression (defined as a respiratory rate of ≤ 8).

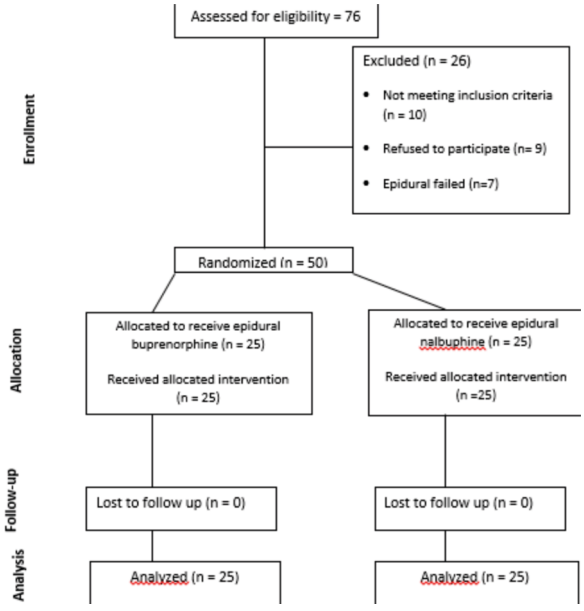
If at any time during the operation the surgeon or the patient felt any discomfort general anaesthesia was instituted immediately and the patient taken off the study. Apart from the study drug and intraoperative fluids the patient did not receive any other medication during the study period unless they had side effects which were treated accordingly.

The statistical analysis was performed using Stata version 14.0, for Windows (StataCorp, Texas, USA). Categorical data, i.e., ASA grade, type of surgery, and the incidence of adverse events (hypotension, bradycardia, respiratory depression, pruritus, and nausea and vomiting) are presented as numbers (percent) and were compared among groups using Chi-square test.

The groups were compared for demographic data (age, height and weight), duration of surgery, time for two segment regression, and total duration of analgesia by t-test. The probability was considered significant if p value was less than 0.05. Data were represented as mean and standard deviation.

Results

76 patients were initially assessed for eligibility of whom 10 patients did not meet inclusion criteria while another 16 patients withdrawn as the patients either refused to participate or the epidural blockade failed to perform. Of the 50 patients conforming to study protocol 25 patients each received either buprenorphine (0.3 mg) or nalbuphine (10 mg) along with epidural levo-bupivacaine as group B and N respectively as per allocation. No patients were lost to subsequent follow-up and analysis.



The two groups in terms of age, height, weight, ASA grade and mean surgical duration were comparable. (Table 1)

Table 1. Demographic and surgical profile

	Group B (n=25)	Group N (n=25)
Age (in years)	37.2± 9.5	38.1±10.2
Weight (in kgs)	51.4±7.4	50.6±8.1
Height (in cm)	157.8±15.2	160.2± 17.6
ASA Grade (1/2)	13/12	12/13
Mean duration of surgery (hr)	1.44±0.4	1.50±0.3

p>0.05

The onset of sensory and motor blocks and the maximum sensory block height were similar in the groups receiving epidural buprenorphine (Group B) and epidural nalbuphine (Group N). However, the duration of analgesia as well as time to two segment regression was significantly prolonged in Group B receiving epidural buprenorhine (p<0.05). (Table 2)

Table 2. Block Characteristics

	Group B	Group N
Onset of sensory block (min)	8.8±2.3	8.2±1.9
Onset of motor block (min)	12.4±2.1	11.8±1.8
Maximum block height reached	T6	T7
Two segment regression time (hour)	8.4±1.8	3.6±1.4*
Duration of analgesia (hour)	16.26±2.4	6.46±1.4*

*p<0.01

The incidence of side effects were comparable in the two groups. (Table 3)

Table 3. Side effects as expressed in percentage

	Group B	Group N
Hypotension episodes	24%	20%
Bradycardia	12%	8%
Respiratory depression	-	-
Pruritus	4%	4%
Nausea and vomiting	12%	16%

p>0.05

Discussion

No studies previously have compared buprenorphine or nalbuphine as an epidural adjuvant or had used levo-bupivacaine for epidural anesthesia in conjunction with either. In the current study 50 patients were randomised to receive either epidural buprenorphine or nalbuphine adjuvants as group B or Group N of 25 patients each. The demographic profile, operation type, surgical duration, onset of both the sensory and motor blockade and incidences of side-effects were similar between the two groups. However, the duration of analgesia of buprenorphine group was significantly greater compared to the nalbuphine group (16.26±2.4 vs 6.46±1.4 hour; p<0.01).

Levo-bupivacaine, the new *S*-enantiomer of bupivacaine was used in this study as it is equi-potent with bupivacaine and safer. Various studies till date have used epidural and intathecal buprenorphine and nalbuphine[2,3,4]. In either epidural or intrathecal injections the duration of buprenorphine have been found to be significantly higher compared to nalbuphine. The duration of analgesia after epidural buprenorphine and epidural nailbuphine in our study was similar to previous studies[2,3]. However, when given intravenously the duration of analgesia of nalbuphine and buprenorphine are similar[5]. The prolonged duration of central neuraxial buprenorphine is attributed to its higher lipophilicity and greater opioid receptor affinity at spinal cord[1].

To conclude, buprenorphine has significantly greater analgesic property as compared to nalbuphine when used as an adjuvant for epidural anaesthesia.

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