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Comparison of Nalbuphine Versus Buprenorphine as an Adjuvant to Intrathecal Bupivacaine for Postoperative Analgesia in Lower Abdominal and Lower Limb Surgeries

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Abstract

Introduction: Opioids when added to local anaesthetics in sub-arachnoid block decreases the dose of local anaesthetics and offers stable hemodynamics. Nalbuphine is an agonist-antagonist act on kappa receptors providing analgesia. Buprenorphine is a mixed agonist-antagonist narcotic with high affinity at both μ and kappa opiate receptors. *Aim:* In this study we have compared the analgesic efficacy of buprenorphine and nalbuphine when added with bupivacaine in spinal anaesthesia. *Material and Methods:* A randomized, double blinded, prospective study on 60 patients of ASA I and II undergoing lower abdomen and lower limb surgery under subarachnoid block was done. Patients were randomly allocated into two groups (n=30). Each group received 15 mg of 0.5% of injection bupivacaine heavy along with either 60ìg of buprenorphine (Group B) or 0.8 mg nalbuphine (Group N). Characteristics of sensory and motor blocks, haemodynamic changes, duration and quality of analgesia, adverse effects, sedation, visual analog score (VAS) score and analgesic requirement were studied at different time intervals. *Results:* Onset of sensory block for Group N is 1.519±0.367 and Group B is 2.665±0.462. Onset of motor block for Group N is 4.639±0.976 and Group B is 3.686±0.373. Duration of sensory block in Group N is 170.60±24.42 and Group B is 237.93±16.43. Duration of motor block in Group N is 257.17±27.74 and Group B is 410.93±17.79. The duration of analgesia (in minute) was 295.60±18.95 in N Group and 566.43±42.19 in Group B. There was no significant difference regarding block characteristics and haemodynamic parameters. The adverse effects were less in N Group. *Conclusion:* Onset of sensory and motor block was faster in Group N compared to Group B. The VAS scores showed that post operative analgesia lasted significantly longer in patients in group B than in group N. No significant side effects were observed in either of the two groups. Sub-arachnoid buprenorphine provides longer duration of post-operative analgesia compared to nalbuphine.

Keywords: Buprenorphine; Intrathecal; Local Anaesthetics; Nalbuphine; Opioids.

Introduction

Sub-arachnoid block is the most commonly performed anaesthetic technique. Pain relief is of most importance in postopera-tive period for lower abdominal and lower limb surgeries. Bupivacaine heavy, the commonly used local anaesthetic when used alone acts for 90 to 120 minutes. Various adjuvants have been tried to prolong the analgesic effect of bupivacaine [1]. Opioids when used as additives in sub-arachnoid block have been found to prolong both anaesthesia and analgesia. They enhance the sensory blockade of local anaesthetics without affecting the sympathetic activity thus improves the quality of analgesia with haemodynamic stability.

Nalbuphine in dose of 0.8 mg, when given intrathecally with bupivacaine heavy, improved the quality of intraoperative and postoperative analgesia. Respiratory depression and abuse potential with nalbuphine is very less on comparing with other centrally acting opioid [2,3]. Buprenorphine in dose of 60 mcg when given intrathecally with bupivacaine heavy, improved the

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quality of intra and postoperative analgesia, as it dissociates slowly from μ-opioid receptor has less addiction potential [4].

Here we have compared the analgesic efficacy of nalbuphine with buprenorphine and their adverse effects. Few studies have investigated intrathecal nalbuphine and buprenorphine individually with hyperbaric bupivacaine, but no study in the literature has compared nalbuphine and buprenorphine [2,5]. Hence, we took up this study to compare the duration of post-operative analgesia when nalbuphine or buprenorphine added to bupivacaine as an adjuvant.

Materials and Methods

This study was conducted in a Medical College Hospital after approval from institutional ethical committee. A bilingual written informed consent was obtained from all the participating patients. A double blinded randomized clinical study was conducted on 60 adult patients of American Society of Anaesthesiologists (ASA) I and II, posted for lower abdominal and lower limb surgeries under subarachnoid block.

Inclusion criteria were; age between 18-60 years, either sex, patients with ASA I and II status and undergoing lower abdominal and lower limb surgery in subarachnoid block which were expected to be of 60-180 minutes. Exclusion criteria were; Patients under ASA III and IV, any contraindication to central neuraxial block, patient with known hypersensitivity to any of the study drugs, pregnancy, coagulation disorders, neurological disorders and spinal abnormalities. Sample size was calculated based on published clinical trials done comparing the adjuvants in subarachnoid blockade. Among total sample size of 60, 30 were allocated in each group. Complete pre anaesthetic check up was done to all the patients posted for surgery. Standard ASA fasting guidelines were followed. Patients were divided into group N & B randomly. All patients were premedicated before night with tablet ranitidine 150 mg, tablet metoclopramide 10 mg & tablet alprazolam 0.25mg. Patients were preloaded with ringer lactate 10 ml/Kg for 20 minutes after shifting to OT. In group N the patients received 15mg of 0.5% hyperbaric bupivacaine plus 0.8mg nalbuphine in sub-arachnoid block. In group B the patients received 15mg of 0.5% hyperbaric bupivacaine plus 60mcg buprenorphine.

Randomization is done by sealed envelope technique. Preparation of drugs is done by an independent anaesthesiologist who is not involved in the study and the drug mixture is administered by another anaesthesiologist who will be blinded and performing subarachnoid block. Spinal anaesthesia is performed in all patients in sitting position using 25G Quinckie spinal needles at L3-L4 or L4-L5 level under aseptic precautions. After observing free flow for CSF spinal solution was administered over 10-15sec. Patient will be moved to supine position immediately after drug administration. Completion of injection was taken as Zero time of induction of anaesthesia. Recordings done during the study were, time to onset of sensory block, time to onset of motor block, quality of sensory block by pinprick/spirit swab, quality of motor relaxation graded according to modified bromage scale, quality of surgical analgesia by surgical incision, intraoperative sedation by Ramsay sedation scoring, post op intensity of pain assessed by visual analog scale (VAS), duration of analgesia, first rescue analgesia. Adverse effects like nausea, vomiting, respiratory depression and pruritis were also recorded.

Surgery was allowed to proceed when T6 level block was achieved. ECG, pulse rate, mean arterial pressure, respiratory rate and arterial oxygen saturation was monitored for every 5 minutes in the initial 30 minutes of surgery, every 10 minutes in the next 1 hour of surgery and every 15 minutes for rest of the procedure. Systolic B.P <90mmhg or >30% decrease from baseline value was treated with Inj. Mephenteramine 6mg IV and extra fluid bolus of 100ml. Bradycardia with HR<50bpm was treated with Inj.Atropine 0.6mg. Oxygen 5L/min is administered via face mask when necessary. Nausea and vomiting was treated with inj. Ondansetron 4mg. Pruritis was treated with anti-histaminics.

The quality of surgical analgesia was scored as: Excellent: No supplementary drug required, Good: Analgesia required, Fair: More than one analgesic required, Poor: General anaesthesia required. Sensory blockade was assessed using pinprick method or using spirit swab .Onset of sensory block was taken as the time taken to attain sensory level of T6 dermatome. Duration of sensory block was defined as the time to two segment regression from the highest level of the sensory blockade. The degree of motor blockade was assessed with modified Bromage scale: O: No paralysis, 1: inability to raise extended knee, 2: inability to flex the knee, 3: inability to flex the ankle joint. Onset of motor block was considered as the time to achieve Grade 3 block from the time of subarachnoid injection. Duration was defined as the time to achieve Grade 0 block. Sedation was assessed using Ramsay sedation

scoring. 1: awake and alert, 2: sedated but responds to a verbal stimulus, 3: sedated but responds to mild physical stimulus, 4: sedated but responds to moderate or strong physicals, 5: not arousable.

Visual analogue scale - VAS consisted of a 10cm horizontal paper strip with two endpoints labelled "no pain" (0) and "worst pain"(10). When patient complains of pain he/she is asked to mark the strip at a point that corresponds to the level of pain intensity they felt presently. VAS was assessed at every 30min intervals from 60 min to 300min or until rescue analgesic was given. Post operatively sensory and motor block was evaluated every 30min during first 2hr, every 60min for next 6hr and at 12 hr and 24hr after entering recovery room. The duration of pain relief was defined as the time from spinal injection to the first request for rescue analgesics. The attending anaesthesiologist was advised to give rescue analgesia on demand with intravenous paracetamol 1gm, if not relieved 100 mg intravenous tramadol as needed. Analgesic requirement was on demand only.

Statistical Analysis

The statistical analysis was done using Statistical Package for Social Science evaluation (presented as mean, standard deviation and range) version 22.0 and data entry was entered in Microsoft excel 2011. Analysis of variance is used to test the hypothesis that several means are equal. The Independent-Samples T Test procedure was used to compare means for two groups. A p-value of 0.05 or less was considered significant.

Results

All the sixty enrolled patients had successfully completed the study. The groups were comparable in demographic data in terms of age, gender, weight, ASA class distribution and duration of the surgery.

The onset of block was significantly earlier group N compared to group B. Onset of sensory block in Group N was 1.519±0.367min, whereas in Group B it was 2.665±0.462 with *P*= 0.000. (Table 1)

Duration of sensory block was 170.60±24.42 in Group N and 237.93±16.43 in Group B with p = 0.000. (Table 2). Group B had significantly prolonged duration of sensory block.

Duration of analgesia was 295.60±18.95 in Group N and 566.43±42.19 in Group B with p = 0.000. Group B had significantly prolonged duration of block (Table 3).

Onset of motor block in Group N was 4.639± 0.976 min, whereas in Group B, it was 3.686±0.373 min which was found to be statistically significant with p = 0.000 (Table 4).

Table 1: Onset of sensory block

Drug	Onset of sensory block (min)		
	Mean	S.D	
Nalbuphine	1.519	.367	t value = -10.63 &
Buprenorphine	2.665	.462	p-value = 0.000

Table 2: Duration of sensory block

Drug	Duration of sensory block (min)		
	Mean	S.D	
Nalbuphine	170.60	24.42	t value = -12.532 &
Buprenorphine	237.93	16.43	p-value = 0.000

Table 3: Duration of analgesia

Drug	Duration of analgesia (min)		
	Mean	S.D	
Nalbuphine	295.60	18.95	t value = -32.073 &
Buprenorphine	566.43	42.19	p-value = 0.000

Table 4: Onset of motor block

Drug	Onset of motor block (min)		
	Mean	S.D	
Nalbuphine	4.639	0.976	t value = 4.990&
Buprenorphine	3.686	0.373	p-value = 0.000

Duration of motor block was 257.17±27.74 in Group N and in Group B was 410.93±17.79 with *P* = 0.000. Duration of motor blockade is significantly prolonged in Group B (Table 5a). Duration of requirement of first rescue analgesia was 296.57±18.95 in Group N whereas 567.43±42.19 in Group B with p = 0.000, thus highlighting the fact that group B had prolonged post operative analgesia (Table 5b).

There was no significant difference in various hemodynamic parameters intra and post operatively between the two groups. (Figure1 and 2).

Three patients in group N and five patients in group B had nausea and vomiting. One patient in Group B had sedation as side effect.

Table 5: Duration of motor block

Drug	Duration of motor block (min)		
	Mean	S.D	
Nalbuphine	257.17	27.74	t value = -25.554 &
Buprenorphine	410.93	17.79	p-value = 0.000

Table 5: Time for rescue analgesia

Drug	Time rescue analgesia (min)		
	Mean	S.D	
Nalbuphine	296.57	18.95	t value = -32.078 &
Buprenorphine	567.43	42.19	p-value = 0.000

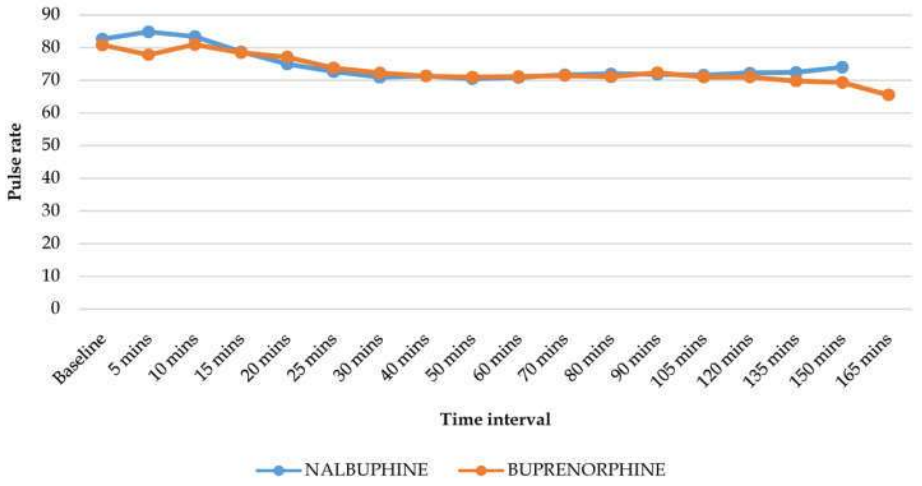

Fig. 1: Heart rate

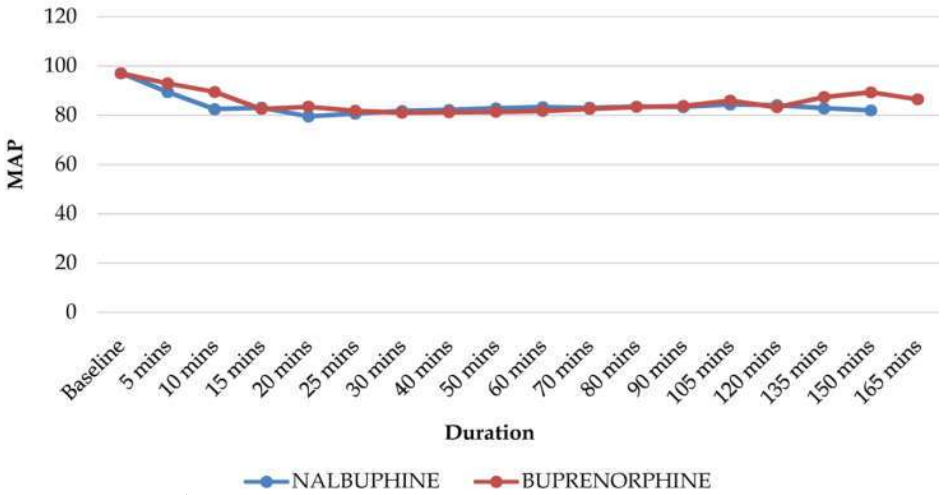

Fig. 2: Mean arterial pressure

Discussion

Spinal anaesthesia is the most commonly used technique for the lower abdominal and lower limb surgeries. Intrathecal opioids are quite commonly used as adjunct to local anaesthetics in regional anaesthesia with multiple advantages like they provide better perioperative sensory and motor blockade with prolonged postoperative analgesia. By reducing the local anaesthetic dosage, they decrease local anaesthetic toxicity and the side effects associated with high spinal. To overcome the side effects of opioids (mu), the partial agonist-antagonist opioids action has been studied extensively. Buprenorphine and nalbuphine competitively displaces other μ antagonists from the receptors without any agonistic effect when bound to the ì receptors. As they bind to kappa receptors, it has agonistic effect. Hence, they are mixed agonist-antagonist. They produce analgesia with minimal ì side effects.

Fournier et al reported faster onset of pain relief with intrathecal nalbuphine compared to intrathecal morphine [6]. Tiwari AK et al., Mukherjee et al., Mostafa MG et al., reported that nalbuphine prolonged duration of analgesia with reduced VAS pain score [7,8,9,10]. Culebras X et al., compared intrathecal morphine with nalbuphine in different doses viz., 0.2 mg, 0.8 mg and 1.6 mg concluded that nalbuphine 0.8 mg prolong postoperative analgesia, without side effects [11]. Ahluwalia et al., also observed Nalbuphine dose of 0.8mg as safer and effective dose, as nalbuphine exhibits a ceiling effect to analgesia [12]. Studies done by Gomaa *et al.*, comparing fentanyl and nalbuphine say prolonged duration analgesia with nalbuphine but results were statistically insignificant [13].

Sapkal et al., and sandhya gujar et al., had proven nausea and vomiting was higher in sub-arachnoid buprenorphine compared to sub-arachnoid clonidine [14,15]. Vadivelu et al. observed that nausea vomiting and light headedness were much prevalent with buprenorphine [16]. Studies done by Khan et al., and Capogna et al., state prolonged duration of analgesia with buprenorphine [17,18].

Our study results were well correlating with above studies. Sedation was also compared in both groups but none of the patients had sedation score more than two except one in buprenorphine group which contradicted our study with others. As studies state that both nalbuphine and buprenorphine produce sedation, which was correlating with study done by Prabhakaraiah et al., comparing nalbuphine with fentanyl [19].

In our present study, we have used preservative free nalbuphine 0.8mg and buprenorphine 60mcg as adjuvants to bupivacaine heavy intrathecally and compared their onset, duration and postoperative analgesia. Our study results showed that onset of sensory block and motor block were quicker in nalbuphine group. But the duration of sensory block, motor block and postoperative analgesia was prolonged in buprenorphine group compared to nalbuphine group. In our study we did not find any statistically significant difference in hemodynamics in both groups which shows that both the opioids did not have any significant sympatholytic activity. Side effects like nausea, vomiting, pruritis, sedation were minimal in both the groups but nalbuphine group has advantage over buprenorphine group. There are differences in pharmacological properties in nalbuphine and buprenorphine which needs to be further evaluated.

Conclusion

From our study, we conclude that both nalbuphine and buprenorphine are good choice of adjuvants to subarachnoid blockade. They shorten the onset of sensory and motor block. Buprenorphine compared to nalbuphine prolongs the duration of sensory and motor blockade and also prolongs postoperative analgesia and duration for first rescue analgesia, with minimal side effects.

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