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Original Research Article

A Comparative Study of Efficacy of Intrathecal Nalbuphine in Different Doses as an Adjuvant to Levo Bupivacaine in Subarachnoid Block

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Abstract: Previous studies are there showing Nalbuphine used intrathecally as an adjuvant to bupivacaine but no study clearly stated the most effective dose of nalbuphine with minimum side effects. Levobupivacaine is less cardiotoxic and there are few studies using nalbuphine with levobupivacaine. The purpose of this study was to compare different block characteristics, hemodynamic effects, postoperative analgesia, and adverse effects of different doses of nalbuphine when used intrathecally with hyperbaric levobupivacaine for spinal anesthesia. The patients were randomly allocated into four groups (30 patients each). Group 1 received levobupivacaine (0.5%) 2.5 with normal saline, group II received Isobaric Levobupivacaine (0.5%) 2.5 ml plus nalbuphine 0.5 mg total made to 3 ml Group III received Isobaric Levobupivacaine (0.5%) 2.5 ml plus nalbuphine 0.75 mg total made 3 ml ,Group IV received Isobaric Levobupivacaine(0.5%) 2.5 ml plus nalbuphine 1 mg diluted and total made to 3 ml. The onset and duration of sensory and motor block, the regression time of sensory and motor block, hemodynamic changes, and side effects were recorded. Patients in Group III and IV had significantly longer sensory and motor block than patients in Groups I and II. Side effects were more with group III and IV compared to group I and II. Intrathecal nalbuphne (0.75mg and 1mg) was associated with prolonged motor and sensory block, compared to 0.5mg and levo bupivacaine alone.
Keywords: Nalbuphine, levobupivacaine, intrathecal.

INTRODUCTION

Nalbuphine hydrochloride is a synthetic opioid agonist – antagonist analgesic of the phenanthrene series. Adding Nalbuphine to epidural analgesic agents provides an increase in the efficacy and the duration of postoperative analgesia [1]. The use of nalbuphine as a sole analgesic agent provides satisfactory cover of mild to moderate types of pain with a low incidence of side effects. The ceiling effect of nalbuphine with increasing the dose, which prevents it from covering the most severe pain, also prevents unwanted sedation and respiratory depression. Nalbuphine provides an increased safety margin, when compared to μ-agonists. When nalbuphine is used concurrently with μ-agonists (e.g. morphine and fentanyl), the benefits of both μ- and κ-analgesia can be obtained, with decreasing the severity of the common μ-agonist side effects (itching, nausea/vomiting, urinary retention, constipation, respiratory depression and prolonged sedation) [2].

Regional anesthesia in children is of utmost importance to potentiate the effect of the general anesthesia and to prevent pain before it is initiated. The use of analgesic combination is best limited to the one, which does not produce respiratory depression or vomiting [3]. The levorotatory isomers of bupivacaine were shown to have a safer pharmacological profile with less cardiac and neurotoxic adverse effects. The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate. Levobupivacaine produces subarachnoid block similar to the sensory and motor effects and recovery of bupivacaine with earlier regression of its motor block. Intrathecal administration of 15 mg of levobupivacaine provides an adequate sensory and motor block lasting for approximately 6.5 h, while smaller doses (i.e., 5–10 mg) are used in day-case surgeries. Low concentrations of levobupivacaine may be favorable for ambulatory surgery. The addition of opioids provides a dose sparing

effect of levobupivacaine, which improves the quality of the block with less hemodynamic changes [4].

The dose of levobupivacaine for infant spinal anesthesia is 1 mg/kg of isobaric 0.5% bupivacaine and ropivacaine and 1.2 mg/kg of isobaric 0.5% levobupivacaine. The recommended dose of levobupivacaine for effective caudal anesthesia has been studied to be 2.5 mg/kg. Post-operative epidural infusions of 0.125% levobupivacaine or ropivacaine in pediatric patients produce significantly less motor blockade with equal analgesia as compared to a similar infusion of bupivacaine. It is important to note that toxicity of local anesthetics may be potentiated in patients with hepatic or renal affection, respiratory diseases and pre-existing heart conditions. The drug toxicity may be potentiated with hypoxia. However, the most common cause of the toxicity is inadvertent intravascular injection [5]. Our aim was to find out that the ideal dose of nalbuphine to be the local anaesthetic intrathecally which will prolong the duration of postoperative analgesia and reduce the need for rescue analgesia.

METHODS

After obtaining approval from the Hospital Ethics Committee and informed consent, 120 adults of either sex belonging to American Society of Anaesthesiology (ASA) class I and II, were enrolled in this prospective, randomized, and double blinded study. Patients with contraindication to regional anaesthesia, history of significant coexisting diseases like ischemic heart disease, hypertension, impaired renal functions, rheumatoid arthritis, and severe liver disease where excluded from the study. All patients were investigated a day prior to surgery, and were explained about visual analogue scale (VAS) [6] for measuring the postoperative pain. In the operation theatre electrocardiogram (ECG), pulse oximetry, and noninvasive blood pressure were attached and baseline parameters were recorded and monitoring was initiated. Intravenous (IV) access was secured and all patients were preloaded with ringer lactate 10 ml/kg. All the patients were randomly assigned using sealed envelope technique to any of the four groups in a double blind manner. Group 1 received levobupivacaine (0.5%) 2.5 with normal saline, group II received Isobaric Levobupivacaine (0.5%) 2.5 ml plus nalbuphine 0.5 mg total made to 3 ml Group III received Isobaric Levobupivacaine (0.5%) 2.5 ml plus nalbuphine 0.75 mg total made 3 ml ,Group IV received Isobaric Levobupivacaine(0.5%) 2.5 ml plus nalbuphine 1 mg diluted and total made to 3 ml. Subarachnoid block was administered at the L 2-3 or L 3-4 vertebral level using 26-gauge Quincke spinal needle with patients in the sitting position. The anaesthesiologist performing the block recorded the intraoperative data. The onset and duration of sensory block, highest level of sensory block, time to reach the highest dermatomal level of sensory block, motor block onset, time to complete motor block recovery, and duration of spinal anaesthesia were recorded. The onset of sensory block was defined as the time between injection of intrathecal anaesthetic and the absence of pain at the T8 dermatome assessed by sterile pinprick every 2 min till T8 dermatome was achieved. The highest level of sensory block was evaluated by pinprick at midclavicular line anteriorly every 5 min for 20 min after the injection, thereafter every 15 min. The duration of sensory block was defined as the time of regression of two segments in the maximum block height, evaluated by pinprick. The motor level was assessed according to modified Bromage score: **[**7]. Bromage 0, the patient is able to move the hip, knee, and ankle; Bromage 1, the patient is unable to move the hip, but is able to move the knee and ankle; Bromage 2, the patient is unable to move hip and knee, but is able to move the ankle; and Bromage 3, the patient is unable to move the hip, knee, and ankle. Time for motor block onset was defined as modified Bromage score of 3. Complete motor block recovery was assumed when modified Bromage score was 0.The duration of spinal anesthesia was defined as the period from spinal injection to the first occasion when the patient complained of pain in the postoperative period. All durations were calculated considering the time of spinal injection as time zero. Surgery was allowed to commence on achieving adequate sensory block height (T8).

Vitals were recorded 5 min before intrathecal injection; 5, 10, 15, 20, and 25 minutes after and subsequently every 15 minutes. Pain scores using VAS were recorded 5 min before intrathecal injection, after the start of surgery, and subsequently every 15 min till the surgery was over; and thereafter VAS was assessed in the postoperative period. IV fluids were given to maintain the blood pressure. Hypotension was defined as a decrease in systolic blood pressure (SBP) by 30% from baseline and was treated with IV boluses of 6 mg ephedrine or crystalloid fluids. Heart rate (HR) less than 50 beats/min was corrected using 0.6 mg of IV atropine sulphate. The incidence of pruritus, nausea, vomiting, and sedation were recorded. De Kock sedation scale [8] was used: 1 = patient somnolent but responding to verbal commands; 2 = patient somnolent, not responding to verbal commands but responding to manual stimulation; and 3 = patient somnolent, not responding to verbal commands or manual stimulation.

Motor block recovery (modified Bromage score of zero), sensory block regression were assessed every 15 min after completion of surgery till the time of regression of two segments in maximum block in the post-anesthetic care unit (PACU) along with the vital signs and VAS scores. Any patient showing VAS more than or equal to 3 was administered a supplemental dose of IV. tramadol 50 mg. The amount required by the patients in the next 24 h was recorded in all the groups. Data obtained were tabulated and analyzed using Statistical Package for Social Science (SPSS 15.0 evaluation version). To calculate the sample size, a power analysis of = 0.05 and = 1.00 showed that 30 patients were needed per study group to detect an increase of 30 min difference between the median duration of spinal sensory block between the groups. Data was expressed as means and standard deviation (SD), medians and ranges, or numbers and percentages. For categorical covariates (sex, ASA class, nausea/vomiting, use of additive analgesia, hypotension, and bradycardia) Chi-square test or Fisher's exact test was used as appropriate, with *P* value reported at the 95% confidence interval (CI). Continuous covariates (age, duration of surgery) were compared using analysis of variance (ANOVA). If *P* value <0.05 was considered significant.

RESULT

The effects of intrathecal 0.5% hyperbaric bupivacaine with nalbuphine hydrochloride at three different doses (0.8, 1.6, and 2.4 mg) was studied and compared with 0.5% hyperbaric bupivacaine alone in 100 patients belonging to ASA grade I and II who underwent lower limb orthopedic and lower abdominal procedures including general surgeries and gynecological surgeries. The four groups of patients I, II, III, and IV included in the study did not differ significantly with respect to age, sex, body weight, height, type, and duration of surgery as shown in [Table1].

The results regarding the characteristics of sensory block are summarized in [Table 2].

Table-1: Demographic profile

variables	Group I	Group II	Group 111	Group IV	P VALUE
age	45.2± 12.8	42.7± 12.4	39.7 1±3.8	41.3± 11.9	0.64
Sex(M:F)	20:10	22:8	!8:12	20:10	0.71
Height(cm)	158.8± 6.12	160.5± 5.66	162.8 ±6.54	160.9 ±6.1	0.68
weight	62.55± 10.7	60.45± 9.22	64.8 ±8.9	61.24± 9.1	0.82
Duration of surgery	90.45± 15.6	95.44± 12.85	94.15± 10.68	96.1 ±8.2	0.59

Table-2: Sensory and motor block characteristics

variable	Group I	Group II	Group III	Group IV	P value
Time of onset of sensory block(min)	2.92± 0.85	2.5± 0.77	2.24± 0.68	2.15± 0.7	<0.001
Time of onset of motor block(min)	4.82± 0.8	4.5± 0.6	4.1± 0.7	3.7± 0.6	<0.001
Time to reach maximum sensory level(min)	8.75 ± 1.3	8.14± 1.2	7.4± 0.7	6.5± 0.4	<0.001
Duration of motor block(min)	148.34± 7.8	160.6± 5.8	186.7± 8.6	204.8± 9.5	<0.001
Duration of sensory block(min)	164.5± 5.7	183.9± 6.1	205.14± 5.4	230.8± 6.3	<0.001
Time to administer first rescue analgesia(min)	185.6± 13.55	208.84± 10.7	235.42 ± 11.49	280.62± 13.95	<0.001

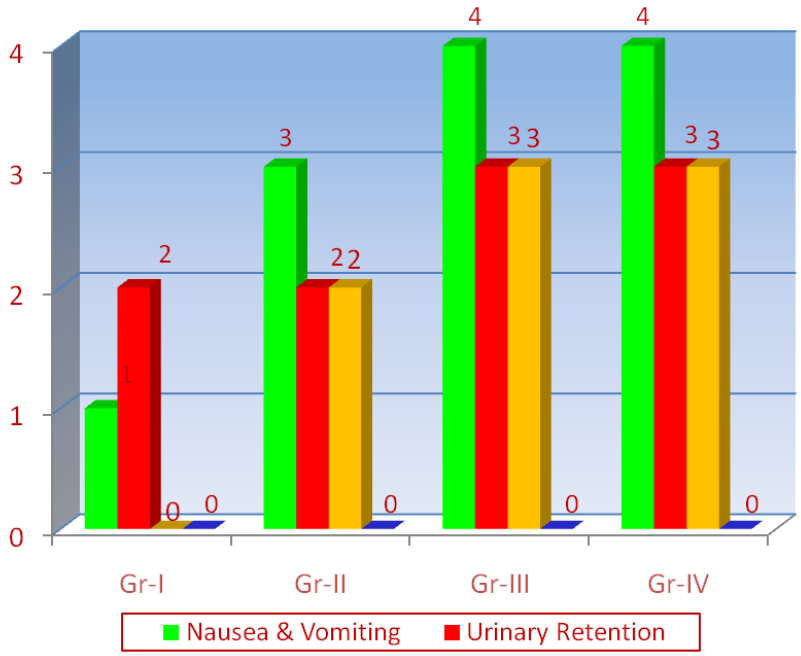

Fig-1: complications

There were no serious complications like nausea, vomiting, urinary retention, shivering, pruritis, hypotension, or respiratory depression as shown in figure1.

DISCUSSION

Recent reports suggest that the intrathecal opioids are safe and effective [10-13]. There were studies of neuraxial administration of nalbuphine with local anesthetics that have shown to produce prolonged analgesia with minimal pruritus and respiratory depression [14-15]. Fuornier *et al.;* In their study, studied 60 obstetric patients under spinal anaesthesia who received morphine 0.1 mg or nalbuphine 1 mg or morphine 0.1 mg with nalbuphine 1 mg in addition to 0.5% bupivacaine 10 mg. They concluded that effective analgesia was prolonged in the morphine with nalbuphine group [16]. Tiwari *et al.;* studied the analgesic effects of intrathecal morphine and nalbuphine and concluded that administration of intrathecal nalbuphine resulted in a significantly faster onset of pain relief and shorter duration of analgesia than intrathecal morphine [17].

Culebras *et al.;* evaluated the analgesic effect of 0.4 mg morphine or 0.4 mg nalbuphine for spinal anaesthesia and found no difference between the groups [18]. There are other studies comparing the different doses of nalbuphine in intrathecal route which has proved nalbuphine as a potent adjuvant to local anaesthetics [19-21].

CONCLUSION

Nalbuphine (2 mg) as intrathecal adjuvant to 0.5% hyperbaric bupivacaine (17.5 mg) for subarachnoid blockade was clinically more efficient than fentanyl for extending the duration of sensory motor block and enhancing the postoperative analgesia following orthopedic surgery of lower limb, with negligible adverse effects.

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