A COMPARATIVE STUDY OF NALBUPHINE IN DIFFERENT DOSES AS AN ADJUVANT TO BUPIVACAINE IN SUBARACHNOID BLOCK

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ABSTRACT

BACKGROUND

Various opioids are used as adjuvants to local anaesthetics in neuraxial block for prolongation of analgesia. Nalbuphine is a synthetic opioid having mixed action, agonist at kappa receptors and antagonist at mu opioid receptors.

The aim of this study is to compare Nalbuphine in different doses as adjuvant to hyperbaric bupivacaine with bupivacaine alone in subarachnoid block. The parameters compared are onset and duration of sensory block, duration of post-operative analgesia, VAS (Visual Analogue Scale) score, haemodynamic changes, sedation score and adverse effect if any.

MATERIALS AND METHODS

A prospective, randomised, double-blind study was carried out on 120 adult patients of ASA Gr - 1, 2 posted for infraumbilical surgeries under spinal anaesthesia. Patients were randomly allocated into four groups with 30 patients in each group. Group I (control group) received hyperbaric bupivacaine 0.5%, 3 mL (15 mg) with 0.5 mL of 0.9% normal saline. Group II, III, IV each received 0.5% hyperbaric bupivacaine 3 mL (15 mg) with 0.5 mg, 0.75 mg and 1 mg Nalbuphine respectively with added normal saline 0.9% making the total volume 3.5 mL in each group.

RESULTS

The onset of sensory block is almost similar in all the groups, but the mean duration of analgesia was prolonged in Gr II, III, IV to 280.84±25.0, 295.12±39.8, 305.8±20.2 minutes respectively in comparison to Gr I: 168.80 ± 22.0 mins. Mean VAS score in Gr I, II, III, IV were 4.05±0.7, 3.5±0.6, 3.5±0.5, 3.4±0.3 respectively. Haemodynamic parameters are within normal range. Addition of Nalbuphine produce conscious sedation with minimal side effects.

CONCLUSION

Addition of Nalbuphine to hyperbaric bupivacaine for subarachnoid block produce longer duration of analgesia. Among different doses of Nalbuphine, 1 mg of Nalbuphine with bupivacaine produce best results with more longer post-operative analgesia.

KEYWORDS

Nalbuphine Hydrochloride, Hyperbaric Bupivacaine, Subarachnoid Block, Post-Operative Analgesia.

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BACKGROUND

Pain is an unpleasant sensory, emotional, psychological response associated with potential tissue damage. Postoperative pain increases the possibility of post-surgical complications, raises the cost of medical care and most importantly interferes with recovery and return to normal activities of daily living.

Subarachnoid block is one of the most popular regional block used for infraumbilical surgeries and hyperbaric bupivacaine is the most common local anaesthetic used for subarachnoid block, but the drawback is single shot bupivacaine cannot be used for prolonged surgeries and it also lack post-operative analgesic action.

So different drug combinations are used to prolong the duration of anaesthesia and to produce post-operative analgesia. Opioids are the most commonly used adjuvants to local anaesthetics in neuraxial block.^{1,2} The rationale for the combination of local anaesthetics and opioids is that local anaesthetics act at nerve axons and opioids at the receptor sites of spinal cord, thereby relieving pain.³

Nalbuphine is an opioid structurally related to oxymorphone. It has agonist action at the kappa receptors (κ) and an antagonist action at the mu (μ) opioid receptors.^{4,5} Previous studies have shown that epidural or intrathecal administration of Nalbuphine produces a significant analgesia accompanied by minimal pruritus and respiratory depression.^{6,7}

In search of ideal agent which can be universally used in all situations, of less side effects, easily available and cost effective we studied the effect of Nalbuphine added in different doses as an adjunct to hyperbaric bupivacaine and compared it with bupivacaine alone in subarachnoid block.

MATERIALS AND METHODS

After taking approval from Hospital Ethical Committee, a prospective, randomised, double-blind study was carried out on 120 adult patients of ASA I and II, of either sex between

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the age group of 18 - 60 years admitted for infraumbilical surgeries under subarachnoid block.

Exclusion Criteria

1. ASA Grade III and IV.
2. Patients under drug abuse.
3. Contraindications for spinal anaesthesia.

After taking written informed consent from patients who were satisfying our criteria, they were randomly allocated into four groups of 30 patients in each group.

Group I received bupivacaine 0.5% heavy 3 mL (15 mg) with 0.5 mL (0.9%) normal saline.

Group II, III and IV received bupivacaine 0.5% heavy 3 mL (15 mg) with preservative free Nalbuphine 0.5 mg, 0.75 mg and 1 mg respectively along with normal saline (0.9%) making the total volume 3.5 mL in each group.

Nalbuphine ampule containing preservative free Nalbuphine hydrochloride 10/20 mg in 1 mL (Glenmark) was used in the study. Accurate dose of Nalbuphine was measured using insulin syringe.

The patients satisfying the inclusion criteria underwent pre-anaesthetic checkup. After checking the basic lab investigations, patients were advised to take tablet ranitidine 150 mg and tablet alprazolam 0.5 mg night before surgery and fasting for 6 hours prior to surgery. The patients were well explained about the procedure of the spinal anaesthesia and VAS (Visual Analog Scale) for expressing pain score.

In the operating room, multipara monitor was connected for continuous recording of Pulse Rate (PR), Non-Invasive Blood Pressure (NIBP), Oxygen Saturation (SpO₂), Respiratory Rate (RR) and ECG. Basal readings were recorded. Intravenous line was secured with 18-G cannula and each patient preloaded with crystalloid 10 mL/kg. Under all aseptic precautions, spinal anaesthesia was given in sitting position at L3-L4 interspace by 25-G Quincke spinal needle. One of the drug regimen was randomly selected and injected into subarachnoid space through the spinal needle followed by which patient was made supine immediately. The patient and the treating anaesthetist were blind about the study drug injected. Vital parameters were recorded every 5 minutes intraoperatively and every 15 minutes post-operatively for 2 hours and then every 2 hours for 24 hours till the rescue analgesia was given, that is VAS > 3. Rescue analgesia was given by Inj. Diclofenac sodium 75 mg IM. Intraoperative hypotension and bradycardia were treated with Inj. Ephedrine and Inj. Atropine respectively. In case of decrease in SpO₂ < 90%, O₂ is given by facemask at 6 litre/min.

The following Parameters were Studied

1. Onset of sensory block, through Pin-Prick method.
2. Time for two dermatomal regression.
3. Duration of effective analgesia that is time from onset of sensory block to the first rescue analgesia or VAS > 3.
4. Haemodynamic changes like hypotension, bradycardia, respiratory depression.
5. Incidence of side effects like nausea, vomiting, urinary retention and pruritus.
6. Sedation was monitored for 12 hours with Campbell Scoring.

Campbell Scoring

Grade I - Wide awake.

Grade II - Sedated, but arousable.

Grade III - Drowsy, difficult to arouse.

Grade IV - Unarousable.

Pain scoring done by Visual Analog Scale (VAS), on scale of 10 points, 0 being no pain and 10 being worst pain.

The results obtained were documented and analysed statistically using SPSS software version 16. Data were analysed in ANOVA analysis. Frequencies expressed as number and percentage.

RESULTS

The demographic variables like age, sex, weight, height and the duration of surgery were comparable in all the groups, $P > 0.05$ (Table 1).

By the addition of Nalbuphine to hyperbaric bupivacaine, the time for two segment regression and the duration of analgesia were prolonged and was statistically significant, $P < 0.05$ as seen in Gr II, III, IV in comparison to Gr I (bupivacaine alone) (Table 2). However, the onset of sensory block was not statistically significant among the groups (Table 2).

The mean VAS score was 4.05 ± 0.7 in Group I, which was significantly higher in comparison to other study groups. It was 3.5 ± 0.6 , 3.5 ± 0.5 and 3.4 ± 0.3 in Group II, III and IV respectively (Table 2).

There was significant difference in the haemodynamic parameters among the study groups. However, it did not require any intervention (Table 4).

Most of the patients had sedation score of 1 in Group I, while it was 2 where the study drug Nalbuphine was added. In Group IV, only 2 patients had a sedation score of 3 (Table 5).

Side effects viz. nausea, vomiting, urinary retention, pruritus and respiratory depression were statistically insignificant among the groups (Table 5).

	Group I	Group II	Group III	Group IV	P value
Age in years	40.8±14.1	39.6±15.2	38.2±14.4	42.2±13.2	> 0.05
Weight in kg	64.9±5.22	66.02±11.87	65.31±10.4	67.9±5.22	> 0.05
Height in cm	164.3±5.7	162.2±4.38	165.3±4.2	168.2±2.24	> 0.05
Sex(m:f)	14:16	17:13	16:14	18:12	> 0.05
Duration of surgery (min.)	105.8±23.2	109.16±24.3	116.2±28.4	114.4±30.1	> 0.05

Table 1. Demographic Characteristics

Parameters	Group I	Group II	Group III	Group IV	P value
Onset of Sensory Block in min	3.3±0.8	3.1±0.6	3.2±0.4	3.1±0.4	> 0.05
Two Dermatomal Regression of Sensory Block in min	92.0±4.2	130.4±6.5	140.7±4.9	160.2±5.4	< 0.05
Duration of Analgesia in min	168.80±22.0	280.84±25.0	295.12±39.8	305.8±20.2	< 0.001
VAS	4.05±0.7	3.5±0.6	3.5±0.5	3.4±0.3	< 0.05

Table 2. Summary of Results

	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	Group IV (n = 30)	P value
Hear rate (Beats/ min)	84.20±9.25	78.25±10.20	75.20±12.25	68.18±10.24	<0.05*
Systolic B.P	124.82±10.25	118.68±9.18	115.20±5.86	112.26±2.4	>0.05
Diastolic B.P	75±7.62	74.2±8.66	72.88±2.8	70.86±6.8	>0.05

Table 3. Comparison of Haemodynamic Parameters

*Did not require any clinical intervention.

Sedation Score	Group I	Group II	Group III	Group IV
1	28(93.33%)	7(23.33%)	5(16.66%)	4(13.33%)
2	2(6.67%)	23(76.66%)	25(83.33%)	24(80%)
3	Nil	Nil	Nil	2(6.67%)
4	Nil	Nil	Nil	Nil

Table 4. Sedation Score

Group	Nausea, Vomiting	Urinary Retention	Pruritus	Respiratory Depression
I	1	2	0	0
II	3	2	2	0
III	4	3	3	0
IV	4	3	3	0

Table 5. Side Effects

DISCUSSION

Nalbuphine is a mixed agonist-antagonist opioid that binds to both mu (μ) and kappa (κ) receptors. It acts by competitively displacing other mu receptor agonists without manifesting any mu agonist activity, but acting as an agonist at kappa receptors. Thus, it has a divergent activity.

Nalbuphine when given for neuraxial block, it binds to kappa receptors present in neuraxis thereby producing analgesia and sedation.

Our study entitled - "A comparative study of Nalbuphine in different doses as an adjuvant in subarachnoid block" for infraumbilical surgery was carried out and the results were compared with the observations of other workers.

In animal studies, it has been proved that Nalbuphine when used as an intrathecal opioid has no neurotoxic activities. Rawal et al⁸ used intrathecal Nalbuphine in large doses 15 - 24 mg in a sheep model and found no histopathological changes of spinal cord.

Tiwari et al⁹ found that addition of Nalbuphine to bupivacaine has no change in onset of time for sensory and motor block. This finding is similar to our study where we did not find any statistically significant change in onset of time

for sensory and motor block. This finding also co-related with Jyothi et al.¹⁰

In our study, two segment regression time and duration of analgesia was prolonged in Group II, III and IV compared to Group I. Moreover, maximum prolongation of analgesia occurred in Group IV, in which higher dose of Nalbuphine - 1 mg was used.

Similar findings were seen in the study conducted by Tiwari et al,⁹ Pugh and Drummond GB,¹¹ and Thoma et al.¹² However, the ceiling properties for analgesic action of Nalbuphine was not seen in our study. By increasing the dose of Nalbuphine from 0.5 mg - 1 mg, we observed prolongation of analgesic activity. Prolongation of duration of analgesia was also similar to study conducted by Lin, Calebras et al¹³ and Mastaffa et al.¹⁴

In our study, there was no statistically significant difference in change of haemodynamic parameters. This observation is similar to the study done by Calebras et al,¹³ Tiwari et al⁹ and Mostaffa et al.¹⁴

In our study, we did not find any case of respiratory depression that is RR < 10/mins. and SpO₂ < 90%. This is similar to study done by Ramagnoli and Keate.¹⁵ This is

because respiratory depression is mu receptor mediated and Nalbuphine is antagonist at this receptor.

In Group I, in which bupivacaine alone was used, patients were conscious, awake and apprehensive, whereas patients who received Nalbuphine as adjuvant to bupivacaine were sedated, calm but easily arousable. This can be correlated with the study done by Calebras et al,¹³ Mostafa et al¹⁴ and Tiwari et al.⁹

CONCLUSION

From the above study, it is concluded that Nalbuphine hydrochloride added to hyperbaric bupivacaine in subarachnoid block prolongs the duration of sensory blockade provides long duration of postoperative analgesia provides good sedation with minimal side effects. Among Nalbuphine-Bupivacaine combination, 1 mg of Nalbuphine (Group IV) as adjuvant to hyperbaric bupivacaine for intrathecal anaesthesia provides best results in comparison to 0.5 mg and 0.75 mg in terms of prolongation of analgesia and sedation scores without side effects.

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