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Comparison of intrathecal nalbuphine and clonidine as adjuvants to hyperbaric bupivacaine in infraumbilical surgeries

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Abstract

Background: Adding adjuvant drugs to the intrathecal local anaesthetics improve the duration of spinal blockade, prolongs postoperative analgesia and it is also possible to reduce the dose of the local anaesthetics. Present study was done to compare and evaluate the efficacy of intrathecal hyperbaric Bupivacaine 12.5mg supplemented with 800µg Nalbuphine and 30µg Clonidine in patients undergoing infraumbilical surgeries under subarachnoid block.

Material & Methods:100 American Society of Anaesthesiology I and II patients who were undergoing infraumbilical surgeries under spinal anaesthesia were enrolled in this prospective randomized double-blinded controlled study. We randomly allocated them into two groups to receive either 800µg nalbuphine (Group I)or 30µg Clonidine (Group II)made up to 0.5 ml and added to 12.5mg of 0.5% bupivacaine. The onset and duration of sensory block and motor block, duration of analgesia, rescue analgesia, vital parameters, and adverse effects were compared between these groups.

Results: In our study, we found that the mean time for 2-segment regression of sensory blockade in group I was 152.64±4.35 minutes while in group II, it was 119.2±10.43 minutes (p value<0.001). There was no significant difference regarding the onset of block and haemodynamic parameters. Number of rescue analgesia dosesin 24 hours period were 2.42±0.49 in group I and 3.2±0.49 in group II. Difference was highly significant (p value <0.001).

Conclusion: Nalbuphine group is better than Clonidine group in terms of prolonged duration of sensory blockade, prolonged Postoperative analgesia and lesser number of doses of rescue analgesia required.

Keywords: Intrathecal, Nalbuphine, Clonidine, Bupivacaine, Adjuvants

Introduction

The main limitations of spinal anaesthesia are it's short duration of action and that it does not provide prolonged postoperative analgesia when it is performed with local anaesthetics alone. Adding adjuvant drugs to the intrathecal local anaesthetics improves the quality and duration of spinal blockade, and prolongs postoperative analgesia. It is also possible to reduce the dose of the local anaesthetics as well as the total postoperative analgesics. Various adjuvants have been used along with local anaesthetics for the prolongation of analgesia both intraoperative and postoperatively in neuraxial blockade. The frequently used adjuvants include: opioids, midazolam, alpha-2 adrenergic agonists, neostigmine, ketamine, etc. However, the use of these adjuvants is often thwarted due to the adverse effects due to them or because of unreliable postoperative analgesia.

Various opioids have been used intrathecally along with bupivacaine to prolong its effect, to improve the quality of analgesia, enhancing analgesia from sub therapeutic doses of local anaesthetic making it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anaesthetic and minimize the requirement of postoperative analgesics.[1-2] Nalbuphine is a semisynthetic opioid agonist-antagonist with mu antagonist and k agonist properties.[3]It has been used as an additive with bupivacaine intrathecally in several clinical settings in doses from 200 to 1600 µg.[4-6]

Intrathecal α2-agonists are used as adjuvant drugs to local anaesthetics, as they potentiate the effect of local anaesthetics and allow a decrease in the required doses. Clonidine is a partial α2-adrenoreceptor agonist used intrathecally, with a well-established record of efficacy and safety.[7] Clonidine has variety of different actions, including antihypertensive effects as well as ability to potentiate the effects of local anaesthetics when added intrathecally to them, prolonging the duration of both motor and sensory spinal blockade.[8-10]

Although nalbuphine is being used more frequently now, there have been relatively fewer studies in literature on the clinical characteristics on intrathecal administration of nalbuphine. This study aimed to build more evidence for it's intrathecal usage as an adjuvant to bupivacaine. We compared it with clonidine, which has been long used as an established adjuvant to bupivacaine intrathecally.

Materials and Methods

After institutional approval and informed written consent, 100 adults of either sex belonging to American Society of Anaesthesiology (ASA) grade I & II, aged 18-60years and scheduled for infra-umbilical surgeries, using subarachnoid block were enrolled in this prospective, randomized controlled study. They were divided into two groups, Group I/Nalbuphine group: receiving 2.5 ml of 0.5% Bupivacaine with 800 µg of Nalbuphine made to 0.5 ml, and Group II/Clonidine group: receiving 2.5ml of 0.5% Bupivacaine with 30 µg of Clonidine made to 0.5ml. A total drug volume of 3.0ml was injected. Patients with contra-indications for subarachnoid block, patients with significant neurological, psychiatric, neuromuscular, cardiovascular, coagulation, pulmonary, renal or hepatic disease or alcohol or drug abuse, malnourished patients, pregnant or lactating women, and patients who refused to be part of this study were excluded.

Pre-anaesthetic checkup was done for all patients and written informed consent was taken. Routine investigations and any specific investigations, if required according to the individual cases were also done. Patients were familiarized with visual analogue scale (VAS) and its use for measuring the postoperative pain. All patients were fasted overnight for 8 to 10 hrs.

Intraoperative: On arrival to the operating room, in all patients, an intravenous line was secured on one arm with a 20G intravenous cannula, & infusion with freely flowing Ringer's lactate was started. All patients were monitored by automated NIBP, pulse oximetry & electrocardiography. Under strict aseptic precautions, with patient in left lateral decubitus position, lumbar puncture was performed at the L3–4 interspace, with a 23-gauge Quincke-point needle. After aspiration of CSF, the patients were given one of the study drugs intrathecally according to the random number chartand the time of injection was recorded as 0 minutes. The study drug was prepared by another investigator to facilitate double blinding. After administering the drug, spinal needle was taken out and the patients were made supine immediately and were given 5 litres per minute of O_2 via an oxygen inhalation mask. The anaesthesiologists performing the technique recorded the intra operative data and followed the patient postoperatively until discharged from post anaesthesia care unit. In case of failed block, general anaesthesia was given and the patient was excluded from the study.

The degree of sensory block was assessed by VAS, the sensory block height was assessed by loss of sensation to pin prick using a 22 G blunt hypodermic needle in the midclavicular line, and the degree of motor block was assessed by the modified Bromage scale. The level of sedation score was assessed by Ramsay sedation scale. Any adverse effects in the postoperative periods like nausea, vomiting, sedation, respiratory depression, pruritus, headache, backache or neurological symptoms etc. were noted.

In both groups I and II sensory and motor blockade characteristics, blood pressure, heart rate, oxygen saturation, respiratory rate and sedation were noted every 2 minutes for first 10 minutes, then every 5 minutes till 30 minutes and then every 15 minutes till the end of surgery. Thereafter, post operatively they were checked every half an hour for the next three hours, every hourly for the next nine hours and then every three hourly till 24 hours.

Small boluses of injection ephedrine (I/V) were given as needed to treat hypotension (MAP < 70 mm Hg or decrease in systolic blood pressure by more than 20% of the base value) & injection atropine (I/V) was given if the heart rate falls below 60 beats per minute. Nausea and vomiting were treated by injection metoclopramide as required.

Results

Both groups were comparable in demographic data like age, sex, height and weight as shown in Table-1.

Table 1: Patient demographics and duration of surgery

	Group I/Nalbuphine	Group II/Clonidine	P Value
Age	37.40±11.72	38.12±13.08	0.72
Weight (kg)	70.02 ± 8.19	71.28 ± 7.85	0.43
Height (cm)	162.9 ± 9.3	164.4 ± 8.9	0.41
Sex ratio (M:F)	35 : 15	36 : 14	0.18
Mean duration of surgery (in minutes)	54.76 ± 3.54	55.06 ± 3.35	0.67

The mean time to onset of sensory block to T10 dermatome was 2.52 ± 0.45 minutes in group I and 2.7 ± 0.72 minutes in group II. The difference between the two groups was non-significant (p>0.05) (Table 2).

The median maximum sensory level achieved in both group I and group II was T6 dermatome and the difference between the two groups was non-significant (p>0.05) (Table 2).

Table 2: Sensory and motor block characteristics

	Group I/Nalbuphine	Group II/Clonidine	P Value
Sensory Block Onset to T10 (mins)	2.52±0.45	2.7±0.72	0.07
Maximum Sensory level	T6	T6	1
Time to Max Sensory level (mins)	9.34±1.81	9.22±1.77	0.73
Max Motor Block (MBmax) Bromage Scale	3	3	1
Time to MBmax (mins)	7.47±0.88	7.63±0.93	0.37
Time for 2-Segment Regression (mins)	152.64±4.35	119.2±10.43	<0.001
Duration Motor Block (mins)	144.5±5.93	157.74±10.28	<0.001
Duration of Analgesia (mins)	273.12 ± 19.80	175.98 ± 14.66	<0.0001
No of rescue analgesia doses over 24 hours	2.42 ± 0.49	3.2 ± 0.49	<0.001

The mean time taken to attain maximum sensory level was 9.34 ± 1.81 minutes in group I and 9.22 ± 1.77 minutes in group II and the difference between the two groups was non-significant (p>0.05) (Table 2).The maximum motor block achieved in both the groups was Bromage score 3 which was comparable and statistically insignificant (Table 2).The time taken to achieve maximum motor block of Bromage 3 in group I was 7.47 ± 0.88 minutes and in group II was 7.63±0.93 minutes. The results were comparable among the two groups and were found to be statistically insignificant (p value>0.05) (Table 2).

The mean time for 2-segment regression of sensory blockade in group I was 152.64 ± 4.35 minutes while in group II, it was 119.2 ± 10.43 minutes. The difference between the two groups was highly significant and it was more prolonged in group I as compared to group II (p value<0.001) (Table 2; Fig 1). The mean total duration of motor block in group I of our study was 144.5 ± 5.93 minutes, while in group II it was 157.74 ± 10.28 minutes. The difference between the two groups was highly significant (p<0.001) (Table 2; Fig 2).

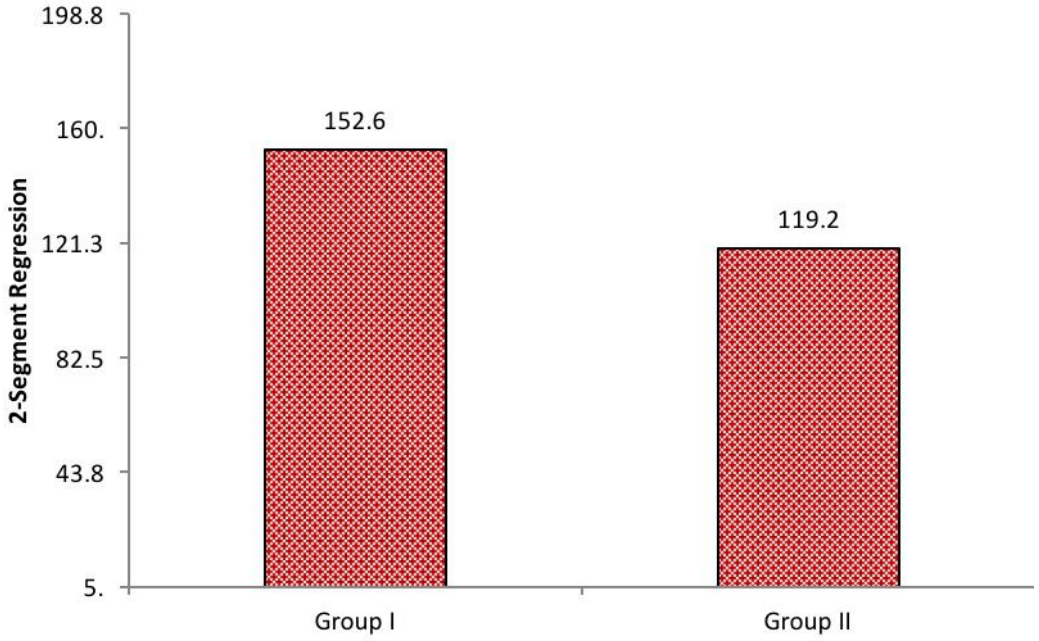

Fig: (1). 2 – Segment Regression

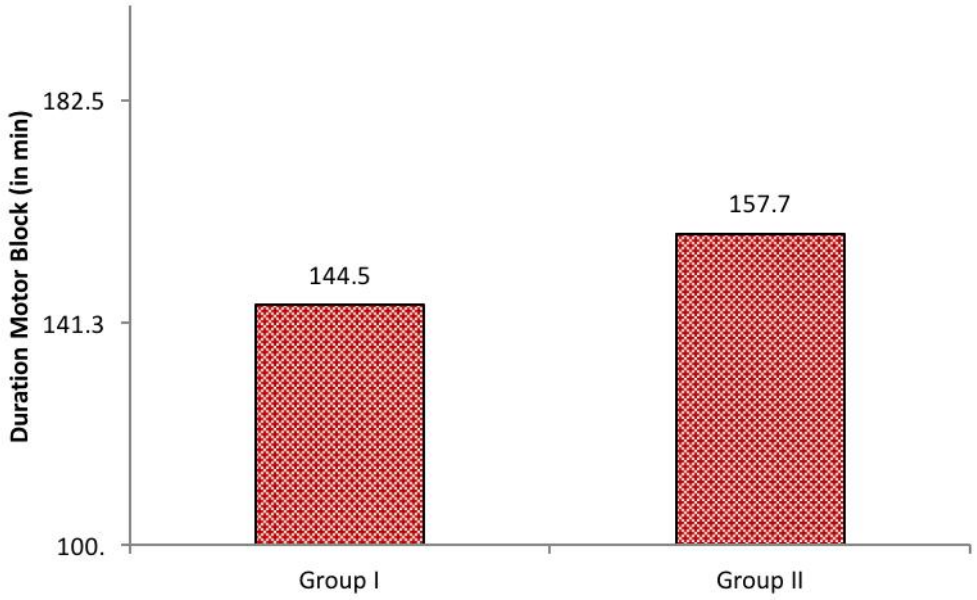

Fig: (2). Duration of motor block (in minutes)

The mean heart rate was comparable in both the groups with the difference being statistically non-significant at all measured intervals. Three patients (6%) in group I and two patients (4%) in group II developed bradycardia with heart rate below 60 beats per minute (Table 3). The incidence of bradycardia was more in Group I as compared to group II but it was statistically non-significant (p value>0.05). The difference between the mean systolic blood pressure was non-significant among the two groups during most of the intraoperative period. Similarly, the difference between the mean diastolic blood pressure was non-significant among the two groups during most of the intraoperative period. Hypotension (fall in blood pressure more than 20%) was seen in 7(14%) patients in group I and 5(10%) patients in group II which was corrected by intravenous fluids. But the difference remained non-significant in both the groups. (p>0.05) (Table 3). The mean respiratory rate, mean peripheral saturation of oxygen measured at various time intervals was comparable in both the groups (p value>0.05).

Table 3: Side effects and complications

Side effects and complications	Group I	Group II	p value with significance	
Hypotension	7	5	>0.05	NS
Bradycardia	5	3	>0.05	NS
Nausea/Vomiting	5	4	>0.05	NS
Pruritus	4	0	0.01	S
Urinary retention	-	-	-	-
Shivering	-	-	-	-

The time of request of first dose of rescue analgesia was delayed in group I, the earliest among which was demanded after the 5th hour, compared to group II, in which the earliest rescue analgesia was after the 3rd hour. The mean duration of analgesia in group I was 273.12 ± 19.80 minutes and it was 175.98 ± 14.66 minutes in group II (Fig 3).

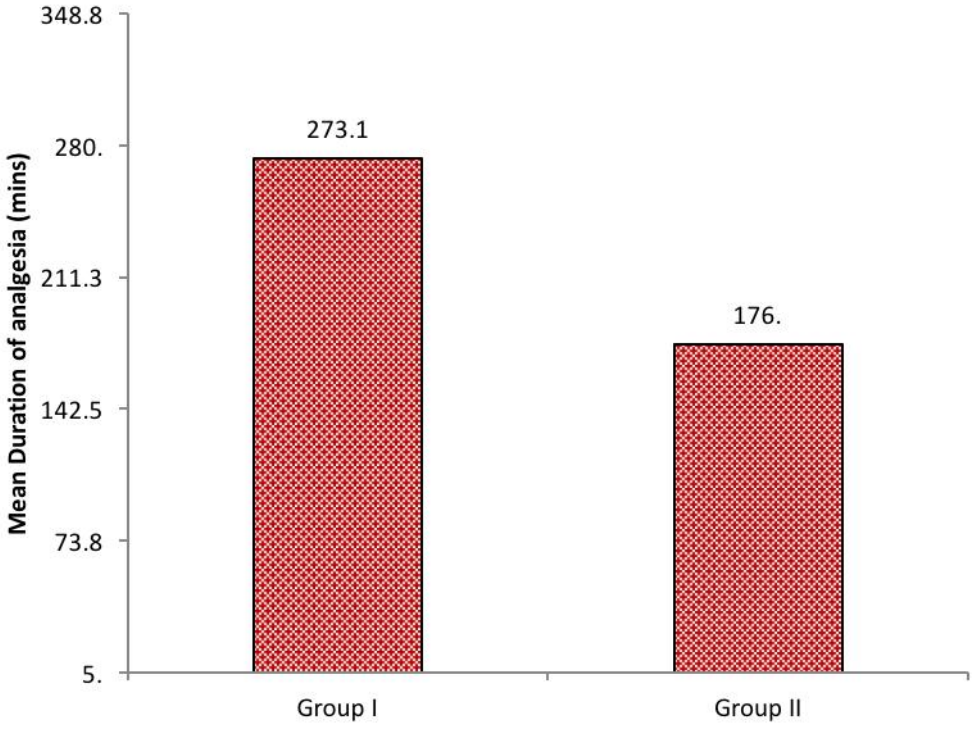

Fig (3): Duration of analgesia (in minutes)

The difference in mean total duration of analgesia between the two groups was highly significant (p value<0.0001). Rescue analgesia was given when the VAS>3.Sedation score in the intra operative period was non-significant in between group I and II.

There was no incidence of pruritus in group II while 4(8%) patients had pruritus in group I. The difference between two groups was statistically significant (p value <0.05). Nausea/vomiting was seen in 5(10%) patients in group I and 4(8%) patients in group II and the difference was statistically non-significant (p value<0.05). Other side effects like urinary retention, shivering, headache, backache, and respiratory depression were not recorded in any of the patients in both the groups (Table 3).

Quality of surgical analgesia was excellent in both the groups.

Discussion

Excessive high regional blocks and local anaesthetics toxicity are the commonest causes of mortality associated with regional blocks. So, the new goals for decreasing mortality associated with regional anaesthesia include reduction in the doses of local anaesthetics, and the use of new techniques to avoid higher blocks and better management of local anaesthetic toxicity.[11] For these purposes, various adjuvant drugs have been used along with the local anaesthetics, including various opioids, midazolam, ketamine, alpha-2 adrenergic agonists, etc.

Opioids work in the intrathecal space by activating opioids receptors in the dorsal grey matter of spinal cord, which modulates the function of afferent pain fibers.[12]Opioids were found synergistic with bupivacaine in reducing pain without measurably increasing sympathetic or motor blockade in dog models.[13]

Clonidine is an antihypertensive agent which mainly acts by central α2 adrenoreceptor stimulation, resulting in diminished sympathetic flow.[14] The intrathecal application of clonidine increases the duration of both sensory and motor block, as well as postoperative analgesia.[15]

In our study we compared nalbuphine 800μg and clonidine 30 μg as adjuvants to intrathecal 12.5mg bupivacaine (0.5%) heavy for various infraumbilical surgeries.

The mean time to onset of sensory block (Time taken from the end of injection to loss of pin prick sensation at T10 dermatome) was 2.52 ± 0.45 minutes in group I and 2.7 ± 0.72 minutes in group II. The difference between the two groups was non-significant (p>0.05). This is in concordance with the studies done by Kumaresan et al[16] and Saikia et al[17]. The mean time for 2-segment regression of sensory blockade in group I was 152.64 ± 4.35 minutes while in group II, it was 119.2 ± 10.43 minutes. The difference between the two groups was highly significant and it was more prolonged in group I as compared to group II (p value<0.001). The results of our study tally with those of the studies done by Mukherjee et al[6] and Bashir et al[18]. The mean time taken to achieve maximum motor block of Bromage 3 in group I was 7.47 ± 0.88 minutes and in group II was 7.63 ± 0.93 minutes. The results were comparable among the two groups and were found to be statistically non-significant (p value>0.05). These results are in accordance with the studies done by Naaz et al[19] and Saikia et al[17]. The mean total duration of motor block in group I of our study was 144.5 ± 5.93 minutes, while in group II it was 157.74 ± 10.28 minutes. The difference between the two groups was highly significant (p<0.001) with the combination of bupivacaine and clonidine providing a longer duration of motor blockade than the combination of bupivacaine and Nalbuphine. These tally with the results obtained in the studies done by Mukherjee et al[6] and Chandrashekarappa et al[20]. In group I, VAS started increasing after 4 hours compared to group II, where the VAS started increasing after 150 minutes. The duration of analgesia following the administration of the study drugs was significantly higher in group I as compared to group II, indicating superior analgesia. The difference in mean total duration of analgesia between the two groups was highly significant (p value<0.0001). Number of rescue analgesia doses were 2.42 ± 0.49 in group I and 3.2 ± 0.49 in group II. Difference was highly significant (p value <0.001), patients in group I required less doses of rescue analgesia as compared to group II.

The incidence of hypotension and bradycardia were comparable in both groups, and the difference was statistically non-significant. Neuraxial opioid induced pruritus is a known side effect of intrathecally administered opioids, and in our study, it was observed only in the Nalbuphine group. While the incidence of nausea/vomiting was comparable in both groups. Nausea/Vomiting were observed in both the groups, but the difference between their incidence

among both the groups were statistically non-significant. While, other side effects like urinary retention, shivering, headache, backache, and respiratory depression were not recorded in any of the patients in both the groups.

Conclusion

From our study we conclude that Bupivacaine when combined with Nalbuphine or Clonidine provided adequate subarachnoid block for infraumbilical surgeries. Both the groups were effective in providing adequate surgical anaesthesia with hemodynamic stability, but Nalbuphine group is better than Clonidine group in terms of

i) Prolonged duration of sensory blockade and postoperative analgesia
ii) Lesser number of doses of rescue analgesia required

The side effects of bradycardia, hypotension, nausea/vomiting were comparable in both groups, except for pruritus, which was seen in the Nalbuphine group.

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Conflict of interest: None declared

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