*Original Research Article*

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# A Study to Compare the Effect of Intrathecal Midazolam and Nalbuphine as an Adjuvant to Bupivacaine for Infra-umbilical Surgeries

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**Abstract**

*Context:* Since spinal anaesthesia provides analgesia for short time with local anaesthetics, many intrathecal adjuvants to local anaesthetic drugs have been addressed to augment the clinical efficiency and duration of anaesthesia intra & post operatively. *Aims:* To compare the efficacy of midazolam and nalbuphine as adjuvants in spinal anaesthesia in infra umbilical surgeries. *Material and method:* This study was conducted on 50 patients aged 18 to 55 years ASA I and II, randomly divided in 2 groups by chit method undergoing elective infra-umbilical surgeries under spinal anaesthesia. Group BM received 0.5% bupivacaine heavy 3 ml, 2 mg preservative free midazolam made 3.5 ml with 0.9% normal saline and Group BN received 0.5% bupivacaine heavy 3 ml, preservative free 1 mg nalbuphine made 3.5 ml with NS. Onset & duration of sensory and motor blockade, hemodynamic changes, sedative effect, time of two segment regression, duration of analgesia and requirement of rescue analgesia, side effects/complications, if any were observed. *Statistical analysis:* Unpaired t-test was used for statistical analysis on IBM Statistical Package for Social Sciences version 21. p-value significant if <0.05. *Results:* Group BM provided short onset of sensory and motor block, longer duration of anaesthesia & post-operative analgesia, sedative effect and longer two-segment regression time as compare to group BN when used as adjuvant to hyperbaric bupivacaine. *Conclusion:* Midazolam is better adjuvant compare to nalbuphine when used intrathecally with bupivacaine 0.5% heavy provides longer duration of anaesthesia, sedation and post operative analgesia.

**Keywords:** Spinal anaesthesia; bupivacaine 0.5% heavy; infra-umbilical surgeries; midazolam; nalbuphine.

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## Introduction

Spinal anaesthesia technique for infra-umbilical surgeries is the best anaesthetic technique as it is simple to perform with rapid onset and complete muscles relaxation Many intrathecal adjuvants have been addressed to augment the clinical efficiency, duration of anaesthesia.

Midazolam, a benzodiazepine group of drug act by occupying benzodiazepine receptor that modulates GABA, the major inhibitory neurotransmitter in the brain [1].

Nalbuphine, a mixed agonist–antagonist opioid are transported supraspinally by bulk cerebrospinal fluid flow where they modulate descending inhibitory pain pathways, and diffuses into the

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epidural space resulting in centrally mediated analgesia.

## Materials and method

This prospective, randomized, interventional study was conducted in department of anaesthesiology. After institutional ethical committee approval a study was conducted on 50 patients undergoing elective infra-umbilical surgeries under spinal anaesthesia. Which included american society of anaesthesiologist (ASA) grade I & II, both sex, aged between 18 to 55 years which divided randomly in 2 groups by chit method. Group BM (midazolam group) received 0.5% hyperbaric bupivacaine 3 ml + 2 mg preservative free midazolam made 3.5 ml with normal saline (NS). And Group BN (nalbuphine group) received 0.5% hyperbaric bupivacaine 3 ml + preservative free 1 mg nalbuphine made 3.5 ml with NS.

*Inclusion criteria*

- Patient willing to sign the written and informed consent
- Age between18 to 55 years
- ASA I & II
- Undergoing elective infra-umbilical surgical procedure

*Exclusion criteria*

- Patients who refuse to sign
- With systemic diseases
- Coagulation disorders or on anticoagulant therapy
- Local infection at the site of proposed puncture for spinal anaesthesia
- Spine deformities and who needed supplementation of general anaesthesia
- Allergy to study drug

All the patients posted for planned infra-umbilical surgery were assessed for detailed pre-anaesthetic check-up. All routine investigations were carried out. All the patients were kept NBM a night before surgery.

On arrival of the patient in the operating room, an intravenous (i.v.) line was secured and preloaded with Ringer's lactate at 10 ml $kg^{-1}$. The patients were connected to multipara monitor. Baseline electrocardiogram (ECG), heart rate (HR), Systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation ($SpO_2$) were recorded. All patients were pre-medicated with inj. glycopyrrolate 0.2 mg, inj. ondansetron 4 mg and inj. ranitidine 50 mg i.v. Patients were given spinal anaesthesia in sitting position via 25G spinal needle in $L_{3-4}$ interspace. Patient were placed supine immediately after injection.

All patients were monitored for vitals and recored at 0, 1, 3, 5, 10, 15, 20, 25, 30, 60, 90, 120, 150 and 180 minuteutes. Onset and level of sensory block by using pinprick test, onset and level of motor block by using Bromage scale. Sedation was assessed by Ramsay sedation scale. Time of onset of sedation was noted when the score was 3 and Duration of sedation was considered when the score returned back to 2.

Pain score was assessed by visual Analogue scale (VAS) in postoperative period. Duration of analgesia were calculated from the time of intrathecal injection to the time when visual analogue scale (VAS) was 2. Time to rescue analgesia inj. diclofenac sodium 75 mg i.m. and total number of analgesics required in the first 24 hours were recorded.

Side effects and complications were noted and treated accordingly.

Bradycardia were defined as pulse rate < 60/ minute and treated with inj. atropine sulfate 0.6 mg i.v. Hypotention were defined as systolic BP<90 mmHg and treated with inj. mephenteraminutee 6 mg i.v.

All patients were shifted to recovery room and observed for HR, SBP, DBP, duration of sensory and motor blockade till patients were able to flex the ankle.

## Results

The distribution of patients with respect to age, height, weight and ASA grade was comparable in both the groups.

**Table 1:** Age, Height, weight & sex distribution (Mean ± SD)

| Demographic Data | Mean ± SD | | p value Significance S - significant NS - not significant |
|---|---|---|---|
| | Group BM | Group BN | |
| Age | 37.36 ± 10.23 | 37.84 ± 11.60 | 0.877 (NS) |
| Height | 160.76 ± 5.79 | 162.00 ± 5.48 | 0.441 (NS) |
| Weight | 59.44 ± 10.84 | 62.28 ± 11.81 | 0.380 (NS) |
| Sex (M/F) | 17/8 | 19/6 | |
| ASA Grade | | | |
| I | 10 (40%) | 10 (40%) | |
| II | 15 (60%) | 15 (60%) | |

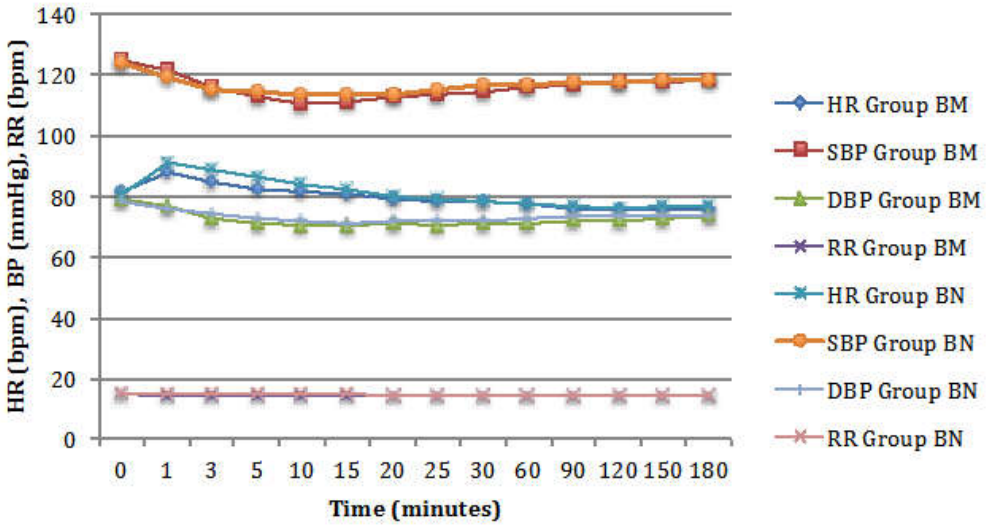


**Chart 1:** Haemodynamic and respiratory rate comparision between both groups

**Table 2:** Onset and duration of sensory & motor block in both groups

| | | Group BM Mean ± SD (minutes) | Group BN Mean ± SD (minutes) | P value Significance |
|---|---|---|---|---|
| Sensory block | Onset at L1 | 3.60 ± 0.76 | 4.28 ± 0.94 | 0.007 (S) |
| | Onset at T10 | 6.00 ± 0.82 | 6.64 ± 1.19 | 0.032 (S) |
| | Time to achieve Highest level | 7.44 ± 1.00 | 8.16 ± 1.46 | 0.048 (S) |
| Motor Block | Onset | 3.84 ± 0.75 | 4.84 ± 0.75 | <0.001 (S) |
| | Segment regression | 134.48 ± 7.23 | 124.16 ± 8.21 | <0.001 (S) |
| | Duration of surgery | 85.20 ± 30.49 | 77.52 ± 32.17 | 0.391 (NS) |
| | Duration of Sensory Block | 222.12 ± 14.49 | 186.96 ± 14.87 | <0.001 (S) |
| | Duration of motor block | 167.20 ± 12.51 | 151.16 ± 10.27 | <0.001 (S) |
| | Duration of Analgesia | 276.08 ± 17.98 | 242.72 ± 15.65 | <0.001 (S) |
| | Total analgesic requirement in 24 hours | 2.08 ± 0.28 | 2.16 ± 0.37 | <0.0001 (S) |

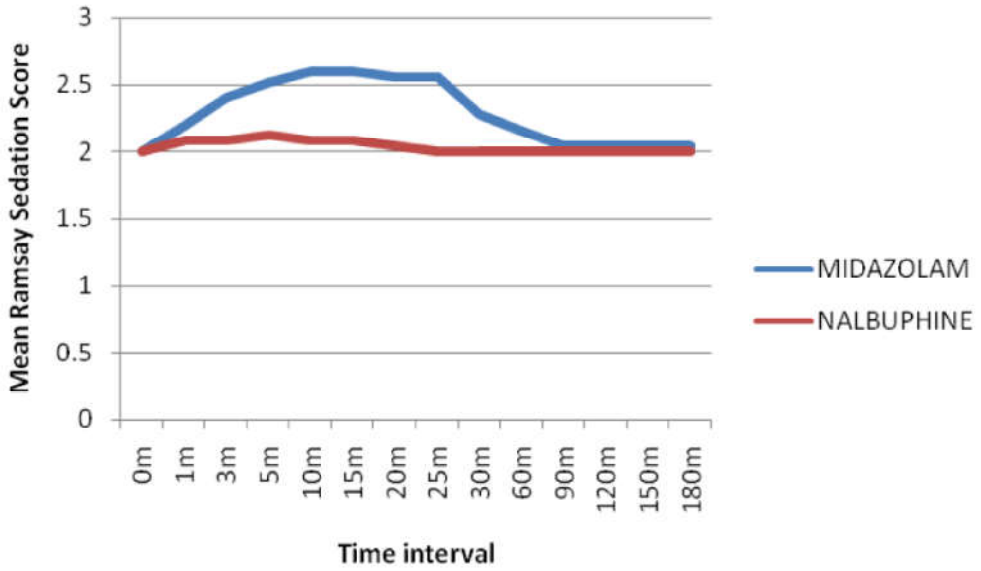


**Chart 2:** Ramsay sedation score

**Table 3:** Complications or side effects

| Complications or Side Effects | Group BM | Group BN |
|---|---|---|
| Vomiting | 0 | 0 |
| Nausea | 1 (4%) | 1 (4%) |
| Bradycardia | 1 (4%) | 0 |
| Hypotension | 1 (4%) | 2 (8%) |
| Chest pain | 0 | 0 |
| Rigors | 0 | 0 |
| Headache | 0 | 0 |
| Backache | 0 | 0 |
| Allergic Reactions | 0 | 0 |

## Discussion

In our study 50 patients were randomly divided in 2 groups, both groups were comparable in gender, age & ASA grading (Table 1).

KumKum Gupta et al. [2], Usha shukla et al. [3] studies were comparable to our study.

As shown in chart 1, perioperatively there was statistically no significant difference in haemodynamics and RR between both groups (p value>0.05).

In our study, the mean onset of sensory block at $L_1$ was 3.60 ± 0.76 minute in group BM and 4.28 ± 0.94 minute in group BN which was statistically significant. The mean onset of sensory block at $T_{10}$ was 6.00 ± 0.82 minute in group BM and 6.64 ± 1.19 minute in group BN which was statistically significant. Syed Ali Aasim et al. [4] observed in their study that the onset of sensory block for midazolam group was 6.8 ± 0.8 minute. Kumkum Gupta et al. in [2] compared in their study that the onset of sensory block at $T_{10}$ level was 3.91 ± 2.25 minute for nalbuphine group and time taken for to achieve sensory block at most cephalic level was 7.13 ± 3.81 minute for nalbuphine group (Table 2).

We observed $T_{10}$ level in 8 patients (32%), $T_8$ level in 6 patients (24%) and $T_6$ level in 11 patients (44%) in group BM compare to $T_{10}$ level in 9 patients (36%), $T_8$ level in 9 patients (36%) and $T_6$ level 7 patients (28%). Duration of mean sensory block in group BM 222.12 ± 14.49 and in group BN was 186.96 ± 14.87 which was statistically highly significant (p value of <0.001). Syed Ali Aasim et al. [4], Joseph attia et all. [5[ study results were comparable with our study (Table 2).

In our study the mean onset of motor block in group BM was 3.84 ± 0.75 minute and in group BN was 4.84 ± 0.75 minute which was statistically highly significant (p value < 0.001). Usha shukla et al. in [3] found in their study that time to reach complete motor block was 6.8 ± 0.6 minutes for midazolam group which was delayed as compare to our study. Hala Mostafa Gomar et al. [6] found in their study that the time for onset of complete motor block was 5.72 ± 0.17 minute for nalbuphine group which was delayed as compare to our study (Table 2).

In our study mean duration of motor block in group BM was 176.20 ± 12.51 and in group BN was 151.16 ± 10.27 with p value of <0.001 which is statistically highly significant. Usha shukla et al. [3] found in their study that duration of motor block was 152.2 ± 2.9 minute for midazolam group which was comparable with our study. Syed Ali Aasim et al. [4] found that duration of motor block was 139.9 ± 12.8 minute for midazolam group which was comparable with our study (Table 2).

In our study duration of surgery in both groups was comparable and statistically not significant with p value 0.391 (Table 2).

In our study, the mean time of 2 segment regression in midazolam group was 134 ± 7.23 minutes and in nalbuphine group was 124.16 ± 8.21 minute which was statistically highly significant (p<0.001). Fareed ahmed et al. in 2016 [9], Kumkum Gupta et al. in 2015 [2] study results were comparable with our study (Table 2).

In our study mean duration of analgesia in group BM was 276.08 ± 17.98 minute and in group BN was 242.72 ± 15.65 minute which shows statistically highly significant prolonged duration of analgesia in group BM with p value <0.0001. Syed Ali Aasim et al. [4], Anirban Chattopadhyay et al. [7] study results in midazolam group was comparable with our study (Table 2).

In our study total requirement of rescue analgisics in 24 hrs were 2.08 ± 0.28 and 2.16 ± 0.37 with midazolam and nalbuphine group respectively which was statistically significant p value <0.001 (Table 2).

In our study, perioperatively there was statistically significant difference in Ramsay sedation score between the two groups (p value<0.05) during first 60 minuteutes in group BM as compare to group BN which is significant. By 90 minuteutes there was statistical insignificant difference since (p value >0.05). Anirban Chattopadhyay et al. [7] found significant difference in sedation level in intraoperative period but not in postoperative period. Whether intrathecal midazolam causes clinically significant sedation or not is a debatable issue; Yegin et al. [8] found that 2 mg intrathecal midazolam causes significant sedation, but others did not. We think that intraoperative sedation may be a desirable property of intrathecal

midazolam (Chart 2).

In our study, in group BM, 1 patient had nausea, 1 had bradycardia & 1 had hypotension while in group BN, 1 patient had nausea & 2 patients had hypotension. There was no respiratory depression or fall of $SpO_2$ in both groups.

## Conclusion

We conclude that addition of inj. midazolam 2 mg to inj. bupivacaine 0.5% heavy provides faster onset and longer duration of sensory and motor block with prolong duration of analgesia when compared to addition of inj nalbuphine 1 mg to inj bupivacaine 0.5% heavy for infraubilical surgeries. Addition of midazolam intrathecally also provides intra-operative sedation with prolonged two segment regression time without respiratory depression with stable hemodynamics as compare to nalbuphine when used intrathecally.

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