

Original research article

## Intrathecal nalbuphine versus dexmedetomidine as an adjuvant in spinal anaesthesia for lowerlimb and lower abdominal surgeries

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**Abstract**

This study aimed to compare intrathecal nalbuphine and dexmedetomidine as an adjuvant in spinal anesthesia for lower limb and lower abdominal surgeries to improve the quality of spinal anesthesia (onset, duration, and side effects) and prolongation of duration of postoperative analgesia

Hyperbaric bupivacaine, a local anesthetic, has a short half-life of 2 to 2 ½ hours. Hence several adjuvants have been tested to enhance and prolong its analgesic effect. Initially, the preemptive combination of intrathecal opioids like fentanyl, nalbuphine, buprenorphine were extensively studied and found to have its own side effects and of late alpha -2 agonist like dexmedetomidine with this local anesthetic for regional anesthesia, is being studied.

**Aim:** In the present study we tried to compare intrathecal nalbuphine and dexmedetomidine as adjuvants in spinal anaesthesia for lower limb and lower abdominal surgeries.

**Methods:** The present study was conducted in the department of anaesthesiology, KIMS, Narketpally during Oct 2021 to Sep 2022.

This study was a prospective, randomised controlled, single blind, study conducted in 60 patients of ASA grade I and II undergoing elective surgeries under spinal anaesthesia. The patients were divided randomly with computer randomizer software into two groups, containing 30 patients in each group. Drugs selected are divided as Group BN: Patients received 3 ml of 0.5% hyperbaric bupivacaine (15mg) plus 1mg nalbuphine and Group BD: Patients received 3 ml of 0.5% hyperbaric bupivacaine (15mg) plus 5 µg Dexmedetomidine. Spinal block characteristics, blood pressure, pulse rate and side effects were studied during intra-operative and postoperative period.

**Results:** It was observed from present study that in Dexmedetomidine group onset and complete motor blockade was early and duration of anaesthesia and analgesia was significantly prolonged compared to the Nalbuphine group. Hemodynamic parameters were preserved both intra-operatively and postoperatively in both groups. However there were a small percentage of patients who developed hypotension and bradycardia with dexmedetomidine which were easily managed without any untoward effect.

**Conclusions:** Intrathecal low dose Dexmedetomidine in a dose of 5µg along with 0.5% hyperbaric bupivacaine is associated with prolonged onset, duration, and side effects sensory and motor blockade compared to 1mg of nalbuphine for spinal anaesthesia in patients undergoing elective lower abdominal and lower limb surgeries.

**Keywords:** Dexmedetomidine, nalbuphine, hyperbaric bupivacaine, spinal anaesthesia, lower limb and lower abdominal surgeries.

**Introduction**

Spinal anesthesia with hyperbaric bupivacaine 0.5%(heavy) is a popular method however there is disadvantage of its short half life. To overcome this disadvantage there is an constant search for an ideal adjuvant. Initially opioids like fentanyl and buprenorphine were tried. Opioids reduce the toxicity and adverse cardiovascular effects of local anesthetics, however this type of combination brings about additional undesirable problems like itching, nausea and vomiting and / or respiratory depression.

Nalbuphine, a drug with mixed µ antagonist and κ agonist properties, has the potential to maintain or

even enhance  $\mu$ -opioid based analgesia while simultaneously mitigating the  $\mu$ -opioid side effect<sup>1</sup> Nalbuphine and other  $\kappa$  agonists have provided potent analgesia in certain models of visceral nociception<sup>2</sup>. They demonstrate complicated interactions with  $\mu$  opiates that suggest dose-dependent synergies and significant antagonisms at larger doses<sup>3</sup> their lipid solubility and rapid clearance. Respiratory depression, pruritus and urinary retention are the events that were considered to be reflective of the actions of spinal  $\mu$ -opioids<sup>4-6</sup>. Dexmedetomidine is a new alpha2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative, analgesic in the intensive care unit<sup>7</sup>. It causes sedation without causing respiratory depression. It has sedative, analgesic, sympatholytic and anxiolytic effect that blunt many CVS responses in perioperative period<sup>8</sup>. It is an S- enantiomer of medetomidine used in veterinary medicine. Drug cannot be given as bolus due to concerns about peripheral alpha – 2 receptor stimulation with resulting hypertension and bradycardia<sup>9,10</sup>. It is thought that intrathecal dexmedetomidine produces its analgesic effect by inhibiting the release of C fibers transmitters and by hyperpolarization of post-synaptic dorsal horn neurons<sup>11</sup>. The prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneurons<sup>12</sup>. Alpha 2 adrenoreceptors do not have an active role in the respiratory center, therefore, dexmedetomidine throughout a broad range of plasma concentration, has minimal effects on the respiratory system<sup>13</sup>.

### Methods

After institutional ethics committee approval, pre anaesthetic checkup was done. Sixty patients of American Society of Anaesthesiologists (ASA) physical status 1 or 2, aged between 20 – 60 years were selected through randomizer software, scheduled for elective lower limb and lower abdominal surgeries were included in this prospective randomized controlled study. An informed written consent was obtained from all the participants.

- Patients with neurological disorders, allergy to study drug, coagulation disorders, local infection at the site of injection, spine deformities, ASA 3 and above, pregnancy were excluded.
- Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of SAB was explained to the patients and written consent was obtained. The patients were educated about the use of visual analogue scale.
- Preparation of patients included period of overnight fasting.
- Patients were premedicated with Tab. Rantidine 150 mg and Tab. Alprazolam 0.5 mg H.S.

### Preparation of operating theatre

- Anaesthesia workstation was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus and necessary monitors were kept ready before the procedure.
- Emergency drug tray consisting of atropine, adrenaline, phenylephrine, ephedrine, dopamine were kept ready.

### Procedure

- Patients shifted to OR table, IV access was obtained on the forearm with No 18G IV cannula and all patients were given inj MIDAZOLAM 1 mg iv for anxiolysis and coloaded with 15 ml / Kg of Ringer's Lactate.
- Patients were randomly allocated into two groups by using randomizer software.
- Baseline vitals parameters were recorded.
- Under strict asepsis, using 25 G Quincke spinal needle, lumbar puncture was performed at L<sub>3</sub> – L<sub>4</sub> space. Free flow of csf was confirmed

Group BN received 3 ml, 0.5% hyperbaric bupivacaine + 1mg Nalbuphine and Group BD received 3 ml, 0.5% hyperbaric bupivacaine + 5ug

### Dexmedetomidine respectively

- Intraoperatively pulse rate, non invasive blood pressure, electrocardiogram, SpO<sub>2</sub> was recorded, every 5 min standard monitoring done till the end of surgery and subsequently every 10 min postoperatively.
- Time of onset of T<sub>10</sub> sensory block and peak sensory block was noted using pin prick method, time of onset of bromage 3 motor block was noted.
- Motor block was assessed with Modified Bromage scale<sup>14</sup>

**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 the hip and knee but able to move the ankle

**Bromage 3:** The patient is unable to move the hip, knee and ankle.

**Modified Ramsay sedation scale<sup>15</sup> was used for intraoperative sedation**

- 1 = agitated, restless
- 2 = cooperative, tranquil
- 3 = responds to verbal commands while sleeping
- 4 = brisk response to glabellar tap or loud noise while sleeping
- 5 = sluggish response to glabellar tap or loud noise while sleeping
- 6 = no response to glabellar tap or loud noise while sleeping

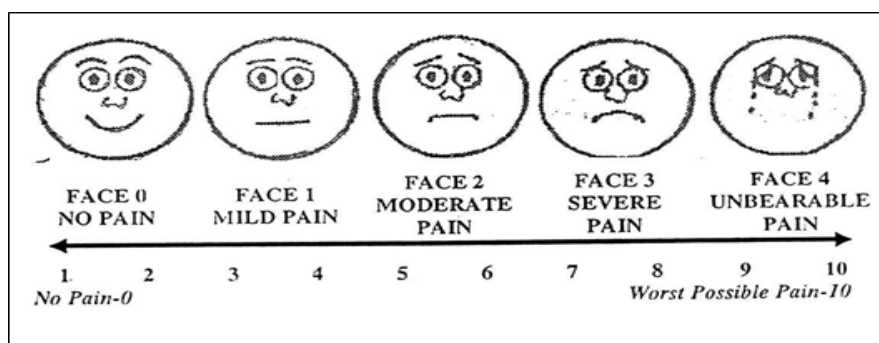
**• Following parameters were recorded**

Hypotension (> 20% fall of baseline blood pressure) was treated with bolus dose of 6 mg ephedrine i.v.

Bradycardia (pulse rate < 50 bpm), was treated with 0.6 mg atropine.iv

Incidence of respiratory depression defined as respiratory rate less than 9 /min and SpO<sub>2</sub> less than 90% on room air, was noted

- Side effects if any were noted Post operatively regression of the sensory block and the motor blockade to reach modified Bromage 0 was noted
- Pain was assessed using “Visual Analogue Scale”, It is linear scale, consists of 10 cm line anchored at one end by a label such as “No pain” and other end by “Worst pain imaginable”. Patient simply marks the line to indicate the pain intensity. Supplemental analgesia was given with inj. TRAMADOL 50mg i.v, for visual analogue score of more than 4, Time of supplemental analgesia was noted.
- Visual analogue scale<sup>16</sup> was used to assess post operative pain.



0 = no pain, 10 = severe pain.

**Statistical Methods<sup>[17, 18]</sup>**

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

- The following assumptions on data is made, Assumption: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent
- Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.
- Study Design: A Comparative two group randomized clinical study with 60 patients with 30 patients in Group BN (Nalbuphine) and 30 patients in Group BD (Dexmedetomidine) is undertaken to study the changes in haemodynamics and side effects.
- Statistical analysis was done by applying Chi-square test, Anova test and students ‘t’ test to analyse the data, p value was determined.

$p > 0.05$  is not significant  $p < 0.05$  is significant

$p < 0.001$  is highly significant

**Results**

**Table 1:** Comparison of age and weight in both groups

	Group BN (n=30)	Group BD (n=30)	P-value
Mean age in years	42.03±11.18	42.1±7.81	$p > 0.05$
Mean weight Kg	58.5±6.98	57.6±8.98	$p > 0.05$

The above table shows there is no significant difference in age ( $p$  value < 0.05) and there is no significant difference in height ( $p$  value > 0.05)

**Table 2:** Comparison of gender in both the groups

Gender	Group BN	Group BD
Male	25(83.33%)	24(80.33%)
Female	5(16.67%)	6(20.67%)

**Table 3:** Comparison of height wise distribution in both the groups

Height in centimeters	Group BN	Group BD
155-164	16(53.33%)	18(60%)
165-174	14(46.64%)	12(40%)

**Table 4:** Comparison of onset and duration of analgesia motor blockade in both the groups

	Group BN (in minutes)	Group BD (in minutes)	P value
Time of onset of analgesia	2.18±0.1	1.546±0.56	p<0.0001
Time of onset of motor blockade	3.78±0.175	1.983±1.541	p<0.0001
Time of 2 segment regression	126±7.25	136.784±11.857	p=0.0001
Time of duration of motor blockade	239.430±12.377	379±19.6	p<0.001
Duration of analgesia	296.4±13.6	410.9±20.0	p<0.0001

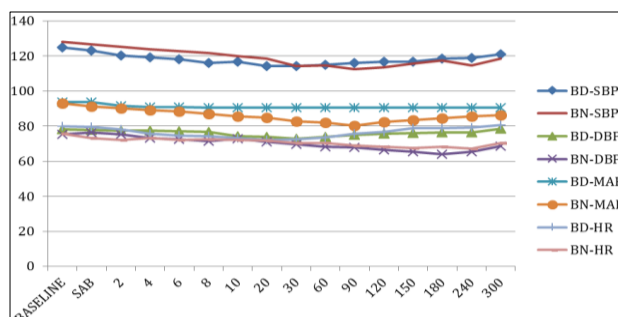
The mean time of onset of analgesia is less in group BD has compared to Group BN ( $p<0.0001$ ).  
 The mean time of onset of motor blockade is less in group BD has compared to group BN ( $P<0.0001$ ).  
 The mean time of two segment regression is prolonged in group BD as compared to group BN ( $p=0.0001$ ).  
 The mean time of duration of Motar blockade is prolonged in group BD as compared to group BN ( $P<0.001$ ).  
 The mean for duration of analgesia is prolonged in group BD as compared to group BN ( $p<0.0001$ ).  
 These values are stastically significant

**Table 5:** Comparison of mean of maximum height of sensory blockade in both the groups

	Group BN	Group BD
Mean of maximum height of sensory Blockade(segments)	T6-T8	T6-T8

**Table 6:** Comparison of maximum height wise distribution of sensory blockade in both the groups

Maximum height of sensory Blockade (segments)	Group BN	Group BD
T4	1(3.33%)	3(10.0%)
T6	12(40%)	13(43.33%)
T8	15(50%)	11(36.66%)
T10	2(6.67%)	3(10.0%)



**Fig 7:** Comparison of maximum heartrate, systolic blood pressure, diastolic bloodpressure, mean arterial pressure in both the groups

**Table 7:** Comparison of occurrence of side effects in both cases

Complications	Group bn	Group bd
Nausea	1(3.33%)	2(6.66%)
Sedation	0	1(3.33%)
Dry mouth	1(3.33%)	2(6.66%)
Bradycardia	1(3.33%)	4(13.3%)
Hypotension	3(10.33%)	5(16.66%)

**Table 8:** Comparison with various studies

	Nalbuphine	Duration of motor blockade	Dexmeditomidine	Duration of motor blockade
Gupta,ragini <i>et al.</i> (2011) <sup>[19]</sup>			5 mcg	421±21
Basunia SR <i>et al.</i> (2016) <sup>[20]</sup>	0.8 mg	140.4±3.09	-	-
Basunia SR <i>et al.</i> (2016) <sup>[20]</sup>	1.2 mg	242.2±3.0	-	-
Suresh <i>et al.</i> (2016) <sup>[21]</sup>	-	-	5 mcg	407.53 ±18.913
Fatemeh Khosravi <i>et al.</i> <sup>[22]</sup> (2020)	-	-	5 mcg	428.64 ± 73.39
Mohamed SA <i>et al.</i> (2021) <sup>[23]</sup> (n=135)	0.8 mg	241.2±0.74	-	-
In present study	1 mg	239.430±12.37	5 mcg	379±19.6

## Discussion

Bupivacaine acts at axonal level. Nalbuphine is mixed  $\mu$  antagonist and  $\kappa$  agonist. Dexmedetomidine, alpha2-agonist produces analgesia by acting at spinal level, laminae 7 and 8 of the ventral horns of the spinal cord. During our study

The mean age in the nalbuphine and dexmedetomidine groups 42.03±11.18 and 42.1±7.81 years respectively,

The mean weight in the nalbuphine and dexmedetomidine groups 58.5±6.98 and 57.6±8.98 kilograms respectively.

The total male patients in the nalbuphine and dexmedetomidine groups is 25 and 24 respectively and female patients are 5 and 6 respectively.

The maximum height of sensory blockade in nalbuphine group (T6-T8) Compared to dexmedetomidine group (T6-T8).So all the above 4 parameters are comparable.

The mean time of onset of analgesia in nalbuphine and dexmedetomidine groups is 2.18±0.1 and 1.546±0.56 ( $p<0.0001$ ).

The mean time of onset of motor blockade in nalbuphine and dexmedetomidine groups is 3.78±0.75 and 1.983±1.541( $p<0.0001$ ).

In the present study, mean duration of motor blockade in nalbuphine and dexmedetomidine groups is 239.430±12.377 and 379±19.6 minutes respectively and it is statistically significant ( $p<0.05$ ).

In the present study, mean duration of 2 segment regression in the nalbuphine and dexmedetomidine groups is 126±7.25 and 136.78±11.857 minutes respectively.It is prolonged in dexmedetomidine group which is statistically significant ( $P<0.05$ ).

In the present study, mean duration of analgesia in nalbuphine and dexmedetomidine groups is 296.4±13.6 and 410±20.0 minutes,so duration of analgesia is more in dexmedetomidine group. In the present study, the changes in the mean values of mean arterial pressure in both the groups,after administration of study drug are statistically not significant ( $>0.05$ )at various intervals of time.

ECG monitoring showed sinus bradycardia in 1 (3.33percent) nalbuphine group and 4 (13.33percent) in dexmedetomidine group. are no ST-T changes or dysrhythmias in ECG in any of the patients of the either group through out the period.

In the present study, occurrence of complications like nausea is 2(6.66 percent) and 1 (3.33percent) in case in nalbuphine group, sedation is 1(3.33%) case in dexmedetomidine group, bradycardia is one in case of nalbuphine group (3.33%) and 4(13.33%) in dexmedetomidine group and hypotension is 3 (9.99%) in nalbuphine and 5(16.66%) cases in dexmedetomidine group.

The mean requirement of first rescue analgesia with nalbuphine and dexmedetomidine is after 296.4±13.6 (min) and 410.9±20.0 (min) respectively.

## Conclusion

Dexmedetomidine 5 $\mu$ g, used as adjuvant to 3ml of 0.5% bupivacaine(heavy) intrathecally for spinal anaesthesia is observed to prolong the duration of intraoperative spinal anaesthesia and post operative duration of analgesia compared to nalbuphine.

## References

- Devendra Verma, Udita Naithani, Dharm Chand Jain, Ajay Singh. —Postoperative analgesic efficacy of intrathecal tramadol versus nalbuphine added to bupivacaine in spinal anaesthesia for lower limb orthopaedic surgery. Journal of Evolution of Medical and Dental Sciences. 2013 Aug 19;12(33):6196-6206.
- Schmauss C, Yaksh TL. *In vivo* studies on spinal opiate receptor systems mediating antinociception. II. Pharmacological profiles suggesting a differential association of mu, delta and kappa receptors with visceral chemical and cutaneous thermal stimuli in the rat. J Pharmacol Exp Ther. 1984;228:1-12.
- Loomis CW, Penning J, Milne B. A study of the analgesic interaction between intrathecal morphine

- and subcutaneous nalbuphine in the rat. *Anesthesiology*. 1989;71:704-10.
4. Henderson SK, Cohen H. Nalbuphine augmentation of analgesia and reversal of side effects following epidural hydromorphone. *Anesthesiology*. 1986;65:216-8.
  5. Penning JP, Samson B, Baxter AD. Reversal of epidural morphine-induced respiratory depression and pruritus with nalbuphine. *Can J Anaesth*. 1988;35:599-604.
  6. Yang T, Breen TW, Archer D, Fick G. Comparison of 0.25 mg and 0.1 mg intrathecal morphine for analgesia after cesarean section. *Can J Anaesth*. 1999;46:856-60.
  7. Clarke KW, Hall LW. Xylazine-A new sedative for horses and cattle. *Vet Rec*; 85:512-517, 1969.
  8. Cormack Jr, Orme Rm, Costello Tg. "The role of alpha2-agonists in neurosurgery". *Journal of Clinical Neuroscience*. 2005;12(4):375-8. DOI10.1016 Hyperlink "<http://dx.doi.org/10.1016%2Fj.jocn.2004.06.008>"
  9. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, *et al*. "Dexmedetomidine Vs Midazolam for sedation of critically ill patients: A Randomized Trial". *Jama*. 2009;301(5):489-99.
  10. Menon Dv, Wang Z, Fadel Pj, Arbique D, Leonard D, Li JI, *et al*. "Central sympatholysis as a novel countermeasure for cocaine-induced sympathetic activation and vasoconstriction in humans". *J Am Coll Cardiol*. 2007;50(7):626-33.
  11. Correa-Sales C, Rabin BC, Maze M. A hypnotic response to dexmedetomidine, an alpha 2 agonist, is mediated in the locus coeruleus in rats. *Anesthesiology*. 1992 Jun;76(6):948-52.
  12. Palmeri A, Wiesendanger M. Concomitant depression of locus coeruleus neurons and of flexor reflexes by an alpha 2-adrenergic agonist in rats: a possible mechanism for an alpha 2- mediated muscle relaxation. *Neuroscience*. 1990; 34(1):177-87.
  13. Hall Je, Uhrich TD, Barney JA, Arian SR, Ebert TJ: sedative, amnestic and analgesic properties of small dose dexmedetomidine infusions. *Anaesth Analg*. 2000;90:699-705.
  14. Bromage PR, Burfoot MF, Crowell DE, Pettigrew RT. Quality of epidural blockade. Influence of physical factors. *Br J Anaesthesia*. 1964;36:342-52.
  15. Ramsay MA, Savege M, Simpson BR, Goodwin R. Controlled sedation withalphaxalone-alphadolone. *Br Med J*. 1974;2:656-9.
  16. Etches RC, Sandler AN, Daley MD. Respiratory depression and spinal opioids. *Can J Anaesth* 1989;36:165-85.
  17. Morgan M. The rationale use of intrathecal and extradural opioids. *Br J Anaesth*. 1989;63:165-88.
  18. ShuJun Sun, JiaMei Wang, NaRen Bao, Ying Chen, Jun wang. Comparison of dexmedetomidine and fentanyl as local anesthetic adjuvants in spinal anesthesia: a systematic review and meta-analysis of randomized controlled trials *Drug Design, Development and Therapy*. 2017;11:3413-3424.
  19. Gupta Rajni, Verma Reetu, Bogra Jaishri, Kohli Monica, Raman Rajesh, Kushwaha, Jitendra Kumar. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine *Journal of Anaesthesiology Clinical Pharmacology*. 2011 Jul-Sep;27(3):339-343.
  20. Basunia SR, Chattopadhyay S, Das A, Laha B, Bhar D, Pal R. A prospective, double-blind dose-ranging study of intrathecal nalbuphine in the lower abdominal and lower limb surgeries. *Indian J Pain*. 2016;30:198-203.
  21. Suresh G, Prasad CG. A comparative study of intrathecal 0.5% hyperbaric bupivacaine with dexmedetomidine and 0.5% hyperbaric bupivacaine with fentanyl for lower abdominal surgeries. *Sri Lankan Journal of Anaesthesiology*. 2016;24(1):22-27.
  22. Fatemeh Khosravi Mehdi Sharifi1 Hashem Jarineshin. Comparative Study of Fentanyl vs Dexmedetomidine as Adjuvants to Intrathecal Bupivacaine in Cesarean Section: A Randomized, Double-Blind Clinical Trial, *Journal of Pain Research*. 2020;13:2475-2482.
  23. Mohamed SA, Elsonbaty A, Elsonbaty M. A Comparison between Intrathecal Nalbuphine and Fentanyl for Intraoperative Pain Management during Uterine Exteriorization in Caesarean Section: A Randomized Controlled Trial. *Open Access Maced J Med Sci [Internet]*. 2021 Jul. 5; 9(B):533-40.