ORIGINAL ARTICLE

Comparative study of efficacy of tramadol versus nalbuphine as an adjuvant to intrathecal bupivacaine

Sathyasuba Meenakshi Sundaram[1], Srinidhi Narayanan[1], Gayathri Ramesh[1], Raghuraman M Sethuraman[1], Bhagawathi B[1]*

[1]Department of Anesthesiology, Sree Balaji Medical College & Hospital, BIHER, Chennai - 600044 (Tamilnadu), India

Abstract

Background: Spinal anesthesia is commonly used for infra umbilical surgeries due to its effective analgesia and favorable safety profile. However, local anesthetics like bupivacaine alone provide limited postoperative pain relief. *Aim and Objectives*: This randomized double-blind study aimed to compare the duration of analgesia of intrathecal tramadol and nalbuphine added to hyperbaric bupivacaine for infra umbilical surgeries, as there are limited studies on this comparison. *Material and Methods:* A total of 60 patients scheduled for elective infraumbilical surgeries at a tertiary care center were randomized into two groups. Group T received 25 mg of tramadol, and Group N received 1 mg of nalbuphine, both as adjuvants to 0.5% hyperbaric bupivacaine. The primary outcome was the duration of analgesia. Secondary outcomes included the onset and duration of sensory and motor blocks, hemodynamic stability, time to rescue analgesia and incidence of side effects. *Results:* Although nalbuphine provided a slightly faster onset of sensory and motor block (4.0 ± 1.0 and 5.7 ± 1.2 minutes respectively) than tramadol (4.3 ± 1.1 and 6.0 ± 1.3 minutes respectively), it was statistically insignificant (p = 0.238, 0.314). Also, the duration of analgesia was significantly longer in the nalbuphine group (8.2 ± 1.3 hours) compared to the tramadol group (7.5 ± 1.2 hours) (p = 0.045). Both groups maintained stable hemodynamic profiles, and there was no significant difference in the incidence of side effects. *Conclusion:* Nalbuphine, when added to intrathecal bupivacaine, provides a longer duration of analgesia with comparable onset times and safety profile. Thus nalbuphine can be considered a more effective adjuvant for enhanced postoperative pain relief.

Keywords: Intrathecal Opioids, Nalbuphine, Tramadol

Introduction

Spinal anesthesia is the cornerstone for anesthesia of infra umbilical surgeries, because of its ability to provide profound analgesia, reduce surgical stress responses, and minimize postoperative complications [1]. For major ambulatory surgeries, spinal anesthesia is a safe, effective, and efficient technique in patients of American Society of Anesthesiologists (ASA) status I-III, when compared to General Anesthesia (GA) [2]. Compared to GA, spinal anesthesia offers distinct advantages such as reduced thromboembolic events, faster postoperative recovery, and better patient satisfaction. The administration of local anesthetics like bupivacaine in the subarachnoid space leads to effective sensory and motor blockade, making it ideal for infraumbilical surgical procedures such as hernia repair, gynecological surgeries, urological surgeries, and orthopedic interventions.

However, one of the main challenges with spinal anesthesia is the limited duration of postoperative

analgesia provided by local anesthetics alone. While long-acting local anesthetics are widely used for spinal anesthesia, they would not extend postoperative analgesia considerably, thus necessitating the use of rescue analgesics soon after surgery. To address this limitation, various adjuvants have been studied for their ability to extend the duration of analgesia without compromising patient safety. Although multiple types of intrathecal adjuvants including alpha-2 agonists [3] and opioids [4] are used, the latter is preferred in terms of better analgesic profile and hemodynamic stability with lesser side effects. Tramadol is a centrally acting analgesic with a dual mechanism of action, i.e. weak μ-opioid receptor agonist, and inhibition of serotonin and norepinephrine reuptake. This unique combination provides effective analgesia while minimizing opioid-related side effects, such as respiratory depression, that is frequently seen with stronger opioids like morphine. Tramadol has been widely studied as an adjuvant in spinal anesthesia and has been found to prolong the duration of analgesia without causing significant hemodynamic instability or serious side effects. It also has been reported to prevent post anaesthesia shivering after subarachnoid block [5].

Nalbuphine, on the other hand, is a mixed agonist-antagonist opioid that acts as an antagonist at μ-opioid receptors and an agonist at κ-opioid receptors. This pharmacological profile allows nalbuphine to provide effective analgesia while reducing the likelihood of respiratory depression and other opioid-related side effects. Studies have demonstrated that nalbuphine when added intrathecally, offers superior analgesia with a faster onset and extended duration compared to traditional opioids [6].

A recent study found that in patients receiving hyperbaric 3 ml bupivacaine (0.5%) and 25 mcg fentanyl in two separate syringes, there was significant improvement in the quality of sensory blockade with relatively less occurrence of hypotension, over the single syringe technique [7].

Though many studies compare intrathecal nalbuphine and water-soluble opioid fentanyl [8-11], to our knowledge, no study on "PubMed search" has compared intrathecal nalbuphine with tramadol to date. Hence, we designed this study to compare the clinical efficacy of intrathecal nalbuphine and tramadol as an adjuvant to bupivacaine.

Material and Methods

This prospective, randomized, double-blinded trial was conducted at a teaching hospital from November 2021 to May 2024. The primary objective of this study was to compare the duration of analgesia between intrathecal tramadol and nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine in spinal anesthesia for infraumbilical surgeries. This study was registered with the Clinical Trials Registry of India [CTRI/2021/11/037784].

The study population consisted of 60 patients scheduled for elective infraumbilical surgeries under spinal anesthesia. Patients were eligible if they were between the ages of 18 and 55, with ASA physical status I or II, and were undergoing infraumbilical surgeries such as hernia repair, gynecological procedures, urological surgeries, etc. Patients were excluded if they refused participation or met exclusion criteria, including ASA grade III or IV, severe anemia, hypovolemia, sepsis, spinal abnormalities, previous spinal surgeries, bleeding disorders, or pregnancy.

Participants were randomly assigned to one of two groups using a sealed envelope randomization

method. Group T (tramadol group) received 25 mg of tramadol added to 2.5 ml of 0.5% hyperbaric bupivacaine for a total intrathecal injection volume of 3 ml. Group N (nalbuphine group) received 1 mg of nalbuphine (0.1 ml), combined with 2.5 ml of 0.5% hyperbaric bupivacaine plus 0.4 ml saline to make a total volume of 3 ml. All injections were administered under aseptic conditions at the L3-L4 interspace with the patients sitting. After the injection, patients were positioned supine, and assessments of sensory and motor block were initiated.

The primary outcome measured was the duration of analgesia, defined as the time from intrathecal injection to the patient's first request for rescue analgesia. Secondary outcomes included the onset of sensory block, defined as the time from injection to the loss of pinprick sensation at the T10 dermatome level, and the onset of motor block, defined as the time to achieve a grade 3 motor block on the modified Bromage scale. Additionally, the study measured the duration of sensory and motor blocks, the time to rescue analgesia, and hemodynamic stability, with continuous monitoring of heart rate, blood pressure, and oxygen saturation. Common side effects, such as nausea, vomiting, pruritus, and urinary retention, were recorded, as were rare side effects like respiratory depression, neurotoxicity, and myoclonus.

The sample size calculation was based on data from a previous study [12] and the minimum sample size was calculated to be 30 in each group with a total of 60 participants.

All patients underwent thorough preoperative assessments, including a detailed medical history and examination, with baseline vitals such as weight, height, pulse rate, blood pressure, and respiratory rate recorded. Patients were kept nil by mouth for a minimum of six hours before surgery. Intraoperative monitoring was performed with ECG, non-invasive blood pressure, and oxygen saturation throughout the procedure. The sensory block was assessed using a pinprick test, while the motor block was evaluated using the modified Bromage scale.

Postoperatively, patients were monitored for 24 hours in the recovery room, where parameters including the duration of sensory and motor blocks, time to rescue analgesia, and the incidence of side effects were recorded. Pain was evaluated at regular intervals using the Visual Analogue Scale (VAS). Rescue analgesia, in the form of intravenous paracetamol, was administered as needed.

Data were collected using a structured proforma and included demographic information such as age, gender, body mass index, and comorbidities, along with intraoperative data on sensory and motor block durations and hemodynamic parameters. Postoperative data included the duration of analgesia, time to rescue analgesia, number of doses of rescue analgesia administered, and the incidence of side effects. Data were entered into an Excel spreadsheet and analyzed using SPSS software. Continuous variables were presented as mean ± Standard Deviation (SD) and analyzed using independent t-tests, while categorical variables were reported as frequencies and percentages, with comparisons made using the Chi-square test. For the numeric data, a t-test was used for comparing both groups. Statistical significance was set at a *p*-value of less than 0.05.

Results

Between the two groups, the duration of analgesia, duration of sensory and motor blocks and time to rescue analgesia were statistically significant ($p =$

0.045, 0.011, 0.021, and 0.038 respectively). Also, the VAS score at 1st and 4th hours were statistically significant ($p = 0.034$ and 0.015 respectively). The onset of sensory and motor block were comparable between the two groups ($p = 0.238$, 0.314 respectively). The side effects profile including nausea, vomiting, pruritis and urinary retention were also comparable (Table 1).

Discussion

Unlike the study comparing intravenous tramadol (1 mg/kg) versus nalbuphine (0.6 mg/kg) for reduction of post spinal anaesthesia shivering that was done earlier [13], this randomized controlled study evaluated the comparative analgesic efficacy of tramadol and nalbuphine as intrathecal adjuvants to bupivacaine for infra umbilical surgeries. Similarly, a study compared the intravenous butorphanol (1 mg) and tramadol (50 mg) for preventing post spinal anaesthesia shivering and concluded that butorphanol was better because of its quicker onset and fewer side effects [14].

Our results indicated that nalbuphine provided a significantly longer duration of analgesia compared to tramadol, with nalbuphine achieving an average analgesia duration of 8.2 ± 1.3 hours compared to 7.5 ± 1.2 hours for tramadol ($p = 0.045$). This extended duration of analgesia with nalbuphine supports findings from previous studies, such as those by Bindra *et al.* [9] that aimed to compare the postoperative analgesia of intrathecal

Table 1: Comparative results between Tramadol and Nalbuphine groups

Parameter	Tramadol Group (Mean ± SD)	Nalbuphine Group (Mean ± SD)	*p*
Duration of Analgesia (hours)	7.5 ± 1.2	8.2 ± 1.3	0.045
Onset of Sensory Block (minutes)	4.3 ± 1.1	4.0 ± 1.0	0.238
Duration of Sensory Block (minutes)	250 ± 20	270 ± 25	0.011
Onset of Motor Block (minutes)	6.0 ± 1.3	5.7 ± 1.2	0.314
Duration of Motor Block (minutes)	230 ± 18	245 ± 20	0.021
Time to Rescue Analgesia (hours)	8.1 ± 1.4	9.0 ± 1.5	0.038
VAS Score (1 hour)	2.1 ± 0.5	1.8 ± 0.4	0.034
VAS Score (4 hours)	3.0 ± 0.7	2.2 ± 0.6	0.015
Incidence of Nausea (%)	16.1%	12.9%	0.724
Incidence of Vomiting (%)	12.9%	9.7%	0.723
Incidence of Pruritus (%)	9.7%	9.7%	1.000
Incidence of Urinary Retention (%)	9.7%	9.7%	1.000

nalbuphine and fentanyl as adjuvants to bupivacaine in cesarean section. They reported that though intrathecal nalbuphine 0.8 mg and fentanyl 20 μg are effective adjuvants to 0.5% hyperbaric bupivacaine in the subarachnoid block, intrathecal nalbuphine prolongs postoperative analgesia maximally. Tiwari *et al*. [15] performed a randomized, prospective double-blind study to evaluate the effects of 2 different doses of intrathecal nalbuphine as adjuvants to hyperbaric 0.5% bupivacaine in lower abdominal, urologic, and lower limb surgeries and concluded that nalbuphine (400 μg) significantly prolonged the duration of the sensory blockade and postoperative analgesia without any side effects. A similar study [16] compared 0.4 mg vs 0.6 mg nalbuphine as intrathecal adjuvant to hyperbaric bupivacaine for lower abdominal and lower limb surgeries and concluded that 0.6 mg was the optimum dose.

Also, there were no gross hemodynamic changes in our study similar to the study by Bindra *et al*. [9] and Tiwari *et al*. [15]. In our study, the onset of sensory block occurred slightly faster in the nalbuphine group (4.0 ± 1.0 minutes) compared to the tramadol group (4.3 ± 1.1 minutes), though this difference was not statistically significant (p = 0.238). Similarly, the onset of motor block was faster in the nalbuphine group (5.7 ± 1.2 minutes) compared to the tramadol group (6.0 ± 1.3 minutes), but again, the difference was not statistically significant (p = 0.314). However, the duration of both sensory and motor blocks was significantly longer in the nalbuphine group. The duration of the sensory block was 270 ± 25 minutes for nalbuphine compared to 250 ± 20 minutes for tramadol (p = 0.011), while the duration of the motor block was 245 ± 20 minutes for nalbuphine and 230 ± 18 minutes for tramadol (p = 0.021). These findings align with those from Deori *et al*. [11] who observed significantly prolonged regression time of both sensory and motor block in intrathecal nalbuphine (p < 0.0001) when compared to intrathecal fentanyl groups.

Nirmal *et al*. [17] did a comparison between intrathecal nalbuphine and butorphanol as adjuvants to isobaric ropivacaine in elective lower limb orthopedic surgeries and observed that the duration of sensory (p < 0.001) and motor blockade (p = 0.02) was significantly prolonged in nalbuphine group than butorphanol group. The onset of blockade was also earlier in the nalbuphine group. A similar study by Kumari *et al*. [18] concluded that intrathecal nalbuphine (0.8 mg) was better as compared to intrathecal butorphanol (25 μg) in prolonging postoperative analgesia, reducing rescue analgesic doses and the onset of sensory block. According to Subedi *et al*. [19], who compared intrathecal fentanyl 10 μg, and tramadol 10 mg, as adjuncts to bupivacaine for a subarachnoid block in caesarean section, intrathecal tramadol showed a longer duration of analgesia. In contrast, Ozer *et al*. [20] who examined the effects of intrathecal tramadol compared with intrathecal fentanyl added to bupivacaine and that of a placebo added to bupivacaine in patients undergoing elective transurethral procedures concluded that fentanyl (50 mcg) added to a local anesthetic provided longer postoperative analgesia compared with tramadol (10 mg) added to a local anesthetic. Likewise, Singh *et al*. [21] compared low-dose tramadol (10 mg) and a placebo, as intrathecal adjuvants to isobaric levobupivacaine in infra umbilical surgeries and concluded that tramadol did not prolong analgesia significantly.

In our study, the time to first request for rescue analgesia was also longer in the nalbuphine group (9.0 ± 1.5 hours) compared to the tramadol group (8.1 ± 1.4 hours) ($p = 0.038$), further supporting the superiority of nalbuphine in providing extended postoperative pain relief. This difference in the timing of rescue analgesia is clinically significant, as it reduces the need for additional postoperative interventions and enhances patient comfort.

Postoperative pain control, assessed using the VAS, was also better in the nalbuphine group. At 1 hour postoperatively, the mean VAS score was 1.8 ± 0.4 in the nalbuphine group compared to 2.1 ± 0.5 in the tramadol group ($p = 0.034$). At 4 hours, the difference in pain control was even more pronounced, with the nalbuphine group reporting a mean VAS score of 2.2 ± 0.6 compared to 3.0 ± 0.7 in the tramadol group ($p = 0.015$). These findings are in accordance with the results of Kumari *et al*. [18] who demonstrated that nalbuphine (800 µg) provides superior pain control in the postoperative period compared to butorphanol (25 µg) as an adjunct to spinal anesthesia for lower limb orthopedic surgeries.

In terms of safety, both groups maintained stable hemodynamic parameters throughout the intraoperative and postoperative periods, with no significant differences observed in heart rate, systolic blood pressure, or diastolic blood pressure. The incidence of side effects, including nausea, vomiting, pruritus, and urinary retention, was also comparable between the two groups. Nausea was reported by 16.1% of patients in the tramadol group and 12.9% in the nalbuphine group ($p = 0.724$), while vomiting was observed in 12.9% of patients in the tramadol group and 9.7% in the nalbuphine group ($p = 0.723$). Pruritus and urinary retention were experienced by 9.7% of patients in both groups ($p = 1.000$). A similar study done by Raut *et al*. [22] also concluded that intrathecal nalbuphine with hyperbaric 0.5% bupivacaine in endoscopic urology surgeries was safe without urinary retention or pruritus.

These findings suggest that nalbuphine is a more effective adjuvant to intrathecal bupivacaine than tramadol, offering longer analgesia and better postoperative pain control with a comparable side effect profile. The superior analgesic efficacy of nalbuphine, combined with its safety, makes it a preferable option for infra umbilical surgeries, where prolonged postoperative pain relief is often required.

Limitations

We have done the study within a small population in a single center with optimal dosage. We recommend using this optimal dosage among large populations in multicentres for both tramadol and nalbuphine as intrathecal adjuvants.

Conclusions

This study demonstrated that nalbuphine, when added to intrathecal bupivacaine, provides a longer duration of analgesia, and superior postoperative pain control compared to tramadol, without an increase in side effects. Nalbuphine should be considered a more effective adjuvant in infra umbilical surgeries, especially when prolonged postoperative analgesia is desired. Future studies should continue to refine adjuvant combinations and dosages to optimize patient outcomes in spinal anesthesia.

References

1. Kalbande JV, Kukanti C, Karim HMR, Sandeep G, Dey S. The efficacy and safety of spinal anesthesia with hyperbaric ropivacaine 0.75% and bupivacaine 0.5% in patients undergoing infra-umbilical surgeries: A Randomized, Double-Blind Study. *Cureus* 2024; 16(3):e57005.
2. Ledesma I, Stieger A, Luedi MM, Romero CS. Spinal anesthesia in ambulatory patients. *Curr Opin Anaesthesiol* 2024; 37(6):661-665.
3. Schwartz RH, Hernandez S, Noor N, Topfer J, Farrell K, Singh N, *et al*. A Comprehensive Review of the Use of Alpha 2 Agonists in Spinal Anesthetics. *Pain Physician* 2022; 25(2):E193-E201.
4. Singh Y. Adjuvants in Neuraxial Anesthesia. In: Sinha, A.C., Pasca, I.F. (eds) Peripartum Care of the Pregnant Patient. Springer, Cham. 2024.
5. Gupta P, Gupta M. Intrathecal tramadol for prevention of postanesthesia shivering after subarachnoid block: A prospective randomized placebo-controlled comparison of two different doses (10 and 20 mg). *Anesth Essays Res* 2018; 12(2):495-500.
6. Raghuraman M.S. Intrathecal nalbuphine – Will it gain wider acceptance? – A narrative review. *Egypt J Anaesthesia* 2017; 33: 289-293.
7. Singam AP, Mankhair SG. Comparison of premixed hyperbaric bupivacaine (0.5%) and fentanyl via single syringe with sequential administration via two syringes in spinal anaesthesia for lower limb orthopedic surgeries. *J Krishna Inst Med Sci Univ* 2021; 10(3):47-53.
8. Satapathy S, Nayak LK, Behera SK, Satapathy GC, Swain R, Das S. A comparative study of intrathecal fentanyl and nalbuphine as an adjuvant to hyperbaric bupivacaine for spinal anesthesia in lower limb orthopedic surgeries: A prospective, double-blind, randomized controlled study. *Cureus* 2023; 15(6):e41230.
9. Bindra TK, Kumar P, Jindal G. Postoperative analgesia with intrathecal nalbuphine versus intrathecal fentanyl in cesarean section: A double-blind randomized comparative study. *Anesth Essays Res* 2018; 12(2): 561-565.
10. Prabhakaraiah UN, Narayanappa AB, Gurulingaswamy S, Kempegowda K, Vijaynagar KA, Hanumantharayappa NB, *et al*. "Comparison of nalbuphine hydrochloride and fentanyl as an adjuvant to bupivacaine for spinal anesthesia in lower abdominal surgeries:" A randomized, double-blind study. *Anesth Essays Res* 2017; 11(4):859-863.
11. Deori KC, Taye MK, Lahkar B. Comparative study on regression time of block and adverse effects of nalbuphine and fentanyl as an adjuvant to intrathecal bupivacaine: a prospective randomized double-blind study. *Ain-Shams J Anesthesiol* 2023; (15): 83.
12. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose? *Anesth Essays Res* 2011; 5(2):171-5.
13. Nirala DK, Prakash J, Ram B, Kumar V, Bhattacharya PK, Priye S. Randomized double-blinded comparative study of intravenous nalbuphine and tramadol for the treatment of postspinal anesthesia shivering. *Anesth Essays Res* 2020; 14(3):510-514.
14. Palan A, Agrawal NK. Control of intraoperative shivering under spinal anaesthesia- a prospective randomized comparative study of butorphanol with tramadol. *J Krishna Inst Med Sci Univ* 2017; 6(1):57-65
15. Tiwari AK, Tomar GS, Agrawal J. Intrathecal bupivacaine in comparison with a combination of nalbuphine and bupivacaine for subarachnoid block: A randomized prospective double-blind clinical study. *Am J Ther* 2013; 20(6):592-595.
16. Raghuraman MS, Rajesh K, Sivaperumal G. Comparison of 0.4 mg versus 0.6 mg of intrathecal Nalbuphine as an adjuvant to hyperbaric Bupivacaine in lower abdomen and lower limb surgeries. *J Krishna Inst Med Sci Univ* 2021; 10(4):49-55.
17. Nirmal A, Singh Y, Mathur SK, Patel S. Comparison between intrathecal nalbuphine and butorphanol as adjuvants to isobaric ropivacaine in elective lower limb orthopedic surgeries: A prospective, randomized, double blind study. *Anaesth Pain Intens Care* 2019; 23(4):382-386.
18. Kumari A, Kullar KK, Gupta R. Duration of postoperative analgesia with Nalbuphine vs Butorphanol as an adjunct to spinal anesthesia for lower limb orthopedic surgeries: A randomized double-blind active control trial. *J Anaesthesiol Clin Pharmacol* 2021; 37(4):592-597.

19. Subedi A, Biswas BK, Tripathi M, Bhattarai BK, Pokharel K. Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: a randomised, double-blind study. *Int J Obstet Anesth* 2013; 22(4): 316-21.
20. Ozer S, Turk HS. Evaluation of anesthetic and analgesic effects of intrathecal administration of tramadol vs fentanyl. *Sisli Etfal Hastan Tip Bul* 2019; 53(1):16-20.
21. Singh DR, Mohamed H, Krishnaveni N, Nag K. Evaluating the efficacy of tramadol as an adjuvant to intrathecal isobaric levobupivacaine for elective infraumbilical surgeries. *Anesth Essays Res* 2017;11(3):572-577.
22. Raut DS, Ninave S, Verma N, Bele A, Nayak A. Assessment of the efficacy of nalbuphine as an adjuvant to intrathecal bupivacaine in endoscopic urological surgeries for the prolongation of postoperative analgesia. *Cureus* 2024; 16(7):e64257.

Author for Correspondence:
Dr. Raghuraman M Sethuraman, Department of Anaesthesiology, Sree Balaji Medical College & Hospital, BIHER, #7, Works Road, New colony, Chromepet, Chennai – 600044, India
Email: drraghuram70@gmail.com Cell: 916379141854

How to cite this article:
Sundaram SM, Narayanan S, Ramesh G, Sethuraman RM, Bhagawathi B. Comparative study of efficacy of tramadol versus nalbuphine as an adjuvant to intrathecal bupivacaine. *J Krishna Inst Med Sci Univ* 2025; 14(1):108-115.

Submitted: *15-Sep-2024* ***Accepted:*** *25-Nov-2024* ***Published:*** *01-Jan-2025*