Section: Anesthesia

Original Research Article

ASSESSMENT OF DEXMEDETOMIDINE, CLONIDINE, AND FENTANYL IN ENHANCING HYPERBARIC BUPIVACAINE FOR ANESTHESIA IN LOWER LIMB SURGERY

Dhrmesh Champaklal Pandya[1], Rinkuben Chandulal Patel[2], Nikulbhai Jivanbhai Prajapati[3], Akshaykumar Vinodbhai Pandya[4]

[1,2,4]Assistant Professor, Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India.
[3]Associate Professor, Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India.

Received *: 04/11/2024*
Received in revised form *: 25/12/2024*
Accepted *: 11/01/2025*

Corresponding Author:
Dr. Akshaykumar Vinodbhai Pandya,
Department of Anesthesia, Nootan Medical College and Research Center, Visnagar, Gujarat, India.
Email: akshaypandya38@gmail.com

DOI: 10.70034/ijmedph.2025.1.35

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (1); 201-205

ABSTRACT

Background: Local anesthetics such as bupivacaine are frequently employed in spinal anesthesia for surgeries involving the lower limbs; however, the duration of spinal anesthesia tends to be quite brief. The duration of action of bupivacaine in spinal anaesthesia can be extended through the incorporation of adjuvants like midazolam, opioids, neostigmine, dexmedetomidine, and clonidine. This study aims to assess and compare the impacts of clonidine and fentanyl when used as intrathecal adjuvants alongside hyperbaric bupivacaine in patients undergoing orthopedic surgery on the lower limbs.

Material and Methods: The current study was carried out in the Department of Anaesthesiology and Intensive Care at a Tertiary Care Teaching Institute in India. It involved patients of both genders, aged between 20 and 60 years, classified as ASA I/II, who were scheduled for lower limb orthopedic surgeries. A total of 210 patients were randomly assigned to three groups of 70 to evaluate the duration and quality of analgesia provided by clonidine and fentanyl when used as adjuvants to intrathecal bupivacaine.

Results: The findings indicate that there were statistically significant differences in the time taken to achieve the T10 block, the mean time until the first request for analgesia, and the duration of motor block across all three groups. The findings indicated that the group receiving clonidine demonstrated superior outcomes compared to those treated with fentanyl and bupivacaine alone. ($P \leq 0.05$).

Conclusion: The administration of intrathecal clonidine at a dosage of 37.5 micrograms results in a faster onset and extended duration of both sensory and motor blocks, while also enhancing the duration of analgesia when contrasted with fentanyl at 25 micrograms.

Keywords: Clonidine, Dexmedetomidine, Fentanyl, Hyperbaric Bupivacaine.

INTRODUCTION

Lower limb surgeries can be conducted using local, neuroaxial, or general anesthesia, with neuroaxial block emerging as the favored approach. The spinal block technique is characterized by its quick onset and profound anesthetic effect, presenting a lower likelihood of infection while also being a cost-effective option. Post-operative pain presents a significant challenge, as the medications utilized often have a limited duration of effectiveness. Consequently, the administration of analgesics after surgery becomes essential.[1,2] Visceral pain, nausea, and vomiting are frequently encountered issues during lower abdominal surgeries performed under spinal anesthesia.[3] Incorporating fentanyl into hyperbaric bupivacaine enhances the effectiveness of subarachnoid blocks during surgery and in the immediate postoperative period.[4] The incorporation of opioids into local anesthetic solutions presents certain drawbacks, including the potential for pruritus and respiratory depression.

Dexmedetomidine, a novel and highly selective α2-agonist, is currently being assessed as a neuraxial adjuvant due to its ability to maintain stable hemodynamic conditions while offering effective intraoperative and extended postoperative analgesia with minimal adverse effects.[5]

Dexmedetomidine, known for its selectivity as a 2 adrenergic agonist, has emerged as a versatile solution for numerous applications and procedures within perioperative and critical care environments.[6] Recent findings indicate that it is becoming an important complement to regional anesthesia and analgesia, with ongoing studies progressively establishing the evidence for its safe application in central neuraxial blocks.[7,8] Drawing from previous human studies, it is suggested that the administration of intrathecal 5 µg dexmedetomidine may enhance postoperative analgesia when combined with hyperbaric bupivacaine in spinal anesthesia, while minimizing side effects.

Fentanyl is a synthetic opioid that acts centrally and is commonly utilized for managing pain. Intrathecal fentanyl is commonly combined with other local anesthetics to enhance both anesthesia and analgesia. The advancements in spinal anesthesia have led to a notable decrease in side effects associated with anesthetic drugs, such as pruritus, nausea, and vomiting.[9]

Clonidine, classified as an alpha-2 adrenergic agonist, has a long-standing history of use as an antihypertensive medication. Recent studies have underscored the appealing anesthetic qualities in humans, such as the ability to lower anesthetic needs, enhance hemodynamic stability, and deliver effective analgesia.[4] The duration of both sensory and motor blockade induced by spinal lidocaine, bupivacaine, and ropivacaine is extended. Research indicates that even minimal doses of clonidine, starting at 15µg, can enhance the effectiveness of spinal anesthesia with ropivacaine and bupivacaine, while avoiding adverse side effects.[10]

Given the limited evidence,[11,12] regarding the efficacy of dexmedetomidine as an adjunct to hyperbaric bupivacaine in spinal anesthesia, we aimed to investigate its potential benefits. Additionally, we sought to compare this novel alpha-2 adrenergic agonist with the well-established adjuncts clonidine and fentanyl, focusing on their effects on spinal block characteristics in patients undergoing lower limb surgery.

MATERIALS AND METHODS

The current study was carried out in the Department of Anaesthesiology and Intensive Care at a Tertiary Care Teaching Institute in India, following the approval of the Hospital Ethical Committee, and spanned a period of one year.

Individuals of both genders, aged between 20 and 60 years, classified as ASA I/II, are set to undergo surgical procedures on the lower limbs.

Exclusion Criteria

- Patients with contraindication for spinal anaesthesia such as patient refusal, bleeding diathesis, coagulation abnormalities, raised intra cranial pressure, infection at the site
- Patients allergic to any of the study drugs.
- Patients with systemic disorders like respiratory, cardiac, renal or hepatic in sufficiency
- Patients refusing to participate in the study

A comprehensive history was taken, followed by both a general and systemic examination. The initial measurements of heart rate, blood pressure, respiratory rate, and oxygen saturation were documented. Baseline demographic data such as weight, height, age, and sex were documented as well. Standard assessments such as haemoglobin levels, bleeding time, clotting time, renal function tests, serum electrolytes, blood sugar levels, electrocardiograms, and chest radiographs were conducted as part of the evaluation. Additional specific investigations were conducted as required for the patient. A total of 210 patients were randomly assigned into three groups of 70 to evaluate the duration and quality of analgesia provided by clonidine and fentanyl when used as adjuvants to intrathecal bupivacaine.

Patient Groups

Group A: Received 15mg of 0.5% bupivacaine and 1 ml of normal saline.

Group B: Received 15mg of 0.5% bupivacaine and 25ugm of fentanyl.

Group C: Received 15mg of 0.5% bupivacaine and 37.5mg of clonidine.

In adherence to strict aseptic protocols, the area was meticulously cleaned and prepared for the procedure. A 25 G Quienkes needle was carefully inserted into the L3-L4 space while the patient was in a sitting position. The drug combination was administered slowly, tailored to the specific group, following confirmation that there was no cerebrospinal fluid present. All patients were administered 6 liters per minute of oxygen via a venturi mask during the surgical procedure. The assessment of sensory block was conducted utilizing the pin prick method. The upper level of T10 was deemed acceptable. The evaluation of motor block was conducted utilizing the Modified Bromage Score. During the surgical procedure, hemodynamic parameters including heart rate, blood pressure, oxygen saturation, and respiratory rate were meticulously recorded at 5-minute intervals for the first hour, followed by measurements every 10 minutes until the conclusion of the surgery. The duration of pain relief was established as the interval from spinal injection to the initial request for rescue analgesia or visual analog scale (VAS) assessment.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2019) and then exported to data editor page of SPSS

version 19 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

RESULTS

The average age in group A is 32.15 years, with a standard deviation of 12.6, and the ages range from 20 to 60 years. The average age in group B is 35.47 years, with a standard deviation of 11.78, and the ages range from 20 to 60 years. The average age of participants in group C is 31.49 years, with a standard deviation of 10.22, and ages ranging from 20 to 60 years. In Group A, the gender distribution revealed a significant majority of 85.71% males compared to 14.28% females. In Group B, the gender distribution revealed a striking 95.71% of participants were male, while females constituted a mere 4.28%. The composition of Group C consisted of 87.14% males and 12.85% females. The three groups exhibited comparable characteristics in terms of age, gender, height, weight, and ASA grade distribution, with no statistically significant differences observed among them. (P>0.05)

In our analysis, we examined the average heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), oxygen saturation (SpO2), and respiratory rate at various time intervals during the intraoperative period, specifically at 0, 5, 10, 15, 20, 30, 40, 50, 60, and 70 minutes. The differences observed in these measurements were found to be statistically insignificant (p>0.05). Statistical analysis revealed significant differences in the time to reach the T10 block, the mean time taken for the first request for analgesia, and the duration of motor block across all three groups. The findings indicated that the group receiving clonidine demonstrated superior outcomes compared to those treated with fentanyl and bupivacaine alone. Statistical significance was observed with a p-value of less than or equal to 0.05.

In our study, two patients in the bupivacaine (15mg) with fentanyl (25µg) group and three patients in the clonidine (37.5µg) group experienced hypotension; however, the difference was not statistically significant. In the study, it was observed that only one patient in both the fentanyl and clonidine groups experienced a single episode of bradycardia. Notably, there were no occurrences of bradycardia reported in the bupivacaine-only group, leading to an insignificant difference among the groups. In a recent study, postoperative vomiting occurred in 2.85% of patients who were administered Bupivacaine (15mg) combined with fentanyl (25µg). This adverse effect was managed with an intravenous injection of Ondansetron at a dosage of 4 mg. Notably, there were no reported cases of vomiting in the group receiving clonidine. The observed difference did not reach statistical significance. (p>0.05) Study patients did not exhibit respiratory depression, and nausea was observed.

Table 1: Distribution of demographic data among the studied group

Variables	Group A (n=70)	Group B (n=70)	Group C (n=70)	P value
Age (years)	32.15±12.6	35.47±11.78	31.49±10.22	0.38
Male	60 (85.71%)	67 (95.71%)	61(87.14%)	
Female	10 (14.28%)	3 (4.28%)	9 (12.85%)	0.07
Weight	58.5 ± 6.78	57.03 ± 4.14	57.8 ± 7.36	0.1
ASA				
I	62 (88.57%)	62 (88.57%)	62 (88.57%)	0.43
II	8 (11.42%)	8 (11.42%)	8 (11.42%)	

Statistically significance at p≤0.05

Table 2: Comparison of duration of motor block (seconds) between group A, B and C

Variables	Group A Mean±SD	Group B Mean±SD	Group C Mean±SD	P value
Time to reach T10 (seconds)	6.48 ± 0.9	6.06 ± 0.5	4.86 ± 0.70	0.002*
Duration of motor block (seconds)	230.35 ± 30.75	274.10 ± 15.48	320.10 ± 17.55	0.03*
First request for Analgesia (minutes)	249.35 ± 50.11	270.22 ± 55.14	325.24 ± 51.10	0.05*

*** Indicate statistically significance at p≤0.05**

DISCUSSION

The exact mechanism through which intrathecal α 2 -adrenoceptor agonists extend the duration of motor and sensory block provided by local anesthetics remains unclear. Their mechanism involves the binding to presynaptic C-fibers as well as postsynaptic dorsal horn neurons. Their pain-relieving effects stem from a reduction in the release of C-fiber transmitters and the hyperpolarization of postsynaptic dorsal horn neurons.[13] Local anesthetic agents function by inhibiting sodium channels. The extended duration of effect could be attributed to the synergistic interaction between local anesthetics and α 2 -adrenoceptor agonists.

Additionally, the extended motor block associated with spinal anesthetics may stem from the binding of α 2 -adrenoceptor agonists to motor neurons located in the dorsal horn.[14] Research indicates that intrathecal α2-receptor agonists exhibit antinociceptive effects for both somatic and visceral pain. Fentanyl is an opioid that acts as a lipophilic μ-receptor agonist. When administered intrathecally, fentanyl interacts with opioid receptors located in the dorsal horn of the spinal cord, potentially leading to effects that extend beyond the spinal level.[15]

Research has explored the application of intrathecal clonidine in conjunction with local anesthetics. There is a notable absence of studies exploring the combination of intrathecal dexmedetomidine with local anesthetics. The chosen intrathecal dose of dexmedetomidine in our study was informed by prior research conducted in animal models. Several animal studies examining the use of intrathecal dexmedetomidine at doses ranging from 2.5 to 100 μg have not indicated any neurologic deficits associated with its administration.[16-18]

Our research indicates that the use of intrathecal clonidine alongside bupivacaine results in extended analgesia when compared to the administration of intrathecal fentanyl with bupivacaine alone. Comparable results were observed by Khezri et al,[19] Bajwa et al,[20] and Chhabra et al.[21] In a study conducted by Mahendru et al., it was suggested that the administration of 30 μg of intrathecal clonidine yields sensory and motor block characteristics that are comparable to those observed with 25 μg of fentanyl.[22] This finding stands in contrast to the results of our own research. Bhure et al,[23] showed that incorporating clonidine, fentanyl, and midazolam with bupivacaine markedly enhances both the onset and duration of sensory and motor block while maintaining relative hemodynamic stability. This combination also extends the duration of analgesia and decreases the need for systemic analgesics compared to using bupivacaine alone. The researchers found that clonidine serves as a valuable adjunct to bupivacaine in spinal anesthesia, extending the duration of analgesia while maintaining a favorable safety profile. Bhattacharjee et al,[24] found in their research that the addition of 75 μg of clonidine and 25 μg of fentanyl to bupivacaine extended the duration of perioperative analgesia for cesarean sections. Postoperative analgesia was found to be more prolonged with fentanyl in comparison to clonidine. Additionally, clonidine was associated with a higher incidence of side effects, including nausea, vomiting, and hypotension. These observations did not align with our study's findings. In spinal anesthesia, local anesthetics are typically administered exclusively through intrathecal injection. However, various adjuvants have been incorporated with the aim of enhancing the quality of the subarachnoid block and augmenting the effects of local anesthetics. In recent years, the application of intrathecal adjuvants has become increasingly favored, as it seeks to extend the duration of anesthesia, enhance patient satisfaction, reduce resource use compared to general anesthesia, and promote quicker recovery times. Clonidine offers a range of additional advantages, including its ability to prevent nausea, decrease postoperative shivering, provide anxiety relief, and induce sedation. These effects can help mitigate the undesirable side effects often associated with opioids, such as itching and respiratory depression.

As interest in regional anesthesia techniques continues to rise, particularly for enhancing the quality of intraoperative and postoperative analgesia while minimizing side effects, the use of intrathecal dexmedetomidine as an adjunct to local anesthetics is steadily advancing. Ongoing clinical studies are demonstrating its efficacy and safety, and will help establish the appropriate dosages of dexmedetomidine needed to complement spinal local anesthetics.

CONCLUSION

It can be concluded that intrathecal clonidine (37.5ugm) provides quicker onset and prolonged duration of sensory and motor blocks simultaneously increasing the duration of analgesia when compared to fentanyl (25ugm).

REFERENCES

1. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med 2008; 33:159-67.
2. Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol 2011; 27:297-302.
3. Mantz J, Josserand J, Hamada S. Dexmedetomidine: New insights. Eur J Anaesthesiol 2011; 8:3-6.
4. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006; 50:222-7.
5. Al Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block. characteristics in gynecological procedures: A double blind controlled study. Am J Appl Sci 2009; 6:882-7.
6. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J 2009;30:365-70.
7. Murphy KR, Myors B. Statistical power analysis: A simple and general model for traditional and modern hypothesis tests. 2nd ed. Mahwah, NJ: Lawrence Erlbaum Associates; 2004.
8. Singh R, Gupta D, Jain A. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain after lower segment caesarean section: A randomized control trial. Saudi J Anaesth. 2013; 7:283– 90
9. Sharan R, Verma R, Dhawan A, Kumar J. Comparison of clonidine and fentanyl as adjuvant to ropivacaine in spinal anesthesia in lower abdominal surgeries. Anesth Essays Res. 2016; 10:526–31.
10. Van Tuijl I, van Klei WA, van der Werff DB, Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric

bupivacaine on postoperative pain and morphine requirements after caesarean section: A randomized controlled trial. Br J Anaesth. 2006; 97:365–70.
11. Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. Reg Anesth Pain Med. 2006;31(6):501–5.
12. Faiz SH, Rahimzadeh P, Sakhaei M, Imani F, Derakhshan P. Anesthetic effects of adding intrathecal neostigmine or magnesium sulphate to bupivacaine in patients under lower extremities surgeries. J Res Med Sci. 2012;17(10):918–22.
13. Eisenach JC, De Kock M, Klimscha W. α2-Adrenergic Agonists for Regional Anesthesia: A Clinical Review of Clonidine (1984 - 1995). Anesthesiology 1996; 85:655-74.
14. Harada Y, Nishioka K, Kitahata LM, Kishikawa K, Collins JG. Visceral antinociceptive effects of spinal clonidine combined with morphine, enkephalin, or U50, 488H. Anesthesiology 1995;83:344-52.
15. Kalso E, Poyhia R, Rosenberg P. Spinal antinociception by dexmedetomidine, a highly selective α2-adrenergic agonist. Pharmacol Toxicol 1991; 68:140-3.
16. Talke P, Xu M, Paloheimo M, Kalso E. Effects of intrathecally administered dexmedetomidine, MPV-2426 and tizanidine on EMG in rats. Acta Anaesthesiol Scand 2003; 47:347-54.
17. Xu M, Kontinen VK, Kalso E. Effects of radolmidine, a novel alpha2- adrenergic agonist compared with dexmedetomidine in different pain models in the rat. Anesthesiology 2000; 93:473-81.
18. Horvath G, Joo G, Dobos I, Klimscha W, Toth G, Benedek G. The synergistic antinociceptive interactions of endomorphin-1 with dexmedetomidine and/or S(+)-ketamine in rats. Anesth Analg 2001; 93:1018-24.
19. Khezri MB, Rezaei M, DelkhoshReihany M, Haji SeidJavadi E. Comparison of postoperative analgesic effect of intrathecal clonidine and fentanyl added to bupivacaine in patients undergoing cesarean section: A prospective randomized double-blind study. Pain Res Treat 2014. 2014 513628.
20. Bajwa BS, Singh AP, Rekhi AK. Comparison of intrathecal clonidine and fentanyl in hyperbaric bupivacaine for spinal anesthesia and postoperative analgesia in patients undergoing lower abdominal surgeries. Saudi J Anaesth. 2017; 11:37–40.
21. Chhabra AR, Jagtap SR, Dawoodi SF. Comparison of clonidine versus fentanyl as an adjuvant to intrathecal ropivacaine for major lower limb surgeries: A randomized double blind prospective study. Indian J Pain. 2013; 27:170–4.
22. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J AnaesthesiolClinPharmacol. 2013; 29:496–502.
23. Bhure A, Kalita N, Ingley P, Gadkari CP. Comparative study of intrathecal hyperbaric bupivacaine with clonidine, fentanyl and midazolam for quality of anaesthesia and duration of postoperative pain relief in patients undergoing elective caesarean section. Peoples J Sci Res. 2012; 5:19–23.
24. Bhattacharjee A, Singh NR, Singh SS, Debberma P, Debberma P, Singh T, et al. A comparative study of Intrathecal clonidine and fentanyl along with bupivacaine in spinal anesthesia for caesarean section. J Med Soc. 2015; 29:145–9.