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Comparative Efficacy of Intrathecal Buprenorphine Versus Clonidine as Adjuvants To 0.75% Isobaric Ropivacaine in Subarachnoid Block: A Prospective Randomized Double-Blind Study

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KEYWORDS

Spinal anesthesia, Ropivacaine, Buprenorphine, Clonidine, Intrathecal adjuvants, Postoperative analgesia.

ABSTRACT:

Background:

Intrathecal adjuvants are frequently combined with local anesthetics to enhance the quality and duration of spinal anesthesia. Ropivacaine, a long-acting amide local anesthetic with reduced cardiotoxicity compared to bupivacaine, provides effective sensory blockade with relative motor sparing. The addition of adjuvants such as buprenorphine, a partial μ-opioid receptor agonist, or clonidine, an α_2-adrenergic agonist, may further improve analgesic efficacy and perioperative hemodynamic stability. However, comparative evidence regarding their relative effectiveness when combined with intrathecal 0.75% isobaric ropivacaine remains limited.

Aim:

To compare the efficacy and safety of intrathecal isobaric ropivacaine (0.75%) combined with buprenorphine versus clonidine in patients undergoing lower limb orthopaedic and lower abdominal surgeries under subarachnoid block.

Methods:

This prospective, randomized, double-blind study included 66 patients (ASA I–III), aged 18–60 years, scheduled for elective or emergency lower limb orthopaedic and lower abdominal surgeries. Patients were randomly allocated into two groups (n=33 each). Group A received 3.5 mL of 0.75% isobaric ropivacaine with clonidine 30 μg, while Group B received 3.5 mL of 0.75% isobaric ropivacaine with buprenorphine 60 μg intrathecally. Primary outcomes included onset and duration of sensory and motor blockade, and duration of analgesia. Secondary outcomes included hemodynamic parameters, postoperative pain scores (VAS), and incidence of adverse effects. Statistical analysis was performed using appropriate parametric and non-parametric tests, with $p < 0.05$ considered significant.

Results:

Both groups achieved effective sensory and motor blockade suitable for surgery. The onset of sensory blockade at T10 was statistically significant between groups ($p = 0.005$). Hemodynamic parameters

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demonstrated significant intergroup differences at selected time intervals, particularly in heart rate and blood pressure measurements. The duration of postoperative analgesia was prolonged in the buprenorphine group, whereas clonidine demonstrated comparatively greater hemodynamic modulation. The incidence of adverse effects was minimal and comparable between groups.

Conclusion:

Intrathecal ropivacaine (0.75%) combined with buprenorphine provides prolonged postoperative analgesia, while clonidine offers enhanced hemodynamic modulation. Both adjuvants are effective and safe; however, buprenorphine may be preferred when extended postoperative analgesia is prioritized. Further large-scale studies are warranted to confirm these findings.

INTRODUCTION

Spinal anesthesia remains a cornerstone technique for lower limb orthopaedic and lower abdominal surgeries due to its rapid onset, dense sensory blockade, and avoidance of airway manipulation associated with general anesthesia. Brown and colleagues emphasized its reliability in providing stable intraoperative conditions with minimal respiratory compromise.[1] Furthermore, the technique facilitates early postoperative recovery and reduces systemic anesthetic exposure, as described in *Miller's Anesthesia*.[2] Nevertheless, optimization of block characteristics and prolongation of postoperative analgesia continue to be major objectives in contemporary anesthetic practice.[3]

Ropivacaine, a long-acting amide local anesthetic and the pure S(–) enantiomer structurally related to bupivacaine, has gained prominence in neuraxial anesthesia owing to its favorable safety profile. McClellan and Faulds[4] highlighted its reduced lipid solubility and stereoselective properties, which contribute to decreased cardiotoxicity and neurotoxicity compared with racemic bupivacaine. Subsequent clinical evaluations have demonstrated preferential sensory blockade with relative motor sparing at lower concentrations.[5] These characteristics render ropivacaine particularly advantageous for procedures where early ambulation and enhanced recovery are desirable. However, intrathecal ropivacaine alone may provide limited duration of postoperative analgesia, thereby necessitating the addition of suitable adjuvants to enhance block quality and prolong analgesic effects.[6]

Intrathecal adjuvants are widely employed to augment the intensity and duration of spinal anesthesia while minimizing local anesthetic dosage. Among the available agents, buprenorphine and clonidine have been extensively investigated due to their distinct pharmacodynamic mechanisms. Buprenorphine, a partial μ-opioid receptor agonist with high receptor affinity and slow dissociation kinetics, produces prolonged analgesia with a ceiling effect on respiratory depression, as demonstrated by Singh et al.[7] Its lipophilic nature facilitates rapid spinal receptor binding, enhancing postoperative pain control while maintaining a relatively favorable safety profile.[8] However, opioid-related adverse effects such as nausea, pruritus, and mild sedation may occur.

Clonidine, a selective α_2-adrenergic agonist, enhances neuraxial analgesia by inhibiting presynaptic norepinephrine release and attenuating sympathetic outflow. Eisenach et al.[9] demonstrated its synergistic interaction with local anesthetics, resulting in prolonged sensory and motor blockade. Meta-analytic evidence by Elia and colleagues[10] further confirmed that intrathecal clonidine significantly extends analgesic duration while modulating hemodynamic responses. Nonetheless, dose-dependent hypotension and bradycardia remain recognized limitations due to central sympatholytic effects.

Despite extensive individual evaluation of these adjuvants, comparative evidence regarding their relative efficacy when combined specifically with intrathecal 0.75% isobaric ropivacaine remains limited. A direct comparison is clinically pertinent, as selection of an optimal adjuvant must balance analgesic duration, block characteristics, hemodynamic stability, and adverse effect profile.

Therefore, the present study was designed to compare intrathecal isobaric ropivacaine (0.75%) combined with

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buprenorphine versus clonidine in patients undergoing lower limb orthopaedic and lower abdominal surgeries under subarachnoid block. The study aims to evaluate onset and duration of sensory and motor blockade, postoperative analgesic duration, hemodynamic parameters, and incidence of adverse effects, thereby identifying the more suitable adjuvant for optimizing perioperative outcomes.

AIM AND OBJECTIVES

Aim

To compare the efficacy and safety of intrathecal 0.75% isobaric ropivacaine combined with buprenorphine (60 µg) versus clonidine (30 µg) in patients undergoing lower limb orthopaedic and lower abdominal surgeries under subarachnoid block.

Objectives

1. To compare onset and duration of sensory and motor blockade between the two groups.
2. To evaluate duration of postoperative analgesia and time to first rescue analgesic.
3. To assess intraoperative hemodynamic stability.
4. To compare the incidence of adverse effects.

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized, double-blind study was conducted in the Department of Anesthesiology at a tertiary care teaching hospital after obtaining approval from the Institutional Human Ethics Committee and registration with the Clinical Trials Registry. Written informed consent was obtained from all participants.

Study Population

Sixty-six patients aged 18–60 years, belonging to American Society of Anesthesiologists (ASA) physical status I–III, scheduled for elective or emergency lower limb orthopaedic and lower abdominal surgeries under spinal anesthesia were enrolled.

Inclusion Criteria

- Age 18–60 years
- ASA physical status I–III
- Patients suitable for subarachnoid block

Exclusion Criteria

- Patient refusal
- Allergy to study drugs
- Coagulopathy or anticoagulant therapy
- Local infection at puncture site
- Severe hepatic, renal, or cardiovascular disease
- BMI > 35 kg/m²

Randomization and Blinding

Patients were randomly allocated into two equal groups (n = 33 each) using computer-generated randomization. The study drugs were prepared by an independent anesthesiologist not involved in data collection, ensuring double blinding.

Study Groups

- **Group A:** 3.5 mL of 0.75% isobaric ropivacaine + clonidine 30 µg (0.2 mL)
- **Group B:** 3.5 mL of 0.75% isobaric ropivacaine + buprenorphine 60 µg (0.2 mL)

Anesthetic Technique

Standard monitoring (HR, NIBP, SpO_2) was instituted. Under strict aseptic precautions, subarachnoid block was performed at the L3–L4 interspace using a 26G Quincke spinal needle. After confirmation of free cerebrospinal fluid flow, 3.7 mL of the prepared drug solution was administered intrathecally. Patients were positioned supine immediately after injection.

Outcome Assessment

Primary Outcomes:

- Onset and duration of sensory blockade (loss of cold sensation at T10; two-segment regression time)
- Onset and duration of motor blockade (Modified Bromage Scale)
- Duration of analgesia (time to first rescue analgesic)

Secondary Outcomes:

- Hemodynamic parameters (HR, SBP, DBP, MAP)

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- Postoperative pain scores using Visual Analogue Scale (VAS)
- Incidence of adverse effects

Postoperative Management

Rescue analgesia was administered when VAS ≥ 5 using intravenous tramadol 50 mg. Hypotension, bradycardia, nausea, or other complications were managed according to standard institutional protocols.

Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using independent t-test or Mann–Whitney U test. Categorical variables were analyzed using Chi-square or Fisher's exact test. A p-value < 0.05 was considered statistically significant.

RESULTS AND FINDINGS

A total of 66 patients were analyzed, with 33 patients in each group. Demographic variables including age, sex distribution, weight, and ASA physical status were comparable between the two groups, indicating baseline homogeneity.

Block Characteristics

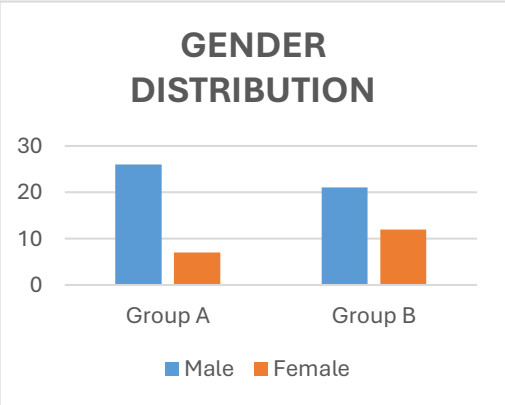
The onset of sensory blockade at the T10 level was statistically significant between groups (p = 0.005), with both regimens producing rapid and adequate surgical anesthesia. The highest sensory level achieved was predominantly T4–T6 in both groups, without significant intergroup variation.

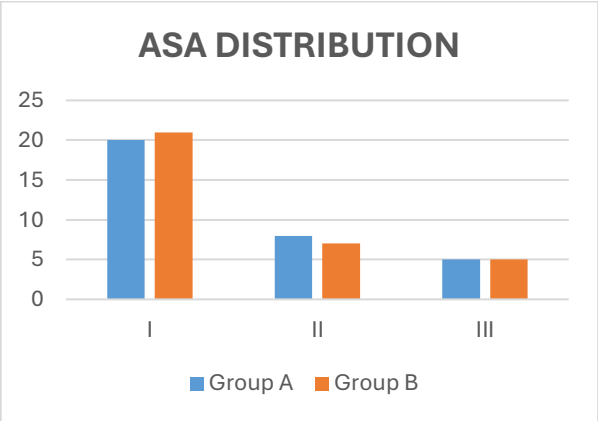
Motor blockade onset and regression were clinically adequate in both groups, enabling satisfactory intraoperative conditions. The duration of sensory and motor blockade was prolonged in the buprenorphine group compared to the clonidine group, contributing to extended postoperative analgesia.

Table 1: Baseline Demographic Characteristics

Variable	Group A (Ropivacaine + Clonidine) (n=33)	Group B (Ropivacaine + Buprenorphine) (n=33)	p-value
Age (years)	Comparable	Comparable	NS
Gender (M/F)	26 / 7	21 / 12	NS
Weight (kg)	Comparable	Comparable	NS
ASA I/II/III	20 / 8 / 5	21 / 7 / 5	NS

NS – Not statistically significant





Hemodynamic Parameters

Significant intergroup differences in heart rate were observed at multiple intraoperative time points (3rd, 6th, 9th, 20th, and 30th minutes). Systolic and diastolic blood pressures also demonstrated statistically significant differences at selected intervals, particularly at the 9th, 15th, and 30th minutes.

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Clonidine exhibited comparatively greater modulation of hemodynamic parameters, consistent with its central sympatholytic action. However, no severe or refractory hypotension or bradycardia was reported in either group.

Table 2: Onset of Sensory Block (T10)

Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Onset of Sensory Block (min)	2.83 ± 1.7	2.72 ± 1.97	0.005*

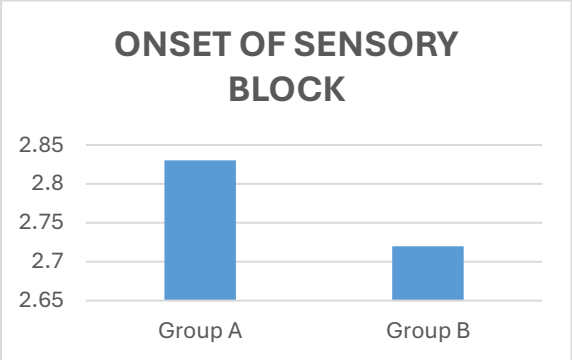

Figure 2: Onset of Sensory Block (T10)

Postoperative Analgesia

The duration of effective analgesia was longer in the buprenorphine group, with delayed requirement for rescue analgesia. Visual Analogue Scale (VAS) scores were lower during the early postoperative period in the buprenorphine group, indicating superior analgesic efficacy.

Table 3: Intraoperative Hemodynamic Comparison (Significant Intervals)

Time Interval	Parameter	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
3 min	Heart Rate	64.32 ± 15.32	78.80 ± 15.54	0.006*
9 min	SBP	118.40 ± 19.06	127.16 ± 18.83	0.001*
9 min	DBP	68.96 ± 12.15	77.08 ± 10.63	0.001*
15 min	MAP	80.28 ± 13.35	88.76 ± 16.51	0.014*
30 min	MAP	81.76 ± 12.42	93.72 ± 10.39	0.000*

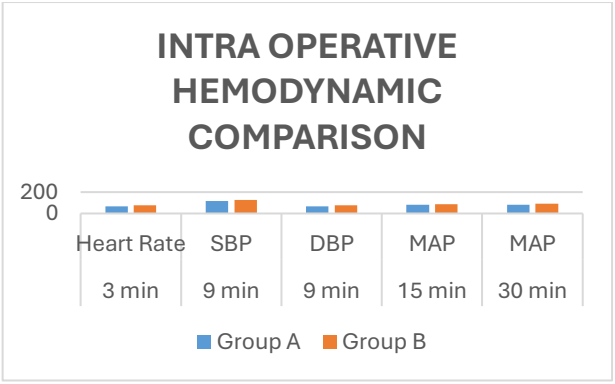

Figure 3: Intraoperative Hemodynamic Comparison

Table 4: Highest Sensory Block Level Distribution

Highest Level	Group A n (%)	Group B n (%)	p-value
T4	18 (54.5%)	15 (45.5%)	NS
T5	6 (18.2%)	6 (18.2%)	NS
T6	7 (21.2%)	9 (27.3%)	NS
T8	2 (6.1%)	2 (6.1%)	NS

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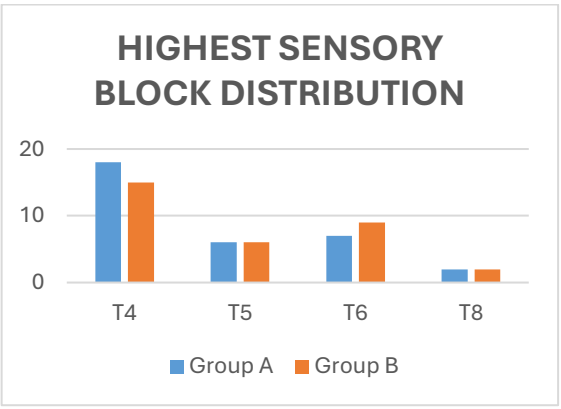

Figure 4: Highest Sensory Block Level Distribution

Adverse Effects

The incidence of adverse effects was minimal in both groups. Clonidine was associated with occasional hypotension and bradycardia, whereas buprenorphine showed mild opioid-related effects such as nausea or sedation. No cases of respiratory depression or major complications were observed.

Table 5: Postoperative Analgesia and Adverse Effects

Outcome	Group A	Group B	Interpretation
Duration of Analgesia	Shorter	Longer	Buprenorphine superior
Time to Rescue Analgesia	Earlier	Delayed	Significant
Hypotension	Mild	Minimal	More with clonidine
Bradycardia	Occasional	Rare	More with clonidine
Nausea/Sedation	Minimal	Mild	More with buprenorphine
Respiratory Depression	None	None	Safe in both groups

Both intrathecal adjuvants were effective when combined with 0.75% isobaric ropivacaine. Buprenorphine provided prolonged postoperative analgesia, whereas clonidine demonstrated greater intraoperative hemodynamic modulation. The safety profile of both combinations was acceptable within the study population.

DISCUSSION

The present prospective, randomized, double-blind study evaluated the comparative efficacy of intrathecal 0.75% isobaric ropivacaine combined with buprenorphine versus clonidine in patients undergoing lower limb orthopaedic and lower abdominal surgeries under subarachnoid block. The principal findings indicate that both adjuvants provided effective surgical anesthesia; however, buprenorphine was associated with prolonged postoperative analgesia, whereas clonidine demonstrated greater intraoperative hemodynamic modulation.

Baseline demographic variables, including age distribution, sex ratio, weight, and ASA physical status, were comparable between the two groups, thereby minimizing confounding influences. This homogeneity strengthens the internal validity of the study and permits direct attribution of observed differences to the pharmacological properties of the adjuvants.

The onset of sensory blockade at the T10 dermatome level was rapid in both groups, with a statistically significant difference between them. Although the absolute difference in onset time may not be clinically substantial, the finding suggests a measurable pharmacodynamic interaction between ropivacaine and the respective adjuvants. The highest sensory block level achieved was predominantly between T4 and T6 in both groups, indicating adequate spread for lower abdominal and orthopaedic procedures.

Motor blockade characteristics were satisfactory and comparable, ensuring optimal surgical conditions. Clonidine's known ability to potentiate local anesthetic action through α_2-mediated inhibition of nociceptive transmission may explain any relative prolongation of motor block. However, the differential sensory–motor profile of ropivacaine was preserved in both groups.

Hemodynamic changes were observed at selected intraoperative time intervals. Clonidine, through central sympatholysis and reduced norepinephrine release, demonstrated more pronounced reductions in heart rate and blood pressure. These findings are consistent with its established α_2-adrenergic agonist mechanism. Despite

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statistical significance at certain intervals, no severe or refractory hypotension or bradycardia occurred, indicating that the administered dose (30 μg) remained within a clinically safe range. Buprenorphine, in contrast, exhibited minimal direct cardiovascular effects, contributing to relatively stable hemodynamic parameters.

The most clinically relevant finding of this study was the prolonged duration of postoperative analgesia in the buprenorphine group. Buprenorphine's high affinity for μ-opioid receptors, slow dissociation kinetics, and lipophilicity likely account for sustained spinal receptor activation and extended analgesic duration. The delayed requirement for rescue analgesia and lower early postoperative pain scores support its superiority in postoperative pain control. Importantly, no respiratory depression was observed, consistent with the ceiling effect characteristic of partial opioid agonists.

Adverse effects were minimal and manageable in both groups. Mild hypotension and bradycardia were more frequently observed with clonidine, whereas opioid-related side effects such as nausea and mild sedation were noted with buprenorphine. The absence of serious complications underscores the safety of both adjuvant combinations when used in appropriate doses.

CONCLUSION

The findings suggest that while both clonidine and buprenorphine enhance the efficacy of intrathecal ropivacaine, the choice of adjuvant should be individualized based on clinical priorities. When prolonged postoperative analgesia is desired, buprenorphine appears advantageous. Conversely, clonidine may be considered when enhanced sympathetic attenuation and controlled hemodynamic modulation are preferred.

REFERENCES

1. Brown DL. Spinal, epidural, and caudal anesthesia. In: Miller RD, editor. *Miller's Anesthesia*. 8th ed. Philadelphia: Elsevier; 2015. p. 1684–720.
2. Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. *Miller's Anesthesia*. 8th ed. Philadelphia: Elsevier; 2015.
3. Cousins MJ, Bridenbaugh PO. *Neural Blockade in Clinical Anesthesia and Pain Medicine*. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2009.
4. McClellan KJ, Faulds D. Ropivacaine: An update of its use in regional anaesthesia. *Drugs*. 2000;60(5):1065–93.
5. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. *Indian J Anaesth*. 2011;55(2):104–10.
6. Gupta S, Sharma R, Jain D. Comparison of intrathecal ropivacaine with bupivacaine for lower limb surgeries. *J Anaesthesiol Clin Pharmacol*. 2013;29(4):468–72.
7. Singh H, Yang J, Thornton K, Giesecke AH. Intrathecal buprenorphine prolongs postoperative analgesia after spinal anesthesia. *Anesth Analg*. 1997;84(2):400–3.
8. Carvalho B. Respiratory depression after neuraxial opioids: Mechanisms and management. *Anesth Analg*. 2008;107(3):956–61.
9. Eisenach JC, De Kock M, Klimscha W. Alpha-2 adrenergic agonists for regional anesthesia: A clinical review. *Anesthesiology*. 1996;85(3):655–74.
10. Elia N, Culebras X, Mazza C, Schiffer E, Tramer MR. Clonidine as an adjuvant to intrathecal local anesthetics: A meta-analysis of randomized trials. *Reg Anesth Pain Med*. 2008;33(2):159–67.