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Efficacy of Analgesic Effect of Dexmedetomidine Versus Clonidine Added to Intrathecal Hyperbaric Ropivacaine in Lower Limb Orthopedic Surgeries – A Randomized Clinical Trial

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KEYWORDS
Anesthesia, Analgesia, Intrathecal clonidine, Dexmedetomidine, Hyperbaric ropivacaine, Spinal anesthesia

ABSTRACT:

Background: The subarachnoid block is widely regarded as the preferred technique for lower-limb orthopedic surgeries due to its ability to effectively block sensory, motor, and sympathetic impulses. Ropivacaine is commonly used intrathecally for this purpose. Various adjuvants, including alpha-2 agonists, have been employed to prolong the duration of analgesia and enhance anesthesia.

Objective: To evaluate the efficacy of dexmedetomidine and clonidine as adjuvants to 0.75% hyperbaric ropivacaine in spinal anesthesia for lower-limb orthopedic surgeries, with a focus on the duration of analgesia.

Methods: This prospective, randomized clinical trial involved 70 patients scheduled for lower-limb orthopedic surgeries under subarachnoid block. The patients were randomly assigned to two groups of 35 each, using a closed opaque envelope method. Group A received 2.5 mL of 0.75% hyperbaric ropivacaine with 10 mcg dexmedetomidine (0.5 mL), while Group B received 2.5 mL of 0.75% hyperbaric ropivacaine with 30 mcg clonidine (0.5 mL). After the subarachnoid block, we monitored the onset of sensory and motor blockade, hemodynamic changes, time to two-segment sensory regression, and the duration of motor blockade and analgesia.

Results: The mean time to onset of sensory blockade in Group A was 4.0 ± 0.7 minutes, compared to 5.2 ± 1.0 minutes in Group B, with a p-value of < 0.001. The time to two-segment sensory regression was significantly longer in Group A (252.4 ± 33.1 minutes) than in Group B (188.6 ± 26.1 minutes) ($p < 0.001$). There was a significant difference in the duration of analgesia between Group A (339.1 ± 29.3 minutes) and Group B (286.6 ± 30.1 minutes) ($p < 0.001$). Complications were more frequent in the clonidine group than in the dexmedetomidine group.

Conclusion: The duration of analgesia and sensory blockade was significantly longer in the dexmedetomidine group compared to the clonidine group, with excellent hemodynamic stability observed in both groups.

Introduction

Spinal anesthesia, also referred to as a sympathetic block, is commonly used in surgical procedures involving the lower limbs, pelvis, and abdomen. It helps to alleviate pain both during and after surgery, while also promoting early mobilization. Sympathectomy offers several benefits, such as reducing postoperative hypercoagulability, enhancing tissue blood flow, decreasing the need for splinting, which leads to improved oxygenation, and reducing stress and

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improving peristalsis due to the suppression of the neuroendocrine response to surgery [1]. However, spinal anesthesia may also result in adverse effects, including bradycardia, hypotension, prolonged motor block, and high spinal anesthesia [2].

Ropivacaine and Levobupivacaine are modern local anesthetics with lower cardiotoxicity compared to bupivacaine [3]. Ropivacaine has been widely used in epidural, intrathecal, and peripheral nerve blocks [4]. It is particularly advantageous due to its tendency to cause less motor block, facilitating early mobilization [5], which contributes to faster postoperative recovery [6]. Initially, hyperbaric ropivacaine was prepared by adding 25% glucose to isobaric ropivacaine, but preconstituted hyperbaric ropivacaine is now available.

Opioids have traditionally been used as adjuvants in anesthesia. In 1979, morphine was the first opioid administered intrathecally [7,8]. These drugs were utilized to extend the duration of anesthesia and provide postoperative pain relief. However, the use of opioids has declined due to side effects such as respiratory depression. Various other agents, including alpha-2 agonists, neostigmine, and vasoconstrictors, have also been used as adjuvants to enhance anesthesia and alleviate pain.

Dexmedetomidine, an α2-adrenergic agonist [9], and Clonidine, a widely used alpha-2 adrenergic agonist, have been employed as additives in intrathecal anesthesia [10]. Dexmedetomidine is considered superior to clonidine in terms of its sedative properties and provides better intraoperative and postoperative comfort for patients [11,12]. Dexmedetomidine also offers better hemodynamic control, although in higher doses it can cause hypertension due to its effect on smooth muscle cells in resistance arteries. In contrast, clonidine tends to induce hypotension, regardless of the dosage, with profound hypotension often observed in hypertensive patients [13].

Against this background, this study was designed to evaluate the efficacy of adding Dexmedetomidine versus Clonidine in lower limb orthopedic procedures, with the hypothesis that Dexmedetomidine will provide superior analgesia compared to Clonidine when administered intrathecally in combination with Ropivacaine.

Materials And Methods

A prospective randomized clinical trial was conducted among 70 ASA grade I and II patients scheduled for lower limb orthopedic surgeries under spinal anesthesia, between November 2022 and May 2024, following approval from the Institutional Ethical Committee (IEC no. AV/IHEC/2022/060) at AVMC&H and registration with the Clinical Trial Registry of India (CTRI/2023/03/050845). The sample size of 70 patients (35 in each group) was calculated based on a similar study by Krishnappa MS et al. [14], with an expected mean difference in the duration of analgesia of 34 minutes and a standard deviation of 50 minutes. The significance level and power were set at 5% and 80%, respectively. After obtaining informed written consent, patients were randomly allocated into two groups of 35 each using a lot system with a closed opaque envelope method, and the study was double-blinded.

Both the investigator and participants were unaware of the study drug administered. Patients aged 18 to 60 years, undergoing lower limb orthopedic surgeries, classified as ASA-I or ASA-II, with a body weight of 50-80 kg, height of 140-180 cm, and surgeries lasting ≥ 2 hours were included. Patients classified as ASA-III or higher, those with hypersensitivity to study drugs, uncontrolled diabetes mellitus, hypertension, kidney or liver failure, cardiac dysrhythmias, or bleeding disorders were excluded.

Group A received a total of 3 ml of the study drug, consisting of 2.5 ml of 0.75% preconstituted hyperbaric ropivacaine and 10 mcg of dexmedetomidine (diluted in 2 ml of distilled water, where 1 ml contains 20 mcg; 0.5 ml was added to the ropivacaine). Group B received 3 ml of the study drug, consisting of 2.5 ml of 0.75% preconstituted hyperbaric ropivacaine and 30 mcg of clonidine (diluted in 1.5 ml of distilled water, where 1 ml contains 60 mcg; 0.5 ml was added to the ropivacaine). After pre-anesthetic evaluation, all patients received oral T. Alprazolam 0.5 mg and T. Pantoprazole 40 mg as premedication the night before surgery. On the day of surgery, patients were preloaded with 10 ml/kg of Ringer lactate over 15 minutes prior to intrathecal drug administration, and baseline vital parameters were recorded. Under aseptic conditions, subarachnoid blockade was performed using a 25G Quincke needle in the L3-L4 intervertebral space. After

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confirming the free flow of cerebrospinal fluid, the study drug was administered, and the patient was positioned supine. Patients were monitored for the onset of sensory and motor blockade, hemodynamic changes, time for two-segment sensory regression, duration of motor blockade, and postoperative analgesia. The time from intrathecal administration to the loss of pinprick sensation at the T8 dermatome was considered the onset of sensory blockade, and the onset of motor blockade was assessed using Bromage score 3. Heart rate, blood pressure, and oxygen saturation were monitored every 5 minutes for the first 30 minutes and then every 10 minutes until the end of surgery. If the mean arterial pressure (MAP) dropped by more than 20% from baseline, it was treated with 6 mg intravenous ephedrine in incremental doses. A heart rate 20% below baseline was considered bradycardia and was treated with intravenous atropine (20 mcg/kg) as needed.

The time from the onset of sensory blockade to two-segment regression (T10) was considered sensory block regression. The time from the onset of motor blockade to reaching Bromage score 1 was considered the duration of motor blockade. The time at which the patient reported pain with a visual analog scale (VAS) score of 3 was considered the point of first rescue analgesia, treated with 100 mg intravenous tramadol. The time from intrathecal drug administration to the administration of the first rescue analgesic was recorded as the duration of analgesia provided by the study drugs. Postoperative complications, including hypotension, bradycardia, nausea, and vomiting, were monitored, and all data were recorded and analyzed.

Statistical Analysis: Statistical analysis will be performed using the Statistical Package for Social Sciences (SPSS) version 20.0. Data will be presented as median (range), number (%), standard error of the mean, or mean (standard deviation). Nominal measurements will be compared using the chi-square test. For ordinal variables, including pain severity, the independent t-test will be used. A significance level of $P < 0.05$ will be considered statistically significant.

Results

The two groups were comparable in terms of demographic data such as age, sex, height, weight, ASA I & II physical status, and duration of surgery (Table 1). There was a statistically significant difference between Group A and Group B in the onset of sensory blockade, with Group A showing an onset of 4.0 ± 0.7 minutes and Group B showing 5.2 ± 1.0 minutes ($P < 0.001$*). However, the onset of motor blockade was not significantly different between Group A and Group B (7.1 ± 1.2 minutes and 7.4 ± 1.1 minutes, respectively; $P < 0.177$*). The time for two-segment sensory regression was slower in Group A compared to Group B (252.4 ± 33.1 minutes vs. 188.6 ± 26.1 minutes; $P < 0.001$*). There was no significant difference in the duration of motor blockade between Group A and Group B (206.57 ± 18.10 minutes and 159.11 ± 19.59 minutes, respectively; $P < 0.06$*). The duration of analgesia was significantly prolonged in Group A compared to Group B, with durations of 339.1 ± 29.3 minutes and 286.6 ± 30.1 minutes, respectively ($P < 0.001$*) (Table 2). Heart rate, as well as systolic and diastolic blood pressure, were better stabilized in Group A compared to Group B ($P < 0.001$*). There was no significant difference in the incidence of adverse effects, such as hypotension, bradycardia, nausea, and vomiting (Table 3).

Discussion

Postoperative analgesia should be long-lasting and effective with minimal side effects. Recently, 0.75% hyperbaric ropivacaine has been used for spinal anesthesia; however, its postoperative analgesic duration is limited. Therefore, the use of additives is a reliable method to prolong the duration of anesthesia. While ropivacaine provides good cardiovascular and hemodynamic stability, the addition of α2 agonists further enhances these properties [15,16]. Although the exact mechanism by which intrathecal α2 agonists prolong sensory and motor blockade of local anesthetics is not fully understood, α2 agonists are known to act by binding to presynaptic C fibers and postsynaptic dorsal horn neurons, whereas local anesthetics block sodium channels. At the same time, intrathecal α2-adrenoceptor agonists produce analgesic effects by inhibiting the release of C fiber transmitters and by hyperpolarizing postsynaptic dorsal horn neurons [13]. Various studies have used different doses of dexmedetomidine for intrathecal blockade, ranging from 3 mcg to 15 mcg, and clonidine from 15 mcg to 300 mcg [10].

In this study, the earlier onset of sensory blockade was statistically and clinically significant in Group A

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compared to Group B (4.0 ± 0.7 minutes vs. 5.2 ± 1.0 minutes), although there was no significant difference in motor blockade between the two groups (Group A: 7.1 ± 1.2 minutes; Group B: 7.4 ± 1.1 minutes). Anusha et al. [17] assessed the same doses of dexmedetomidine, and clonidine used in this study, combined with isobaric ropivacaine, and demonstrated that the onset of sensory blockade at the T10 level was significantly faster in the dexmedetomidine group (3.68 minutes) compared to the clonidine group (6.1 minutes). The onset of motor block was not significantly different between the dexmedetomidine group (11.4 minutes) and the clonidine group (12.66 minutes). A similar study by Tushar et al. [18] compared three groups: clonidine (6.00 ± 1.258 minutes), dexmedetomidine (6.32 ± 1.472 minutes), and plain ropivacaine (6.00 ± 1.28 minutes) in terms of time to reach the T10 sensory blockade level, with no substantial differences among the groups. In this study, the dexmedetomidine group significantly prolonged the duration of analgesia (339.1 ± 29.3 minutes) compared to the clonidine group (286.6 ± 30.1 minutes). Similarly, Tushar et al. [18] concluded that both clonidine (301 ± 51.5 minutes) and dexmedetomidine (316 ± 55.9 minutes) considerably prolonged analgesia compared to plain ropivacaine (204 ± 16.9 minutes). Another study by Vani et al. [19] found that the average duration of analgesia was 204.7 ± 20.61 minutes for plain ropivacaine and 430.9 ± 33.08 minutes when dexmedetomidine was used as an adjuvant.

Heart rate between the two groups was significantly different from 5 minutes to the end of surgery, with better maintenance in the dexmedetomidine group, consistent with studies by Shah et al. [20] and Shukla et al. [21]. Systolic blood pressure was better maintained in Group A after 30 minutes until the end of the procedure, while diastolic blood pressure stabilized within 10 minutes after study drug administration. Consequently, dexmedetomidine has been reported to have more significant hemodynamic effects compared to clonidine. The incidence of hypotension was similar in both groups at the doses used in this study, but bradycardia occurred in Group B, with none observed in Group A.

The limitations of this study include its single-center setting, which limits the external validity of the findings. Additionally, the study population consisted of healthy individuals or those with controlled comorbidities.

Conclusion

A study comparing dexmedetomidine and clonidine as adjuvants to ropivacaine in spinal anesthesia found that the duration of postoperative analgesia and sensory blockade was longer in the dexmedetomidine group compared to the clonidine group. Dexmedetomidine also demonstrated better hemodynamic stability with minimal adverse effects.

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Table 1: Demographic data

Parameters	**Group A (n = 35) Mean ± SD**	**Group B (n = 35) Mean ± SD**	**P value**
Age	55.46 ± 16.17	44.0 ± 14.103	0.6
Sex (M:F)	62.9% : 37.1%	68.6% : 31.4%	0.6
Height (cm)	158.57 (5.90)	159.49 (6.47)	0.53
Weight (kg)	58.09 (6.45)	58.91 (4.76)	0.54
ASA I:II	45.7% : 54.3%	80.0% : 20.0%	0.003
Duration of surgery	126.6 ± 15.5	129.1 ± 13.1	0.228

Table 2: Subarachnoid block characteristics in both groups

Characteristics	**Group A (n = 35) Mean ± SD**	**Group B (n = 35) Mean ± SD**	**P value**
Beginning of sensory blockade	4.0 ± 0.7	5.2 ± 1.0	<0.001

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till T8			
Beginning of motor blockade (Bromage score 3)	7.1 ± 1.2	7.4 ± 1.1	0.177
Time of two segment sensory regression (T10)	252.4 ± 33.1	188.6 ± 26.1	<0.001
Duration of motor blockade (Bromage score 0)	206.57 ± 18.10	159.11 ± 19.59	0.06
Analgesic duration (1st rescue analgesia)	339.1 ± 29.3	286.6 ± 30.1	< 0.001

Table 3 : Complications

Side effect	Group A	Group B
Hypotension	3 (8.6%)	3(8.6%)
Bradycardia	0	1 (2.9%)
Nausea	0	0
Vomiting	0	0

Figure 1: CONSORT flow diagram