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Original Research Article

Analgesic Efficacy of Clonidine as an Adjuvant with Ropivacaine in a Caudal Epidural Block in Lumber Spine Surgery: A Randomized Double-Blind Interventional Study

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Conflict of interest: Nil

Abstract:

Background and Aim: Caudal epidural analgesia is a common regional anesthesia technique for lumbosacral region surgeries. This study aimed to compare the efficacy of ropivacaine 0.2% with clonidine versus ropivacaine 0.2% in caudal epidural analgesia in lumbosacral spine surgeries under general anesthesia.

Materials and Methods: This prospective, randomized, double-blinded study was conducted, on 72 patients who underwent lumbosacral spine surgery. The patients were aged 18–65 years, of either gender, American Society of Anesthesiologists (ASA) grade I and II, and randomly allocated into two groups (36 in each group). Group A received ropivacaine (0.2%) 18 ml + normal saline 2 ml, whereas Group B received ropivacaine (0.2%) 18 ml + clonidine 1μg/kg in normal saline 2 ml (total volume 20 ml) administered in caudal epidural block in prone position after the administration of general anesthesia. Hemodynamic parameters such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), heart rate (HR), visual analog score (VAS), duration of analgesia, sedation score, and side effects were recorded at regular intervals postoperatively for 24 hours. Student's t-test and Chi-square tests were used for statistical analysis.

Results: Mean VAS was significantly lower in Group B than in Group A for the first 12 hours postoperatively. Group B showed a significantly prolonged duration of analgesia as compared to Group A. No significant differences were observed with respect to hemodynamic parameters, sedation score, or side effects between the groups.

Conclusion: Clonidine is a safe and effective adjuvant to 0.2% ropivacaine in caudal epidural block for postoperative analgesia.

Keywords: Ropivacaine, Clonidine, Caudal Epidural Block, Lumber, Spine.

Introduction

Caudal epidural block is a well-accepted regional anesthesia technique for infraumbilical surgeries in the distribution of T10-S5 dermatome [1]. It has multiple benefits when combined with general anesthesia, such as reducing the requirement of inhaled and intravenous anesthetic agents, attenuating the stress response to surgery, facilitating a rapid and smooth recovery, and providing good postoperative analgesia [2]. Local anesthetic agents, such as bupivacaine, levobupivacaine, and ropivacaine, are commonly used for caudal block. Local anesthetic agents alone in caudal block provide good operative conditions but have a shorter duration of analgesia. The addition of various adjuvants to local anesthetic agents has gained popularity to increase the efficacy and duration of analgesia; various drugs, such as opioids, α-2 agonists, epinephrine, midazolam, ketamine, and neostigmine, are used as adjuvants. Ropivacaine, a local anesthetic agent that is a new long-acting amide S (-) enantiomer, has benefits over bupivacaine in terms of long

duration of action with less cardiovascular and central nervous system (CNS) toxicity and more preferential blockade of sensory nerve fibers [3]. Clonidine, an α-2 agonist, is an adjuvant with hemodynamic stabilizing properties due to enhanced sympathoadrenal stability ultimately responsible for the decreased requirement of systemic analgesic and anesthetic agents [4]. Our study aimed to evaluate and compare the analgesic effect of ropivacaine versus ropivacaine with clonidine in caudal epidural block for lumbar spine surgeries.

Material and Methods

This study was a prospective, hospital-based, randomized, double-blind, and controlled interventional study. The study was performed after the approval from the institutional review board and ethical committee.

The study period was from June 2020 to December 2020. After obtaining written informed consent, we recruited a total of 72 patients (n = 36 per group). Inclusion criteria were patients aged 18–65 years, male or female, ASA grade I and II, and undergoing lumber spine surgery under general anesthesia. Patients were excluded from the study if they had coagulation disorders and were on anticoagulant treatment, had puncture site infections, had neurological and psychological disorders, were allergic to local anesthetics drugs, or had undergone previous spine surgeries.

Pre-anesthesia check-ups were conducted 1 day before surgery in all patients. After explaining the procedure and obtaining written informed consent, the patients were kept nil by mouth for 6 hours before surgery. Randomization of group allocation was done using a computer-generated random number table, and random numbers were kept in sequential sealed envelopes.

The patient and observer both were blinded about group allocation, as presented in the consort flow chart (Figure 1). After confirmation of written consent and overnight fasting, the patients were taken to the operation theatre.

All standard monitors were connected and baseline monitoring done for noninvasive blood pressure (NIBP), heart rate (HR), oxygen saturation (SPO_2), and electrocardiogram (ECG). An intravenous line taken with an 18G cannula and a balanced salt solution infusion was started. Preoxygenation was done with 100% oxygen for 3–5 minutes in all patients. Standard anesthesia protocol was followed for induction and maintenance in all patients.

After that, all patients were positioned prone on a Wilson's frame, and a caudal epidural block was given under all aseptic precautions using the conventional blind technique with a 20G IV cannula needle. After confirming the proper position of the needle with the whoosh test and loss of resistance technique, the study drug (total volume: 20 ml) was injected after negative aspiration of blood and cerebrospinal fluid (CSF). Group A received 0.2% ropivacaine 18 ml + normal saline 2 ml, whereas Group B received 0.2% ropivacaine 18 ml + 2 ml of injection clonidine 1μg/kg with normal saline.

Hemodynamic parameters were noted at different time intervals, including baseline, just after intubation, 5 minutes after intubation, after the prone position, just after the caudal block, then every 15 minutes throughout the procedure. Hypotension and bradycardia were managed accordingly if observed. When surgery was over, patients were turned into a supine position, and reversal was done with an injection of neostigmine (0.05 mg/kg IV) and an injection glycopyrrolate (0.008 mg/kg IV). Extubation was done when the criteria for adequate reversal were met.

In the postoperative period, all patients were monitored, and hemodynamic parameters, visual analog score (VAS), and sedation score were recorded at different time intervals, initially just after extubation, and then at 30 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, and 24 hours. Duration of analgesia and request of first rescue analgesia was noted. Patients were observed for any side effects, such as nausea, vomiting, hypotension, shivering, respiratory difficulty, and sedation postoperatively up to 24 hours.

Duration of analgesia is defined as the time between caudal analgesia and the first request of rescue analgesia. VAS was used to assess postoperative pain relief with scores ranging from 0 to 10 (0 = no pain; 1, 2, 3 = mild pain; 4, 5, 6 = moderate pain; 7, 8, 9 = severe pain; 10 = worst imaginable pain. At a VAS greater than or equal to 4, injection diclofenac 75 mg IV was given as rescue analgesia.

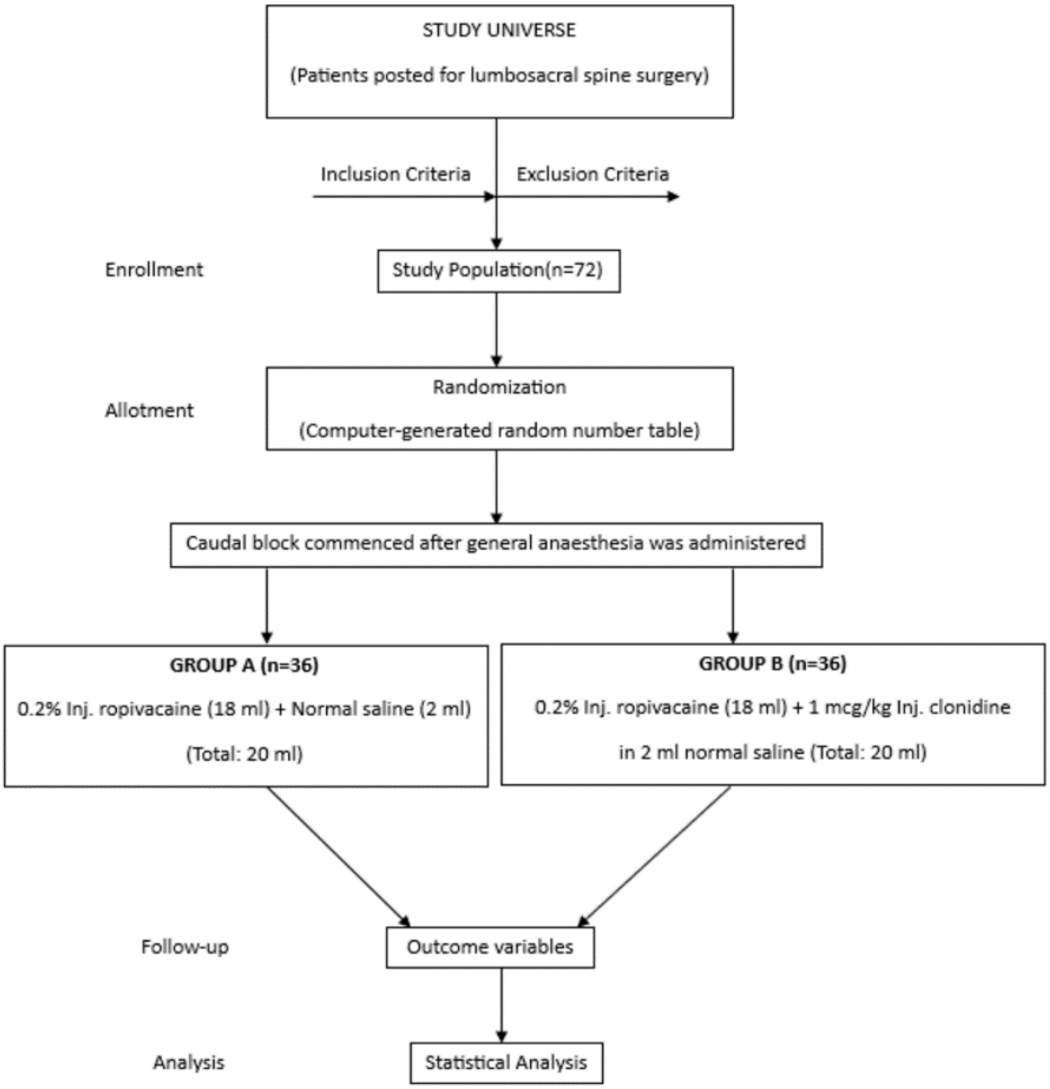

Figure 1: Consort flow chart

Statistical Analysis:

Statistical analysis was conducted using the statistical software package SPSS version 21 for windows (SPSS Inc., Chicago, IL, USA). The categorical data were offered as numbers (percentage) and compared among groups using the Chi-square test.

The quantitative data were offered as mean and standard deviation and were compared using the student's t-test. Probability was deemed significant if the p-value $\leq$ 0.05. The sample size was determined by SPSS to evaluate the statistical difference with a significance level (α) of 0.05 (i.e., 95% confidence) and a power of test of 80%.

The sample size of 36 for each group was adequate at 95% confidence and 80% power to verify the projected difference of 1.17 ($\pm$1.21) in VAS at 8 hours postoperatively in both groups, according to the seed article.[1] This sample size was adequate to account for all other study variables in this study. So, for the purpose of this study, 36 patients comprised each of the two groups.

Results

Both study groups were comparable in terms of demographic and clinical characteristics (age, gender, weight, ASA grade) and mean duration of surgery (Table 1).

Table 1: Demographic profile of Groups A and B

Demographic profile	Group A	Group B	p-value
Age (years)[a]	40.81 ± 13.94	40.83 ± 13.56	0.993 (NS)
Weight (kg)[b]	65.58 ± 7.90	70.75 ± 6.13	0.197 (NS)
ASA grade (%)[c]	Grade 1: 75%	Grade 1: 83.33%	0.562
	Grade 2: 25%	Grade 2: 16.67	

Sex[d]	Male: 50% Female: 50%	Male: 50% Female: 50%	
Mean duration of surgery (minutes)[e]	72.50 ± 21.06	75.42 ± 19.47	0.543

Note: a, b, e: student's t-test; c, d: Chi-square test; NS: non-significant

Figures 2 and 3 depict the comparison and changes in mean HR and MBP intraoperatively at various time intervals. Both groups were comparable with respect to intraoperative and postoperative hemodynamic parameters (HR, SBP, DBP, and MBP).

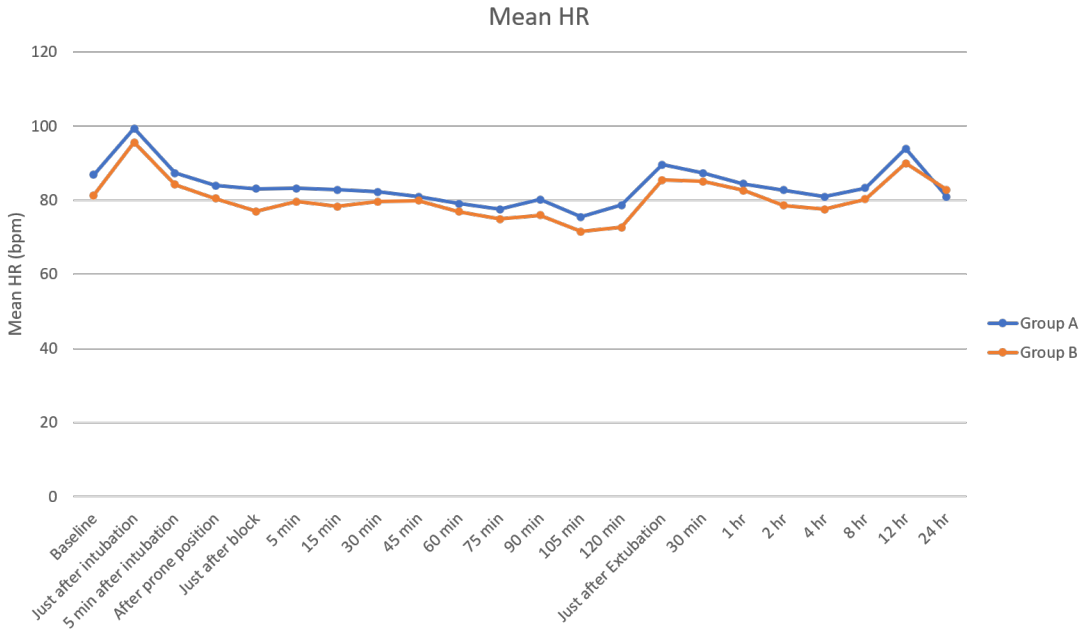

Figure 2: Comparison of mean heart rate (BPM) at different time intervals among the groups from baseline (student's t-test used)

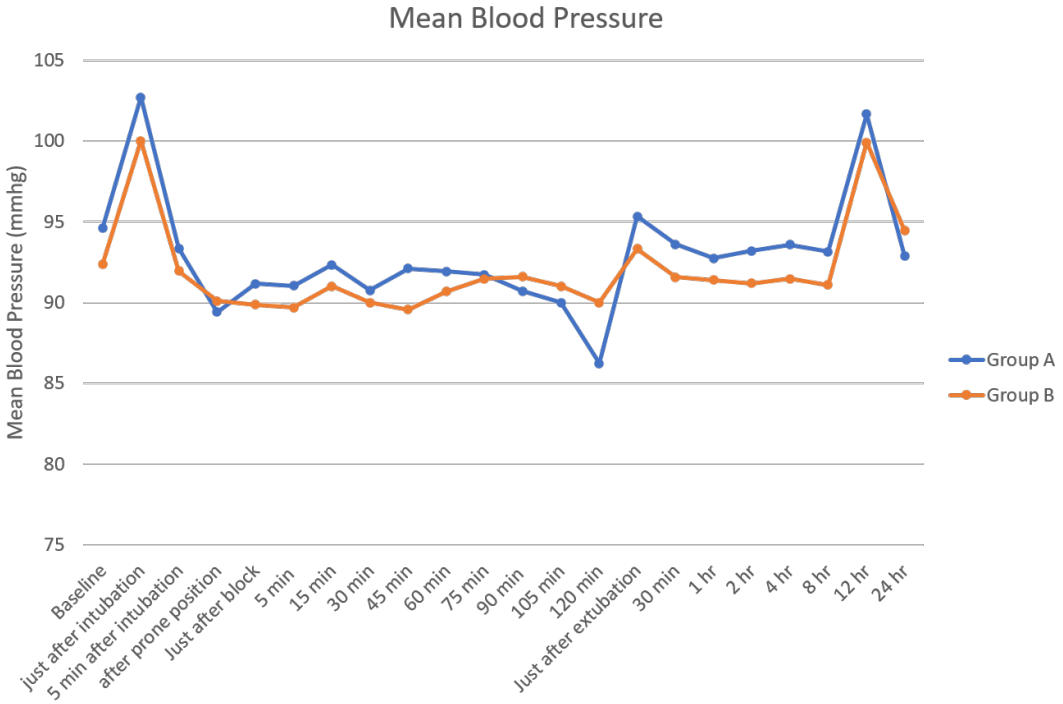

Figure 3: Comparison of mean arterial pressure (mmHg) at different time intervals between the groups from baseline (student's t-test used)

Figure 4 depicts postoperative VAS at different time points. Postoperatively, VAS was found to be significantly lower ($p < 0.001$) in Group B than in Group A. The mean duration of postoperative analgesia was higher in Group B (mean ± SD = 23.69 ± 2.01) than in Group A (mean ± SD = 15.06 ± 1.72), which was found to be statistically significant ($p < 0.001$; Figure 5).

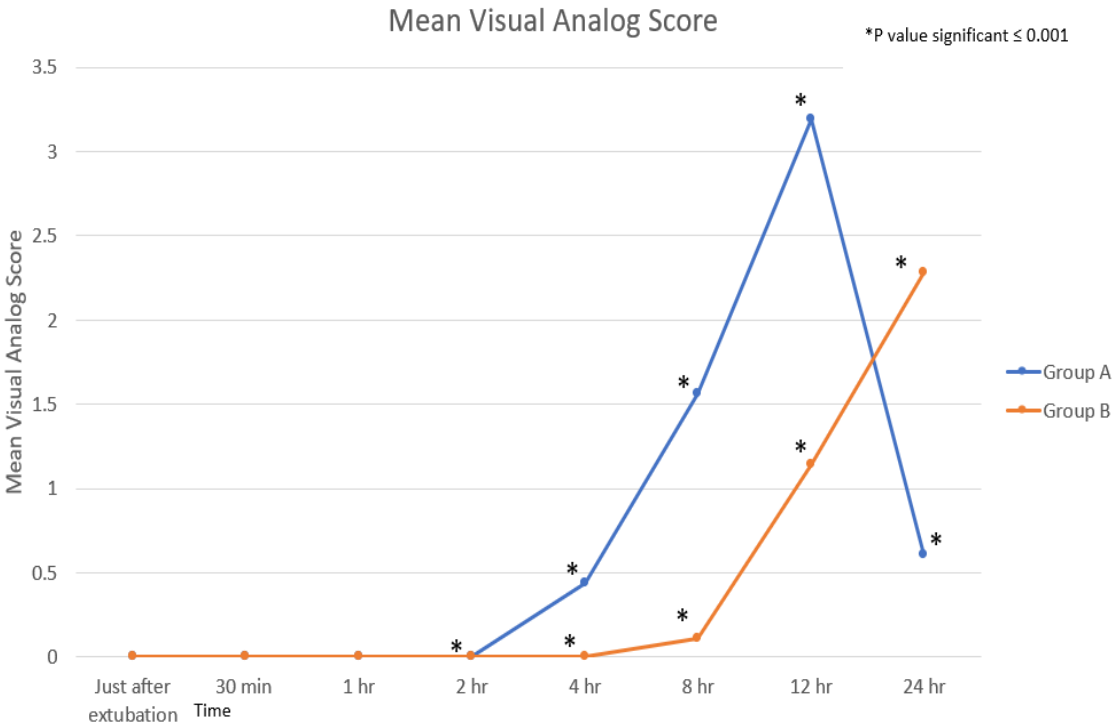

Figure 4: Comparison of VAS (visual analog score) postoperatively at different time intervals between the groups (student's t-test used)

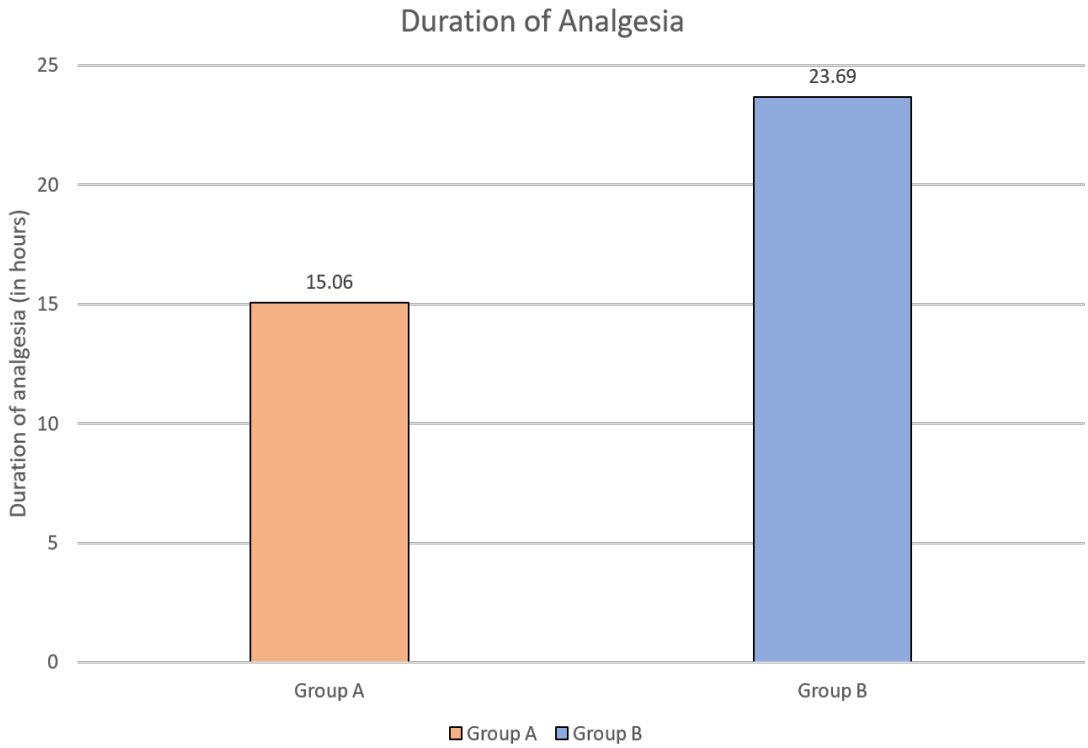

Figure 5: Comparison of mean duration of analgesia between the groups (student's t-test used)

No statistically significant difference was observed between the groups in the postoperative period with respect to sedation score. No statistically significant side effects or complications (e.g., nausea, vomiting, hypotension, bradycardia, or respiratory difficulty) were found in either study groups.

Discussion

Postoperative pain following spine surgery is an acute pain that starts with surgical stress due to systemic inflammation and irritation of afferent neuronal damage [5]. The pain is severe and intense and lasts for one week after surgery. The severity of postoperative pain is directly proportional to the number of vertebrae involved in the surgery.

Adequate postoperative pain control is associated with better patient satisfaction, reduced postoperative opioid requirement, briefer duration of stay in the hospital, and therefore lower costs [6]. Selection of the most appropriate analgesia for postoperative pain of spine surgery poses a challenge to anesthesiologists due to specific indications and contraindications to individual drugs as well as side effects. The neuraxial analgesia technique may be used for effective pain relief and is superior to systemic opioids [7]. Moreover, pain relief with neuraxial block promotes earlier mobilization and better wound healing [7], [8], [9]. Caudal epidural block is a reliable and safe regional analgesic technique for lumbar spine surgeries that is usually given along with general anesthesia. Among the local anesthetics, ropivacaine is the agent of choice given its extended duration of action, safety, and preferential blockade of sensory nerve fibers [10]. The addition of adjuvants, such as epinephrine, ketamine, opioids (morphine, fentanyl, and buprenorphine), midazolam, tramadol, and α-2 agonists, extends the duration of caudal analgesia [11], [12], [13]. However, opioids have more side effects, such as delayed respiratory depression, nausea, vomiting, and constipation. Ketamine prolongs the median duration of postoperative analgesia but is associated with a risk of neurotoxicity, most likely because of the preservative agent (Benzethonium chloride); however, preservative-free ketamine is rarely available [14].

Epinephrine, when used with local anesthetics either intrathecally or locoregionally, extends analgesia and motor block for no more than 60 minutes, but the effect of adding it to the epidural route remains uncertain [15]. According to various studies, midazolam has its dose-dependent analgesic effect through the gamma aminobutyric acid-benzodiazepine (GABA-BZD) system in the spinal cord without any adverse neurological effects; nevertheless, the caudal administration of midazolam remains contentious [14]. Tramadol is an opioid with analgesic potency identical to meperidine without respiratory depression. It has been used in caudal epidurals, but recent literature found no benefit of using caudal epidural tramadol given that it is absorbed systemically and has equal efficacy via the parenteral or caudal route [14]. Although it is an α-2 agonist, clonidine, as an adjuvant, enhances the action of local anesthetic agents for caudal epidural analgesia. The duration of analgesia was increased with epidural clonidine due to the direct inhibition of the spinal cord nociceptive neurons and suppression of nerve transmission in A-delta and C nerve fibers and/or crossing of the blood brain barrier (BBB) and interaction with α-2 adrenergic receptors at supraspinal and spinal sites [16]. Bosenberg et al. compared three doses of ropivacaine in caudal block and observed that 0.2% ropivacaine provides satisfactory postoperative pain relief as compared to 0.1% and 0.3% ropivacaine whereas 0.3 % ropivacaine cause higher motor blockade with minimal improvement in pain relief and 0.1% ropivacaine less effective for analgesia [17]. Sharpe et al. compared the two doses of clonidine 1 and 2 mcg/kg with bupivacaine in caudal block and found no significant advantage of prolonging postoperative analgesia with the higher dose of clonidine (2 µg/kg) [18].

With this background, we compared and evaluated the analgesic efficacy of clonidine (1 µg/kg) as an adjuvant with 0.2% ropivacaine in caudal epidural block in lumbar spine surgery. Demographics such as age; weight; gender; duration of surgery; and hemodynamic variables like HR, SBP, DBP, and MBP were comparable, and no statistically significant differences were found between the study groups. We observed statistically significantly lower VAS and prolonged analgesia with no sedation or side effects among the ropivacaine-clonidine group as compared to the ropivacaine group. The results of our study in terms of hemodynamic variables coincide with the results observed by various authors, including Bajwa et al. [19], Laha et al. [20] Nagappa et al. [1], Mondal et al. [21], and Soni et al. [22].

In our study, we found statistically significantly lower VAS in the postoperative period among the ropivacaine-clonidine group as compared to the ropivacaine group. The first rescue analgesia (VAS ≥ 4) was given to patients of the ropivacaine group at 13–18 hours, whereas the ropivacaine-clonidine group was given it after 20–29 hours, which corresponded with the results of Nagappa et al. [1] and Singh et al. [23]. Thus, the mean duration of analgesia was higher in the ropivacaine-clonidine group (23.69 ± 2.01 hours) as compared to the ropivacaine group (15.06 ± 1.72 hours) ($p < 0.001$).

Similar findings were also observed by Nagappa et al. [1], Solanki et al. [16], Mondal et al. [21], and Soni et al. [22]. Similarly, the effect of caudal clonidine in enhancing postoperative analgesia was observed by Balasubramanian et al. [24], Ivani et al. [25], and De Negri et al. [26]. In our study, a statistically significant difference was not observed for postoperative sedation scores of both groups, which aligns with other studies by Balasubramanian et al. [24], Nagappa et al. [1], Solanki et al. [16], Mondal et al. [21], Soni et al. [22], and Prasad et al. [27]. For both groups, comparable results were observed for side effects (e.g., hypotension, bradycardia, urinary retention, pruritis, postoperative nausea, and vomiting). Nagappa et al. [1], Shukla et al. [28], and Laha et al. [20] reported similar results regarding side effects.

Conclusion

Caudal block with an injection clonidine 1 µg/kg added to 0.2% ropivacaine provide longer postoperative pain relief, lower VAS with good hemodynamic stability, and no significant side effects or sedation as compared to alone 0.2% ropivacaine. This finding suggests that clonidine is an effective adjuvant to 0.2% ropivacaine in caudal epidural block in lumber spine surgery.

Limitations

As a single-center study with a small sample size (n = 36), our results could not be validated and is inconclusive. In future, multicentric and large sample-size studies might be required to prove the hypothesis.

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