MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.7.154.159

OPEN ACCESS

Key Words
A2 agonist, bupivacaine, clonidine, dexmedetomidine, spinal anaesthesia

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Received: 13 May 2024
Accepted: 10 June 2024
Published: 11 June 2024

Citation: D. Preethi Fatima, Sneha Susan Koshy, Saranya and C.M. Ragashree, 2024. Comparison Between Intravenous Dexmedetomidine and Clonidine as Adjuvants to Bupivacaine Spinal Anaesthesia. Res. J. Med. Sci., 18: 154-159, doi: 10.36478/makrjms.2024.7.154.159

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Comparison Between Intravenous Dexmedetomidine and Clonidine as Adjuvants to Bupivacaine Spinal Anaesthesia

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Abstract
Regional anesthesia is preferred as it keeps patients awake, maintains airway reflexes, provides cardiovascular stability but has a discomfort of puncture site pain and recollection of surgery. Recently, there has been interest in inclusion of Intravenous Clonidine and Dexmedetomidine as adjuvants, to overcome patient's discomfort. To compare the effects of intravenous Dexmedetomidine or Clonidine as adjuvants during bupivacaine spinal anaesthesia. A prospective, randomized trial was carried on 80 patients scheduled for elective surgeries under spinal anesthesia, forty in each group. Group A received 1 µg/kg of Dexmedetomidine with an infusion rate of 0.5 µg/kg/h, whereas Group B received 1 µg/kg of Clonidine with an infusion rate of 1 µg/kg/h. Maintenance infusion was administered after Subarachnoid block, following a loading dose that lasted for ten minutes. Patients were tested for time required to reach target sedation, analgesia, sensory and motor blockade. Additionally, the visual analogue score, side effects and hemodynamic parameters were noted and analyzed. Dexmedetomidine has significantly high sedation score, increased duration of sensory block-412.88±10.19mins, motor block-358.61±9.11mins, extended postoperative analgesia -488.05±12.27mins compared to Clonidine 283.51±11.42mins, 217.32±8.56mins and 372.67±13.22mins respectively. When compared, the groups receiving Clonidine and Dexmedetomidine, it was observed that the VAS scores of the former group were much lower. Premeditation with intravenous Dexmedetomidine was superior to intravenous Clonidine in terms of providing early sensory and motor block, extended postoperative analgesia and adequate sedation.

INTRODUCTION

The administration of spinal anesthesia is thought to be a very simple regional anesthetic technique[1]. The safe application of spinal anesthesia involves numerous critical actions, such as the patient's meticulous selection and preparation, precise identification and retrieval of the cerebrospinal fluid (CSF), administration of appropriate anesthetic drugs and adjuvants, efficient handling of physiological side effects and ongoing patient monitoring during the procedure and early post-operative phase[2].

Spinal blocks are widely used due to two main reasons: one is because they have well-defined termination sites and anesthesiologists can continuously administer them with one injection[3]. A wide range of local anesthetics and additives contribute to spinal anesthesia's adaptability by allowing you to control the extent, onset time and duration of the anesthetic. The dispersion of local anesthetic solutions across the subarachnoid region determines the extent of neuronal blockage caused by spinal anaesthesia[4].

The use of hyperbaric bupivacaine with a concentration of 0.5% in spinal anesthesia is commonly recommended. Spinal anesthesia frequently involves the use of bupivacaine, a popular local anesthetic with a relatively short half-life. Several adjuvants have been used intrathecally in conjunction with local anesthetics to improve intra operative analgesia and prolong its duration during the recovery period[5].

The addition of clonidine and dexmedetomidine to local anesthetics supplied via intrathecal, epidural, caudal, and peripheral nerve blocks is a frequent practice in regional anesthesia delivered via intravenous injection. Injecting alpha-2 adrenergic agonists concurrently with local anesthetics enhances the nerve block property of the former via either local vasoconstriction and C fiber blockade facilitation, or spinal action resulting from simple diffusion along the nerve or retrograde axonal transport[6].

Clonidine is an imidazole substance that selectively binds to α2 receptors in the alpha-adrenergic system. According to studies, clonidine causes analgesia by suppressing the release of C-fiber transmitters and causing postsynaptic dorsal horn neurons to become hyper polarized. Motor block may be prolonged if clonidine binds to dorsal horn motor neurons. Blood pressure is complexly affected by clonidine when administered systemically or by neuraxial injection. By directly suppressing sympathetic pre-synaptic α2 adrenoceptor neurons in the spinal cord and activating postsynaptic α2 adrenoceptors in the brain stem, it causes hypotension[7].

Dexmedetomidine is a pharmacologically active d-isomer of medetomidine that is selective to the α2 adrenergic receptor and belongs to the second generation. Selective α2 adrenoreceptor agonist action is exhibited by dexmedetomidine, especially for the 2A receptor subtype. Because of this, it can be used as an analgesic at lower dosages than clonidine, which needs greater dosages. Furthermore, the negative cardiovascular consequences linked to a1-receptor activation are absent with dexmedetomidine[8,9].

Clonidine and dexmedetomidine are α-2 adrenergic agonists with some α-1 agonist activity. Compared to clonidine, dexmedetomidine exhibits an approximately eight to ten-fold higher selectivity at α2 receptors[9]. Several investigations have been carried out to validate the efficacy of these adjuvants in isolation. Few studies have been conducted on the intrathecal administration of clonidine and dexmedetomidine in combination with bupivacaine.

Aims and Objectives: To compare the effects of intravenous dexmedetomidine or clonidine as adjuvants during bupivacaine spinal anaesthesia

MATERIALS AND METHODS

A prospective, randomized study was conducted in Department of Anaesthesia, Sree Mookambika Institute of Medical Sciences, Kulasekharam for a period of 8 months from June 2023 to February 2024. The study comprised eighty patients scheduled for elective lower limb and abdominal surgery under spinal anesthesia who were in physical status I and II according to the American Society of Anesthesiologists (ASA). The study excluded patients with uncontrolled diabetes mellitus, heart disease, systemic hypertension, chronic obstructive airway disease (COPD), hepatic and/or kidney disease, psychological disorders, spinal deformities, conditions contraindicating subarachnoid anesthesia, pregnant or lactating women, individuals on adreno receptor agonist or antagonist therapy and patients who were unwilling to participate.

Following a random assignment of patients into two groups (n = 40), each group received intravenous administration of the following medications: Dexmedetomidine group, or Group A: An intravenous loading dosage of 1 µg/kg dexmedetomidine diluted to 20 ml with normal saline was administered over a 10-minute period prior to Sub-Arachnoid block (SAB), with a subsequent maintenance dose of 0.5 µg/kg/h. Group B (Clonidine group) received an intravenous dosage of 1 µg/kg diluted to 20ml with normal saline and administered over 10 minutes prior to SAB, followed by a maintenance dose of 1 µg/kg/hour. The study medication solutions were given to the attending anesthesiologist, who performed the SAB procedure but was uninformed regarding the group allocation.

A valid and informed written consent was obtained from each patient following a preoperative examination. Peripheral venous cannulation using 18-gauge (G) venflon was performed after the patient

was admitted to the operating room. Vital signs were recorded and all of the standard sub-arachnoid block monitors were fitted.

For the first ten minutes, a 20ml drug solution according to the study group (loading dose: 1 µg/kg of clonidine or dexmedetomidine) was injected. After the loading dosage, 15mg of 0.5% heavy bupivacaine was administered after aspirating clear cerebrospinal fluid, and SAB was carried out in a sitting position at the L3-L4 level while adhering to all aseptic precautions. A typical midline approach was used and a 25 G Quincke spinal needle was used. Following SAB, the patient was placed in a supine position and an infusion pump was used to start the maintenance dose according to protocol for the study group. Throughout the process, additional oxygen was administered via a face mask at a rate of 5 L/min. Surgeons were permitted to begin surgery once sensory block reached level T8.

The sensory level was assessed using the bilateral sterile pin-prick method and the motor blockage was evaluated using a modified Bromage scale (5 grades: 0: No paralysis, 1: Unable to raise extended leg, 2: Unable to flex knee, 3: Unable to flex ankle). Up to six hours after surgery, sensory and motor block assessments were made every minute for the first ten minutes and then every thirty minutes after that. The duration of the blockade, the frequency and need for postoperative analgesics, the onset of analgesia, intraoperative hemodynamic changes every 30 minutes, and sedation were monitored in both studies. The sensory and motor block was evaluated every minute for the first ten minutes following surgery, and then every thirty minutes for the next six hours. The duration of sensory block has been defined as the time it took for the sensory block to regress to the S1 dermatomal level. The time taken by the block to regress to Bromage scale 0 was used to define the motor block duration. From the moment of the sub-arachnoid block, all durations were recorded.

The study drug infusion was discontinued around five minutes before the completion of the surgery. The patients were moved to the post-anesthesia care unit (PACU) following surgery. Every 30 minutes for six hours, an anesthesiologist blind to the group assignment recorded the pain score in the PACU using the Visual Analogue Scale (0 = No discomfort, 10 = Worst agonizing pain). Intravenous diclofenac 75 mg was administered as a rescue analgesic to patients with a VAS score greater than 3.

The SPSS 20.0 trial version was used to statistically analyze the gathered data. The range, mean and standard deviations of the results were displayed. ANOVA was used as a one-way analysis of variance to compare normally distributed continuous variables among the groups. The chi-square or Fisher's exact test can be used to compare nominal categorical data between research groups. A 'p' value of less than 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSIONS

The demographic data, ASA grade, were comparable between the two groups. Basic characteristics such as age, gender, height and weight were not significantly significant between both groups. (Table 1).

Intravenous dexmedetomidine, as opposed to clonidine, also produced an earlier degree of sensory and motor block during bupivacaine spinal anaesthesia. ($p<0.05$). When comparing Group- A to Group B, the mean duration of sensory block and motor block was higher in the former. ($p = 0.001$). Moreover, those who got dexmedetomidine had a longer period of effective analgesia. ($p = 0.001$) (Table 2).

At 30 and 60 minutes, the clonidine group significantly exhibited lower mean blood pressure(MAP) and heart rate (HR) than the dexmedetomidine group (p-value<0.05). (Table 3).

The clonidine group had a significantly lower systolic blood pressure(SBP) at 60 minutes compared to the dexmedetomidine group (p-value of 0.03). The rest of the period exhibited no difference in the SBP of the two group. With the exception of the intervals of 5, 10 and 60 minutes, there are no statistically significant differences ($p>0.05$) in the diastolic blood pressures(DBP) between the two groups. In these cases, the SBP of the clonidine group was considerably lower than that of the dexmedetomidine group ($p<0.05$). (Table 4).

The group receiving dexmedetomidine during the third, fifth and sixth hours demonstrated significantly lower Visual Analogue Scale (VAS) scores than the group receiving clonidine. It was found that there were statistically significant differences in the VAS scores between the two groups, with p-values of 0.001, 0.021 and 0.006, respectively. (Table 5).

Patients receiving intrathecal clonidine were significantly more likely to experience side symptoms, such as bradycardia and hypotension. In the clonidine group, hypotension was noted in 4 (10%) of the patients, while in the dexmedetomidine group, no patients had this adverse effect ($p<0.001$). Similarly, bardycardia was noted in 5 (12.5%) of the clonidine group patients, but not in any of the dexmedetomidine group patients. ($p<0.001$).

Postoperative analgesia requires the use of therapies with a long duration, maximum efficacy and low side effects. Hyperbaric bupivacaine 0.5% is the most widely used local anesthetic for spinal anesthesia. However, it has a limited duration of analgesic effects following surgery[10].

The most common class of analgesics, opioids are frequently employed as the mainstay of treatment for

Table 1: Demographic and clinical Characteristics of Study Participants

Variable	Dexmedetomidine group (n = 40)	Clonidine group(n = 40)	p-value
Age (years)	38.23±5.1	37.62±4.9	0.402
Gender (M/F)	28/12	31/9	0.253
Height (cm)	159.3±4.9	161.5±4.3	0.278
Weight (kg)	69.1±6.7	72.5±5.7	0.651
BMI (kg/m2)	28.3±3.7	29.8±4.1	0.137
ASA score, I/II	36/4	32/8	0.479
Surgical duration (min)	75.00±11.13	71.99±14.26	0.812

Table 2: Comparison of Sensory Block and Motor Block among both groups

Variable	Dexmedetomidine group (n = 40)	Clonidine group(n = 40)	p value
Onset of sensory block (secs)	105.32±9.17	133.56±10.05	0.005
Onset of motor block (secs)	120.57±8.17	145.33±9.22	0.042
Duration of sensory block (mins)	412.88±10.19	283.51±11.42	0.001
Duration of motor block (mins)	358.61±9.11	217.32±8.56	0.001
Duration of effective analgesia (mins)	488.05±12.27	372.67±13.22	0.001

Table 3: Comparison of HR and MBP among study participants at different intervals

Variable	HR			MBP		
	Group A (n = 40)	Group B (n = 40)	p value	Group A (n = 40)	Group B (n = 40)	p-value
Base line	82.31±4.12	81.71±4.08	0.271	95.32±4.54	93.45±4.02	0.314
5 min	79.56±4.88	78.64±4.65	0.174	88.25±3.56	87.25±3.59	0.111
10 min	75.26±4.03	73.44±3.65	0.211	86.32±3.16	84.24±3.57	0.287
30 min	70.25±4.27	67.13±4.05	0.001*	78.66±3.68	74.33±3.65	0.041*
60 min	72.14±4.62	68.54±4.12	0.011*	80.52±3.44	76.58±3.48	0.001*
120 min	71.98±3.49	71.74±3.69	0.205	82.15±3.06	80.87±2.99	0.207
180 min	76.22±3.15	75.28±3.84	0.254	84.05±2.74	83.73±3.01	0.264

Table 4: Comparison of SBP and DBP among study participants at different intervals

Variable	SBP			DBP		
	Group A (n=40)	Group B (n=40)	p value	Group A (n = 40)	Group B (n = 40)	p-value
Base line	122.17±3.24	12152±4.25	0.142	80.22±3.25	79.09±4.02	0.288
5 min	118.11±3.51	115.14±3.47	0.106	78.34±3.17	75.21±3.25	0.017*
10 min	113.02±3.12	110.45±3.22	0.371	72.47±3.08	70.18±3.33	0.045*
30 min	104.65±3.63	98.74±3.58	0.232	63.26±3.65	62.66±3.82	0.051
60 min	107.87±3.89	101.88±3.07	0.031*	67.88±3.09	60.37±3.95	0.001*
120 min	109.58±3.05	107.29±3.16	0.211	69.05±2.94	67.32±3.21	0.310
180 min	111.97±2.67	110.08±2.49	0.172	69.73±2.99	69.04±2.78	0.122

Table 5: Comparison of VAS score among both groups

VAS Score	Dexmedetomidine group	Clonidine group	p-value
2 hours	0.0±0.0	0.0±0.0	0.000
3 hours	1.35±0.25	2.28±0.31	0.001*
4 hours	2.65±0.43	2.79±0.72	0.287
5 hours	3.14±0.51	3.87±0.77	0.021*
6 hours	4.27±0.48	4.91±0.39	0.006*

managing pain following surgery. However, it should be noted that this approach may cause respiratory depression, pruritus, vomiting, nausea and urinary retention. Better adjuvants were therefore required in order to potentially prolong the duration of analgesia while reducing the previously noted negative effects of opioids[11].

Intrathecal α2-agonists have been shown to have anti-nociceptive effects on both visceral and somatic pain. For this reason, these drugs are added to bupivacaine to achieve spinal anaesthesia. The purpose of this study was to determine the effects of dexmedetomidine and clonidine on analgesia duration, sensory and motor onset, regression of sensory and motor and side effects.

The current study revealed that, in comparison to the clonidine group, the dexmedetomidine group experienced an earlier onset of sensory and motor block. Furthermore, in comparison to the clonidine group, the duration of the motor and sensory block was significantly longer in the dexmedetomidine group. Statistically significant difference was observed in the findings. ($p<0.05$).

In the study conducted by Patil KN[12]. Dexmedetomidine (231.20+24.84 min) and clonidine (200+23.67 min) significantly extended the duration of sensory block compared to placebo (171+12.25 min) ($p<0.001$). Motor block duration was 180.40+24.70 min with clonidine, 205.20+25.56 min with dexmedetomidine and 135.20+12.87 min with placebo ($p<0.001$). This was similar to the current study.

Dalwadi JM[13] also carried out a study to evaluate intrathecal clonidine and dexmedetomidine as adjunctive medications to bupivacaine for the purpose of enhancing intra operative and postoperative pain management and preserving steady hemodynamics. In comparison to the clonidine group, the mean duration of analgesia was higher in the dexmedetomidine group. The study found that intravenous dexmedetomidine infusion was superior to intravenous

clonidine because it extends analgesia as well as motor blockade following bupivacaine spinal anesthesia and offers an earlier onset of sufficient sedation.

Singh AN[14] also observed that the onset of motor blockage is faster with dexmedetomidine than with clonidine. The duration of post-operative analgesia was longer in the dexmedetomidine group (250.46±52.10 minutes) compared to the clonidine group (180.56±50.28 minutes).

During most of the duration between the two groups under examination, there were no significant changes observed in hemodynamic measures such as HR, MBP, SBP and DBP. Comparing the clonidine group to the dexmedetomidine group, the clonidine group has considerably reduced SBP, DBP and MBP. The SBP of the clonidine group was much lower than that of the dexmedetomidine group ($p<0.05$), as reported by Mir WK[15].

The present study revealed that there were statistically significant variations in the VAS scores between the two groups, with p-values of 0.001, 0.021 and 0.006, respectively. The study by Mir WK[15]. found that in the 3rd, 5th and 6th hours, the VAS scores were considerably lower in the group receiving dexmedetomidine compared to the group receiving clonidine, with p-values of 0.001, 0.01 and 0.006, respectively.

Patients receiving intrathecal clonidine were significantly more likely to experience side symptoms, such as bardycardia and hypotension. According to a study by Basumatary K[16] intravenous dexmedetomidine 0.5 µg/kg is superior to clonidine 0.5 µg/kg in controlling post-spinal anesthesia shivering during caesarean section due to its early onset of effect, higher response rate without recurrence, good sedation, stable cardiorespiratory function and favorable neonatal outcome.

CONCLUSIONS

When combined with spinal bupivacaine during surgical procedures, the administration of dexmedetomidine appears to offer a strong substitute for clonidine. When used in conjunction with bupivacaine spinal anesthesia, intravenous dexmedetomidine infusion is superior to intravenous clonidine because it prolongs analgesia and motor blocking and offers an earlier start of sufficient sedation. This method gives good postoperative analgesia, minimalizes side effects, maintains stable hemodynamic conditions and provides high-quality intra operative analgesia.

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