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Original Research Article

Effects of Intravenous Dexmedetomidine on the Quality of Subarachnoid Block with Hyperbaric Intrathecal Bupivacaine for Lower Limb Surgery: A Randomized Study

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Conflict of interest: Nil

Abstract:

Background: The present study has been conducted to evaluate the intraoperative and postoperative effects of intravenous dexmedetomidine as an adjuvant on the characteristics of bupivacaine spinal anaesthesia in lower limb surgeries.

Materials and Methods: One hundred subjects of ASA Grade I and II of either sex undergoing elective lower limb surgery under spinal anaesthesia were randomized into two groups of 50 each. Dexmedetomidine group (Group D) received 3ml (15mg) 0.5% Heavy Bupivacaine via subarachnoid block with intravenous dexmedetomidine at 0.5 mcg/kg bolus over 10 minutes, then maintenance infusion at 0.5 mcg/kg/hr and control group (Group C) received 3ml (15 mg) 0.5% Bupivacaine Heavy via subarachnoid block with normal saline of equivalent amount as bolus and maintenance infusion. Along with demographic parameters, block characteristics, haemodynamic parameters, intraoperative sedation score and perioperative complications were assessed and compared between the two groups.

Results: Onset of sensory and motor blocks did not differ significantly between the groups. Time for sensory regression to S1, time for motor recovery and time to rescue analgesia was significantly prolonged in Group D. The mean intraoperative heart rate of the patients of Group D was significantly lower than that of Group C from 5 minutes after subarachnoid block till the end of surgery but the mean arterial pressure and respiratory rate were comparable. The intraoperative sedation score was significantly higher in Group D. No significant difference in perioperative complications were seen between the groups.

Conclusion: Intravenous dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine spinal anaesthesia and provides excellent intraoperative sedation and postoperative analgesia in patients undergoing lower limb surgeries.

Keywords: Dexmedetomidine, Spinal Anesthesia, Adjuvants.

Introduction

Central neuraxial blocks are routinely administered for lower limb surgeries. Subarachnoid block (SAB) with hyperbaric bupivacaine is preferred as it has rapid onset, deep block, cost-effective and easy to administer. The duration of analgesia is limited with spinal anaesthesia as Bupivacaine is appropriate for procedures lasting 2 to 2.5 hours only. [1] If the duration of surgery is prolonged, it may have to be converted into general anaesthesia or supplemented with an intravenous anaesthetic agent. Postoperative pain control is also a major concern because spinal anaesthesia using only local anaesthetics is associated with a relatively shorter duration of action, and thus an early analgesic intervention is needed in the postoperative period. Therefore, many adjuvants were introduced either intravenously or intrathecally to prolong the analgesic duration and decrease the potential side effects by reducing the dose of local anaesthetics. [2,3] Dexmedetomidine is a highly selective α2-adrenoceptor agonist recently introduced to anesthesia1. It causes sedation and analgesia in a dose-dependent manner without causing respiratory depression. [4,5] It was primarily used for

intravenous sedation.[6] Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective α2-adrenoceptor agonism. The molecular mechanism of the analgesic action of α2-agonists is through activation of inwardly rectifying G1-protein-gated potassium channels, resulting in membrane hyperpolarization, thus decreasing the firing rate of excitable cells in the central nervous system. In addition, α2-agonists inhibit neurotransmitter release through reduction in calcium conduction into the cell.[7] These two mechanisms represent two very different ways of affecting analgesia: first, by preventing the nerve from firing, and second, by inhibiting propagation of the signal to its neighbour. Dexmedetomidine administered as an adjuvant drug to local anaesthetics via the intrathecal route provided analgesic relief in postoperative pain without sedation, but it also caused bradycardia and hypotension. To overcome these problems, it may be used intravenously (either bolus or continuous infusion or both) as an adjuvant, in order to position the patient with minimum or no pain, attenuate stress responses and to prolong the duration of postoperative analgesia.[8]

Thus, the present study is designed to evaluate the effect of intravenous Dexmedetomidine as an adjuvant on the characteristics of bupivacaine spinal anaesthesia in lower limb surgeries.

Materials and Methods:

Sampling

After obtaining approval from the institutional ethics committee and written informed consent from the patients, 100 patients from 18 to 65 years of age and ASA Grade I and II of either sex scheduled for lower limb surgeries under spinal anaesthesia were included in the study. Sample size of 50 in each group was estimated using nMaster software based on the study by Al-Mustafa et al.[9] who concluded that intravenous dexmedetomidine prolongs bupivacaine spinal analgesia, considering the sensory regression time to S1 segment in dexmedetomidine group (261.5 ± 34.8 min) and control group (165.2 ± 31.5 min). The precision considered was α-error as 5%, β-error as 10%, and minimum expected difference (clinically significant difference) as 20 min.

Patients were assigned in two groups of the study with the help of computer generated random numbers. Unwilling patients, patients allergic to dexmedetomidine, patients with significant cardiovascular, pulmonary, hepatic or renal impairment, pregnant patients, obese patients (BMI more than 30 kg/m2), patients on β-blocker and Ca2+ channel blocker, patients with contraindications for regional anesthesia including coagulopathy, or local skin infection, patients preferring general anesthesia, prolonged surgery (lasting for over 2 hours) were excluded from the study.

Blinding

A two operator technique was used to maintain blinding. Principal investigator who was supposed to give the block waited outside the operation room (OR). Inside the OR the 2nd physician prepared the drugs in 2 similar syringes of 5ml each for drawing local anaesthetics for subarachnoid block and in another 50 ml syringe normal saline or dexmedetomidine was loaded. After preparing, 2nd physician left the OR. The principal investigator then entered the room and performed the block and made the sensory and motor tests to confirm block success. The patients were unaware of whether receiving intravenous NS or Dexmedetomidine with local anaesthetic in subarachnoid block. A third physician not involved in the study did the data collection.

Procedure

Patients were examined properly for a preoperative counselling. Anaesthesia technique to be performed was also explained to patients at our indoor pre-anaesthesia clinic. A detailed history was obtained from every patient regarding any trauma to head, drug allergy, unconsciousness, seizure, bleeding disorder, any previous surgery, symptoms of breathlessness, asthmatic attack and prolonged medication. Functional status was also assessed. Heart rate, blood pressure, anaemia, jaundice, cyanosis, clubbing, oedema were noted. Assessment of airway was done to anticipate any difficulty in intubation. Examination of the back for any anatomical abnormality or any localized infection was done. Routine investigations were carried out in all patients as per our institutional protocol. These included: complete blood count, urea and serum creatinine, fasting blood sugar, coagulation profile, 12 lead ECG, chest X-ray PA view. Evening before surgery, the patient was explained about the study and they were asked about their willingness to participate in their study. If they agreed to take part, informed consent was taken. The Visual Analog Scale of Pain was explained to them. Solid food was given 6 hours prior to surgery and clear fluid was given 2 hours prior to surgery.

At the operation theatre all the standard base line monitors eg. Non-invasive blood pressure monitor (NIBP), peripheral oxygen saturation monitor (SpO2), electrocardiography monitor (ECG) were attached. The baseline values of blood pressure (systolic blood pressure, diastolic blood pressure and mean arterial pressure), pulse rate, SpO2 and electrocardiography were obtained. Intravenous

access was done with 18G IV cannula and the patients were pre-loaded with 10 ml/kg of lactated Ringer's solution/normal saline. Spinal anaesthesia was given in the midline approach maintaining full asepsis. L3-L4 or L4-L5 intervertebral space was located, skin infiltrated with Lignocaine (2%). Spinal Needle of 25G (Quincke's or Whitacre) was inserted and 3ml of 0.5% Bupivacaine heavy (15mg) was given.

Dexmedetomidine group (Group D) received 3ml (15mg) 0.5% Heavy Bupivacaine via subarachnoid block with intravenous dexmedetomidine at 0.5 mcg/kg bolus over 10 minutes, then maintenance infusion at 0.5 mcg/kg/hr and control group (Group C) received 3ml (15 mg) 0.5% Bupivacaine Heavy via subarachnoid block with normal saline of equivalent amount as bolus and maintenance infusion.

Sensory blockade was evaluated by testing the loss of pinprick sensation with a blunt 25-gauge needle and the time taken for the highest level of sensory blockade, two-dermatomal regression from the maximum level, and regression to S1 level was noted. Motor blockade was assessed by modified Bromage scale (modified Bromage 0, the patient is able to move the hip, knee, and ankle; modified Bromage 1, the patient is unable to move the hip, but is able to move the knee and ankle; modified Bromage 2, the patient is unable to move the hip and knee, but is able to move the ankle; and modified Bromage 3, the patient is unable to move the hip, knee, and ankle).[10,11] Both sensory and motor blocks were assessed at regular intervals from the administration of the block till adequate sensory and motor block was achieved.

Post operatively the blocks were assessed 30, 60 90 and 120 minutes and then hourly, until the regression of the block. Onset of sensory block was defined as the time interval in minutes from Min_1 (after administration of the local anaesthetic) till the sensory block is complete. Duration of sensory block/duration of analgesia was assessed by VAS score and defined as the time interval in minutes from Min_1 (after administration of SAB) till the VAS score >4. Onset time of motor block was defined as the time interval in minutes from Min_1 (after administration of local anaesthetic) till MBS Grade 2. Duration of motor block was defined as the time to the recovery of complete motor function of the lower limbs after administration of the block.

Intraoperatively, level of sedation was assessed according to the Modified Ramsay Sedation Scale (RSS) [12] from 1-6 (1 = anxious and agitated; 2 = cooperative and tranquil; 3 = drowsy but responsive to verbal commands; 4 = asleep but briskly responsive to tactile stimulation; 5 = asleep and sluggish responses to stimuli; 6 = asleep and no response). Excessive sedation was defined as score greater than 4/6.

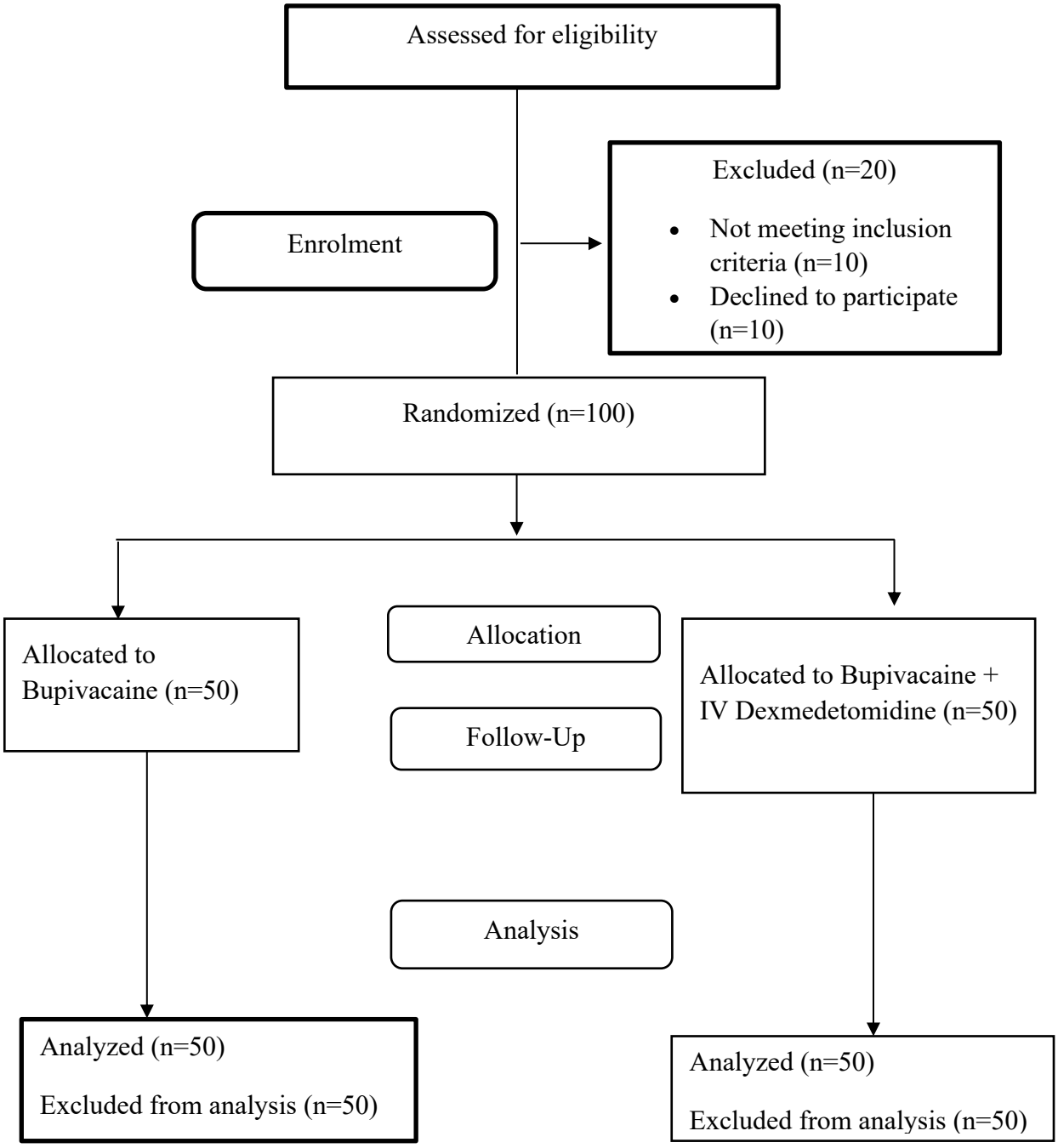
Adverse effects comprised hypotension (20% decrease in MAP relative to baseline), bradycardia (HR<50 beats/ min), nausea, vomiting and hypoxemia (SpO2<90%).IN case of hypotension, injection Phenylephrine 0.2 mg single dose IV bolus was administered; in case of bradycardia, injection Atropine 0.5 mg IV was administered; in case of nausea/ vomiting, injection Ondansetron 4 mg slow IV was administered.

Post-operative pain was assessed using Visual Analogue Scale (VAS). Monitoring of haemodynamic parameters continued in post-operative period. Injection Paracetamol 1 gm IV was administered as rescue analgesia when VAS was more than 4.

Statistical analysis

The data was tabulated in Microsoft excel and analysed with SPSS V.24 software. The continuous variables are presented with mean and standard deviation. The categorical variables are presented with frequency and percentage. Independent t test and chi square test are used for the comparisons. The p value ≤ 0.05 is considered as statistically significant.

Consort Flow Diagram



Results:

Demographic characteristics of the patients including age, gender, height, weight, ASA status and BMI of the two groups in the study are shown in Table 1. There were no significant differences between the groups in terms of these characteristics.

Table 2 shows the comparison of the block characteristics between the two groups. Duration of sensory block and motor block was significantly higher in Group D as compared to Group C (p=0.000) Rescue Analgesia time was also significantly prolonged in Group D as compared to Group C (p=0.000) There was no significant difference in the onset of sensory and motor block in the two groups.

The mean intraoperative heart rate of the patients of Group D was significantly lower than that of Group C from 5 minutes after subarachnoid block till the end of surgery but the mean arterial pressure and respiratory rate were comparable (Figure 1-3). The intraoperative sedation score was significantly higher in Group D (Table 3).

No significant difference in perioperative complications were seen between the groups: only 4 patients in the Group C developed hypotension, 3 patients in the Group D developed hypotension and 1 patient in the Group D developed bradycardia.

Table 1: Demographic characteristics

Parameters	Group	N	Mean	SD	P
Age (years)	Group C	50	49.34	13.12	.567
	Group D	50	47.74	14.72	
Sex	Group C	50	Male: 34 (68%); Female: 16 (32%)		0.829
	Group D	50	Male: 35 (70%); Female: 15 (30%)		
ASA	Group C	50	ASA I: 28 (56%); ASA II: 22 (44%)		0.840
	Group D	50	ASA I: 29 (58%); ASA II: 21 (42%)		
Height (cm)	Group C	50	166.48	9.35	.455
	Group D	50	167.80	8.23	
Weight (kg)	Group C	50	65.52	6.92	.739
	Group D	50	65.98	6.86	
BMI	Group C	50	23.90	4.08	.650
	Group D	50	23.57	3.11	

Table 2: Block characteristics

Parameters	Group	N	Mean	SD	P
Onset of sensory block (min)	Group C	50	11.66	2.04	.094
	Group D	50	11.01	1.80	
Onset of motor block (min)	Group C	50	3.28	0.51	.722
	Group D	50	3.24	0.50	
Time for sensory regression to S1 (min)	Group C	50	160.68	5.79	.000*
	Group D	50	213.74	14.93	
Time for motor recovery (min)	Group C	50	186.48	7.04	.000*
	Group D	50	226.24	13.87	
Time to Rescue Analgesia (min)	Group C	50	119.84	4.77	.000*
	Group D	50	194.90	9.77	

*Statistically significant difference exists (p<0.05)

Table 3: Intraoperative sedation scores

Parameter	Group	Score 1	Score 2	Score 3	Score 4	Total	P value
Baseline	Group C	50	0	0	0	50	-
	Group D	50	0	0	0	50	
15 minutes	Group C	23	27	0	0	50	0.000*
	Group D	4	41	5	0	50	
30 minutes	Group C	43	7	0	0	50	0.000*
	Group D	0	15	20	15	50	
45 minutes	Group C	24	26	0	0	50	0.000*
	Group D	0	8	24	18	50	
60 minutes	Group C	23	27	0	0	50	0.000*
	Group D	0	1	24	25	50	
90 minutes	Group C	20	30	0	0	50	0.000*
	Group D	0	0	35	15	50	
120 minutes	Group C	48	2	0	0	50	0.000*
	Group D	19	28	3	0	50	
150 minutes	Group C	50	0	0	0	50	0.007*
	Group D	41	7	2	0	50	

*Statistically significant difference exists (p<0.05)

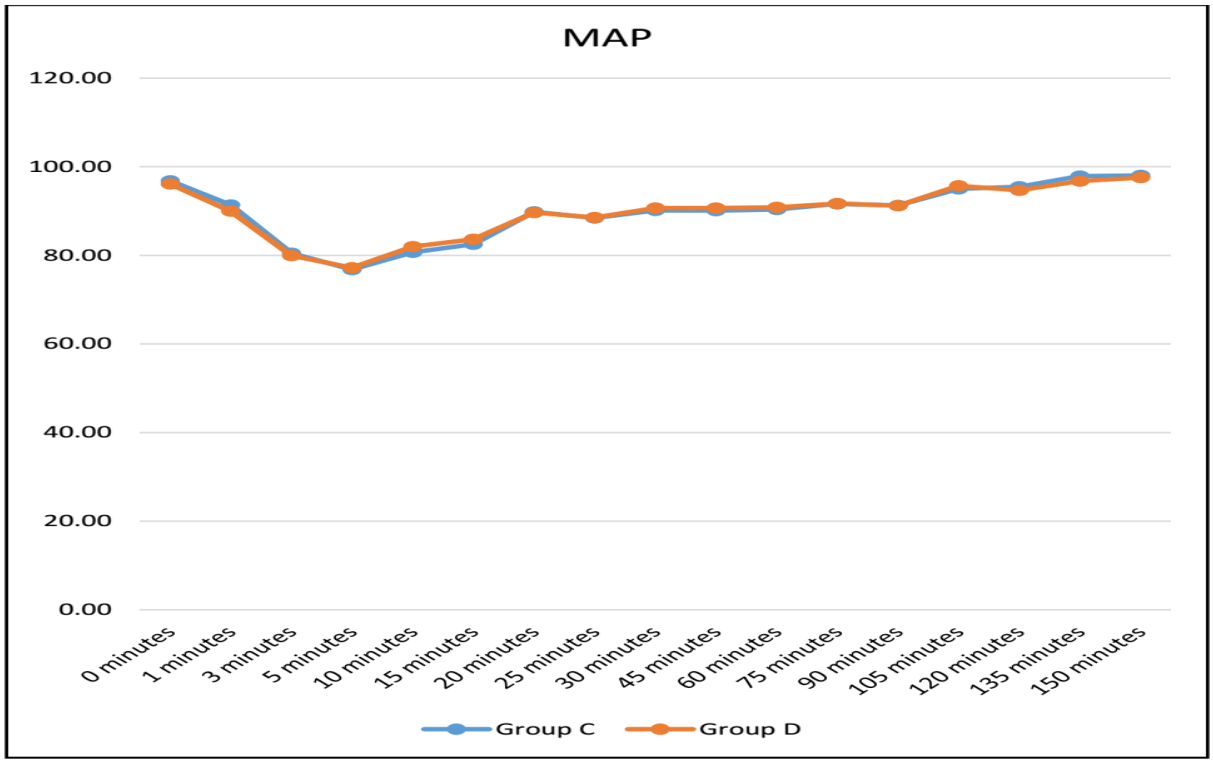


Figure 1: Heart rate at different intervals in the groups

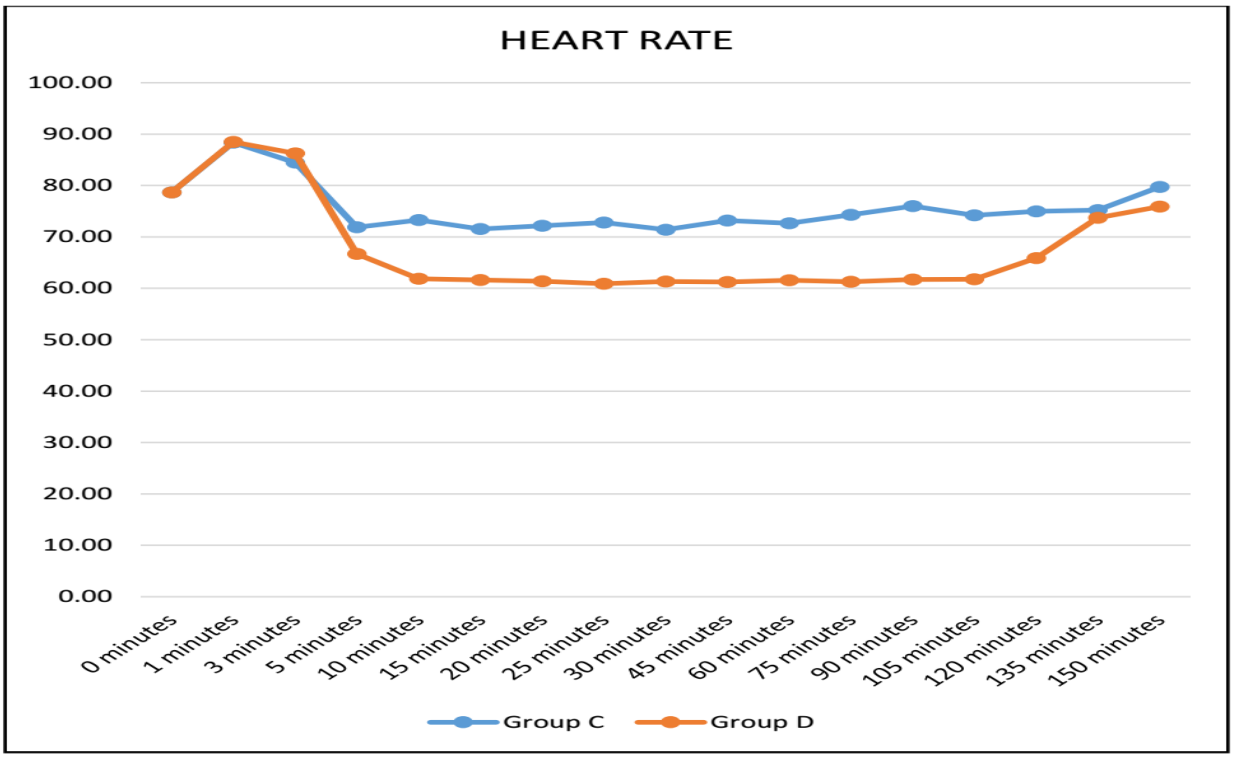


Figure 2: Mean arterial pressure at different intervals in the groups

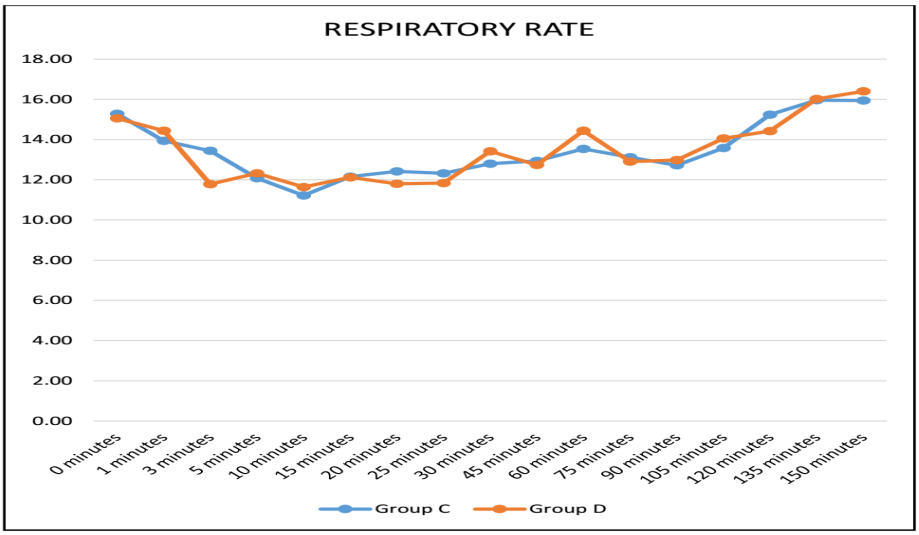


Figure 3: Respiratory rate at different intervals in the groups

Discussion:

Alpha2 agonists have been widely used in intrathecal and intravenous routes as an adjuvant to prolong the effects of spinal anaesthesia. Dexmedetomidine is a suitable adjuvant to spinal anaesthesia as it has more sedative and analgesic effects due to its highly selective alpha 2A receptor agonist activity.[13,14] Systemic and intrathecal injection of Dexmedetomidine produces analgesia by acting at spinal level, laminae VII and VIII of ventral horns. The drug also acts at locus coeruleus and dorsal raphe nucleus to produce sedation and analgesia. This supra spinal action explains the prolongation of spinal anaesthesia after intravenous Dexmedetomidine.[15]

Both the groups in our study showed similar onset of sensory and motor blockade. Previous studies done by Hamed et al [16] compared three groups, group B received NS, group IV received intravenous dexmedetomidine 5 mins after SAB and group IT received intrathecal dexmedetomidine. They found that the time to reach Modified Bromage 3 motor block was significantly shorter in both IV and IT groups than in group B with no statistically significant difference between each other. Harsoor et al [17] who studied the effect of supplementation of low-dose intravenous dexmedetomidine (bolus 0.5 mcg/kg then infusion 0.5 mcg/kg/h before SAB) on characteristics of bupivacaine spinal anaesthesia reported that administration of intravenous dexmedetomidine prolonged the duration of motor block and accelerated the onset of sensory block, but this accelerated motor and sensory block can be attributed to the time as they had initiated infusion 10 mins prior to administration of SAB.

In our study, mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group (213.74 ± 14.93) compared to control group (160.68 ± 5.79) (P value < 0.001). Significant prolongation in mean time for two dermatomal regression of sensory blockade was also reported by Kaya et al [18] (145 + 26 min vs 97 +27 mins; P < 0.001), Tekin et al [19] (148.3 mins vs 122.8 mins; P value < 0.001) in dexmedetomidine and control groups respectively. Similarly Hong et al [20] reported that the mean time to two-segment regression was prolonged in dexmedetomidine group [78 mins vs 39 mins for cold, for dexmedetomidine group and control group respectively. Similar results were reported by Lee et al [21] and Dinesh CN et al [22] who used Dexmedetomidine as 1.0 mcg/kg bolus and 0.5 mcg/kg/hr as infusion.

In the present study the regression time to reach the modified Bromage Scale 0 scale was significantly prolonged in dexmedetomidine group (226.24 ± 13.87) as compared to control group (186.48 ± 7.04). Statistical analysis showed a significant difference with p value of <0.001 indicating a longer duration for regression in Group D patients (P value < 0.001). The results are consistent with that of Al Mustafa et al [9] (199 ± 42.8 min vs. 138.4 ± 31.3 min; P value < 0.05), Whizar-Lugo et al [23] (191±49.8 mins vs 172±36.4), Tekin et al [19] (215 mins vs 190.8 mins; P value < 0.001) for dexmedetomidine group and control group respectively. Elcıcek et al [24] and Hong et al [20] also found that complete resolution of motor blockade was significantly prolonged in dexmedetomidine group. Contrary to all the above studies, Kaya et al [18] reported no significant prolongation in the duration of motor block in dexmedetomidine group compared to control group.

The mean intraoperative heart rate was significantly lower in dexmedetomidine group as compared to control group (P value<0.001). The lowest mean heart rate after subarachnoid block was significantly lower in dexmedetomidine group

as compared to control group (P value < 0.001). No patient in our study had heart rate less than 50 bpm or needed atropine. Similar to our study, the mean heart rate was significantly lower in dexmedetomidine group [as compared to control group at 20 minutes (P value = 0.02) in the study done by Tekin et al [19]. A study by Al Mustafa et al [9] also reported no significant difference in atropine requirement between dexmedetomidine and control groups.

Whizar-Lugo et al [23] reported higher incidence of bradycardia in dexmedetomidne group (32%) compared to control group (20%). Atropine was required in higher proportion of patients in dexmedetomidine group as compared to control group in the present study. Atropine requirement was found to be significantly higher in dexmedetomidine group than in control group in studies by Tekin et al [19] (30% vs. 6.6%) and Hong et al [20] (24.0% vs. 3.8%). No incidence of severe bradycardia requiring atropine recorded in our study can be attributed to lower loading and maintenance dose of dexmedetomidine. There was no significant difference in systolic, diastolic and mean blood pressure variations between the dexmedetomidine and control group in our study.

Previous studies have shown that the hypotensive effect of dexmedetomidine persists in the intraoperative as well as in the postoperative period. Eliceck et al [24] reported significant decrease in mean arterial pressure after 20, 25, and 30 min after dexmedetomidine infusion as compared to control group. Contrary to above studies and consistent to our present study, Al Mustafa et al [9] and Tekin et al [19] reported no significant difference in mean arterial pressures in dexmedetomidine and control groups. Similar to our study, Tekin et al [19] reported no significant difference between groups in the number of patients who received ephedrine to treat hypotension. No significant difference in the incidence of hypotension was reported in dexmedetomidine and control groups in the studies by Al Mustafa et al [9] (0% and 20%) and Whizar-Lugo et al [23] (8% and 4%). In our study intraoperative Ramsay sedation scores were significantly higher in dexmedetomidine group as compared to control group (P value <0.001). However, there was no significant difference in sedation scores between the groups in the postoperative period. Ramsay sedation score was 2 in all patients in control group and ranged from 2-5 in dexmedetomidine group in the study done by Al Mustafa et al [9]. In their study the maximum score was 5 in 12% of patients, 4 in 79% of patients and 3 in 4% of patients. The maximum mean score of sedation (3.96 + 0.55) was attained 30 min after starting dexmedetomidine infusion. Hong et al [20] noted that the median sedation scores during surgery were 4 in the dexmedetomidine group and 2 in the control group (P value < 0.001). A significantly higher average sedation score in the dexmedetomidine group was also reported by others.

Dexmedetomidine inhibits the release of substance P from the dorsal horn of the spinal cord, leading to primary analgesic effects. Dexmedetomidine was found to be effective in providing postoperative analgesia in the present study. The time to first request for postoperative rescue analgesic was significantly prolonged in dexmedetomidine group (194.90 ± 9.77) as compared to control group (119.84 ± 4.77) (P value < 0.001). Similarly, Hong et al [20] noticed that post-operative pain intensity was lower and the mean time to first request for post-operative analgesia was longer in the dexmedetomidine group compared to the control group (6.6 hrs vs. 2.1 hours). Kaya et al [18] in their study observed that dexmedetomidine increased the time to first request for postoperative analgesia (P value < 0.01 compared with midazolam and saline) and decreased analgesic requirements (P value < 0.05). Whizar-Lugo et al [23] in their study noticed that the time to first request for postoperative analgesic in dexmedetomidine group was [220 + 30 mins] significantly prolonged as compared to control group [150 + 20 min] (P value < 0.05). Chan IA et al [25] also demonstrated significant opioid sparing effects with intravenous dexmedetomidine at loading and maintenance dose of 0.5mcg/kg and 0.5 mcg/kg/hr for total knee arthroplasty ((P value = 0.003).

Conclusion

Dexmedetomidine in the loading dose of 0.5 microgram/kg over 10 minutes and 0.5 microgram/kg as intravenous infusion to patients who underwent lower limb surgery under bupivacaine spinal anaesthesia, significantly prolonged the duration of sensory and motor blockade. Dexmedetomidine provided excellent intraoperative sedation and was effective in providing post-operative analgesia. All these effects were achieved without causing deep level of sedation and with minimal hemodynamic side effects. The present study was done in a single tertiary care centre. Therefore, multicentric studies on larger samples are recommended to explore various other aspects that can help in achieving better outcomes.

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