Research Article

A comparison between dexmedetomidine and midazolam infusion on characteristic of spinal anesthesia

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Abstract

Background: Different adjuvants have been used to extend spinal anesthesia, with the probable benefits of late commencement of postoperative pain and reduced analgesic requirements. Alpha-2 adrenoceptor agonists have been recently used for their sedative, analgesic, and perioperative sympatholytic and cardiovascular stabilizing effects with reduced anesthetic requirements.

Objective: In this prospective, randomized, double-blind study, we evaluated the intravenous dexmedetomidine and compared it with intravenous midazolam for effect on sensory and motor blockade, sedation, hemodynamic parameters, duration of analgesia, and side effects during spinal anesthesia.

Materials and Methods: A total of 60 patients scheduled for lower abdominal and lower limb surgery were selected. Group D (n = 30) received dexmedetomidine (1 μg/kg) over 10 min before spinal anesthesia, followed by infusion of 0.5 μg/kg/h during surgery. Group M (n = 30) received midazolam (0.04 mg/kg) over 10 min before spinal anesthesia, followed by infusion of 0.04 mg/kg/h during surgery. Time for onset of sensory and motor blockade, sedation score using Ramsay Sedation Score (RSS), hemodynamic parameters, and duration of analgesia were assessed.

Result: The mean time to achieve the highest sensory level and onset of grade 3 motor block were comparable in both the roups ($p > 0.05$). The mean time to complete regression of sensory analgesia (261.17 ± 23.81 vs. 234.83 ± 22.61 min; $p < 0.001$) and duration of motor block (232.17 ± 27.94 vs. 199.67 ± 22.36 min; $p < 0.001$) were significantly longer in group D when compared with group M. The total duration of analgesia (356.67 ± 54.56 vs. 260.33 ± 18.84 min) was significantly longer in group D when compared with group M ($p < 0.001$).The mean time to achieve RSS of three was significantly shorter in group D when compared with group M ($p < 0.05$). Statistically significant decrease in heart rate was observed in group D when compared with group M.

Conclusion: When compared with intravenous (IV) midazolam, administration of IV dexmedetomidine during spinal anesthesia prolongs the duration of sensory and motor blockade and provides a longer duration of postoperative analgesia, with satisfactory arousable sedation and minimal side effects.

KEY WORDS: Dexmedetomidine, midazolam, comparison, spinal anesthesia

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Introduction

Different adjuvants have been used to extend spinal anesthesia, with the probable benefits of late commencement of postoperative pain and reduced analgesic requirements.[1] Alpha-2 adrenoceptor agonists have been recently used for their sedative, analgesic, and perioperative sympatholytic and cardiovascular stabilizing effects with reduced anesthetic requirements.[2] Dexmedetomidine (1300:1) is more selective

to the α-2 adrenoceptors than clonidine (39:1) and shows potent sedative analgesia-sparing properties. At therapeutic doses, dexmedetomidine is not related to respiratory depression in spite of often-times profound levels of sedation. Because of these properties (sedation, analgesia, and respiratory-sparing), dexmedetomidine is used for sedation during regional anesthesia.[3]

Various studies have demonstrated that intravenous infusion of dexmedetomidine prolongs the sensory and motor blockade with intrathecal bupivacaine. Its effects are readily reversible with atipamezole, an α-2 adrenoceptor antagonist. Potential desirable effects include decreased requirements of anesthetics and analgesics, a diminished sympathetic response to stress, and the potential for cardioprotective effects against myocardial ischemia with minimal effects on respiration.

So, we evaluated and compared the efficacy of intravenous infusion of dexmedetomidine with midazolam on onset and duration of sensory and motor blockade and intraoperative sedation and duration of postoperative analgesia during spinal anesthesia with 0.5% bupivacaine.

Materials and Methods

A prospective, randomized, double-blind comparative study was conducted after obtaining approval from the institutional ethics committee and written informed consent from the patients. Sixty American Society of Anesthesiologists' class I–III patients, aged 20–65 years scheduled for lower abdominal or lower limb surgery under spinal anesthesia at our hospital were enrolled in this study.

Patient with history of sleep apnea, obesity (BMI>30), second- or third-degree heart block, hepatic and renal dysfunction, psychiatric illness, allergy to local anesthetic or study drugs, spinal deformities, and any contraindication to spinal anesthesia (coagulopathy, infection at puncture site, and preexisting neurological deficits in the body) were excluded from the study. Patients were randomly and equally divided into two groups—group D (dexmedetomidine) and group M (midazolam) using computer generated random numbers. In the preoperative room, after securing 18-gauge intravenous (IV) cannula, all the patients were preloaded with inj. Ringer's lactate (10 mL/kg) and premedicated with inj. glycopyrolate (0.004 mg/kg) (IV) 30 min prior to induction.

On arrival to operation room, Group D patients received a loading dose of 1 μg/kg of dexmedetomidine (IV), and group M received a loading dose of inj. midazolam (0.04 mg/kg) (IV) over 10 min by infusion pump. After that, lumber puncture was performed in sitting/lateral decubitus position given at the level of L_3-L_4/L_2-L_3 space with 23/25-gauge spinal needle. After ensuring free flow of cerebrospinal fluid, 3 mL of inj. bupivacaine (0.5%) was injected. When required level of spinal anesthesia was achieved and position had been given, group D received infusion of dexmedetomidine at 0.5 μg/kg/h (IV), and group M received infusion of midazolam at 0.04 mg/kg/h (IV) throughout the surgery. Infusion rate was decreased to half or increased to twice to maintain Ramsay Sedation Score (RSS) of three. Pulse rate, electrocardiography, and SpO_2 were monitored continuously. Oxygen was delivered by an oxygen mask (4 L/min) to all patients throughout procedure.

Sensory blockade was assessed by with pinprick method, and motor blockade was assessed by modified Bromage Scale (grade 0, able to move the hip, knee, and ankle; modified Bromage 1, unable to move the hip but is able to move the knee and ankle; modified Bromage 2, unable to move the hip and knee but is able to move the ankle; and modified Bromage 3, unable to move the hip, knee, and ankle). Sensory and motor blockade were checked at 2, 5, 8, and 10 min after spinal anesthesia, and, then, every 5 min till 30 min, and, then, every 15 min throughout the surgery. Time to achieve T10 sensory level, grade 3 motor blockade, and complete regression from sensory and motor blockade were noted. All the durations were calculated considering the time of spinal injection as time 0.

The level of sedation was evaluated every 5 min throughout the study period using RSS.

Postoperatively analgesia was assessed by the visual analog scale (VAS). Inj. diclofenac sodium (75 mg intramuscular) was given when VAS ≥ 3. The time at which analgesia was first received and total analgesic requirement in 24 h was recorded.

Patients were observed for any adverse effects such as nausea, bradycardia, hypotension, and respiratory depression and treated accordingly.

Statistical Analysis

Data were analyzed by computer statistical software system SPSS software, version 17 (Statistical Packages for the Social Sciences, Chicago, IL). All data were presented as mean and standard deviation (SD), except where specified. The unpaired Student's *t*-test was used for intergroup comparisons. Probability values of $p < 0.05$ were considered significant, and $p < 0.001$ were considered highly significant.

Result

Demographic data and duration of surgery were comparable in both the groups, which are presented in Table 1.

Time to achieve T10 sensory level was comparable in both the groups ($p > 0.05$), but the time required for complete regression of sensory analgesia was significantly longer in group D (261.17 ± 23.81 min) when compared with group M (234.83 ± 22.61 min), ($p < 0.001$).

The mean time from for the onset of grade 3 motor block was comparable in both the groups ($p > 0.05$), but time to complete regression of motor block was significantly longer in group D (232.17 ± 27.94 min) when compared with group M (199.67 ± 22.36 min) ($p < 0.001$).

None of the patients from either group required rescue analgesic during intraoperative period.

Total duration of analgesia was significantly longer in group D (356.67 ± 54.56 min) when compared with group M (260.33 ± 18.84 min) ($p < 0.001$).

Table 1: Demographic data

	Group D (*n* = 30)		Group M (*n* = 30)		*P*
	Mean	SD	Mean	SD	
Age (years)	39.93	11.68	41.53	11.32	>0.05
Gender (M:F)	19:11		11:19		
Total duration of surgery	119.5	45.17	120.17	38.41	>0.05
Type of surgery					
Lower abdominal	15		11		
Lower limb	15		19		

Table 2: Effect on spinal anesthesia

	Group D (*n* = 30)		Group M (*n* = 30)		*P*
	Mean	SD	Mean	SD	
Highest sensory level	T4-T10		T4-T10		
Time to achieve T10 sensory level (min)	4.53	2.29	4.4	2.28	>0.05
Time to complete sensory regression (min)	261.17	23.81	234.83	22.61	<0.001
Onset of grade 3 motor block (min)	5.1	0.55	5.33	1.27	>0.05
Time to return of grade 0 motor block (min)	232.17	27.94	199.67	22.36	<0.001
Total duration of analgesia	356.67	54.56	260.33	18.84	<0.001

Table 3: Sedation score

	Group D (*n* = 30)		Group M (*n* = 30)		*P* value
	Mean	SD	Mean	SD	
Time taken to achieve RSS score of three intraoperatively	17.9	8.39	28.33	6.74	<0.05
RSS score reached at 2 point after stoppage of infusion	31.00	8.14	31.33	6.94	>0.05

The mean time to achieve RSS of three was significantly shorter in group D (17.9 ± 8.39 min) when compared with group M (28.33 ± 6.74 min) ($p < 0.05$).

To maintain RSS three, four patients in group D required decrease infusion rate by half, and six patients in group M required increase infusion rate to double.

At the end of surgery, time to achieve RSS of two after stoppage of infusion of study drug was comparable in both the groups ($p > 0.05$).

Basal hemodynamic parameters were comparable between the groups. Intraoperatively, there was significant decrease in heart rate in group D after 10 min of loading dose and persisted to be lower for 45 min after spinal anesthesia. None of the patients in either group developed clinically significant bradycardia.

Mean arterial pressure (MAP) remained comparable throughout the study ($p > 0.05$) except at 120 min and 180 min, where significant decrease in MAP was observed in group D when compared with group M ($p < 0.001$). One patient from each group developed a single episode of hypotension (blood pressure < 80 mm of Hg) intraoperatively, which was treated by rapid infusion of Ringer's lactate solution and single bolus of inj. ephedrine (6 mg IV).

Respiratory rate and oxygen saturation were comparable between both groups throughout surgery. None of patients showed fall in SpO2 below 98% or respiratory rate <12/min.

None of the patients developed nausea, vomiting, bradycardia, or respiratory depression. One patient from either group developed hypotension.

Discussion

In our study, we found that dexmedetomidine infusion used as a loading, followed by an infusion prolonged the duration of sensory and motor blockade during bupivacaine spinal anesthesia. In addition, it also increased the time until first request of analgesic for postoperative pain relief. It also provided sedation comparable to midazolam infusion.

As rapid administration might produce tachycardia, bradycardia, and hypertension, because of direct action on peripheral α_2 receptor, we administered loading dose of dexmedetomidine slowly over 10 min. in our study.

Al-Mustafa et al.[4] reported prolonged duration of motor block following use of 1 μg/kg initial bolus dose, followed by 0.5 μg/kg/h infusion. Elcicek et al.[5] observed observed that dexmedetomidine bolus of 1 μg/kg, followed by infusion at

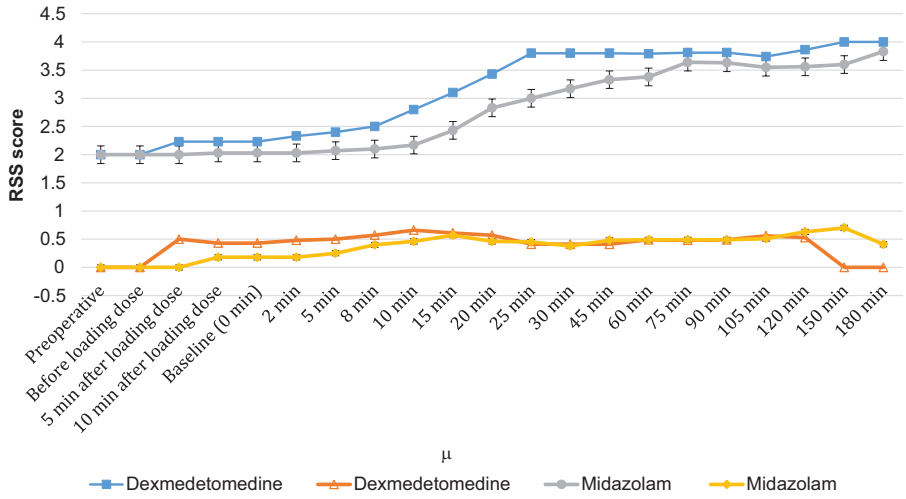

Figure 1: Comparison of intraoperative sedation.

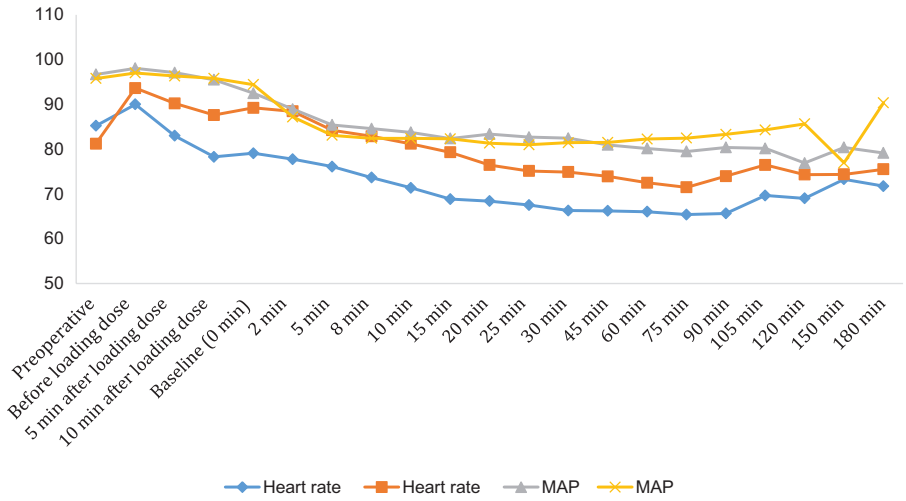

Figure 2: Comparison of intraoperative hemodynamic parameter.

0.4 μg/kg/h prolonged the duration of sensory and motor regression following spinal anesthesia with ropivacaine. Lugo et al.,[6] in their study noted prolongation of sensory block and duration of analgesia without significant effect on motor block while using 1 μg/kg bolus, followed by 0.5 μg/kg/h infusion of dexmedetomidine. Administration of single bolus of 1 μg/kg and 0.5 μg/kg also were reported to prolong the duration of analgesia and sensory blockade. However, in a study by Kaya et al.,[1] use of a single dose of 0.5 μg/kg of dexmedetomidine did not affect the duration of motor block. Harsoor et al.[7] observed that loading dose of dexmedetomidine at 0.5 μg/kg, followed by 0.5 μg/kg/h produce longer duration of analgesia and motor blockade.

The effect of dexmedetomidine on spinal anesthesia is not dependent on the route of administration. Midazolam has been reported to show an antinociceptive effect through the neuroaxial pathway. However, the effects of midazolam on nociception may depend on the route of administration, with analgesia observed after spinal or epidural application but not after systemic administration of this agent. This may be the reason why in our study the duration of sensory and motor blockade and postoperative analgesia was longer with dexmedetomidine infusion when compared with midazolam.

A significant decrease in pulse rate and MAP were observed when compared with baseline in both the groups throughout the surgery. But the fall in pulse rate was greater with dexmedetomidine infusion up to 45 min after spinal anesthesia when compared with midazolam infusion. ($p < 0.05$).

Most studies have noted fall in pulse rate and MAP when compared with baseline value with both dexmedetomidine and midazolam infusion without significant difference between the groups.[1,2,3,8] Many studies have noted bradycardia as a

prominent side effect following dexmedetomidine infusion.[3,9,10] However, we did not note any incidence of bradycardia in our study. Incidence of hypotension was comparable with other studies.[1,2,3,8]

The lower heart rate and MAP observed with dexmedetomidine infusion could be explained by the decreased sympathetic outflow by activation of postsynaptic α2-A receptor in central nervous system and decreased circulatory levels of catecholamines caused by dexmedetomidine.[11]

Duration of postoperative analgesia was longer with dexmedetomidine infusion when compared with midazolam infusion. Celik et al.[2] and Kaya et al.[1] also had similar observation regarding duration of analgesia in their study.

Intraoperative sedation provided by dexmedetomidine or midazolam eliminates the need of additional sedatives. Dexmedetomidine produces sedation by its central effect and seems to be dose-dependent. Most of the patients were sedated in both the groups but easily arousable. Respiratory rate and oxygen saturation were maintained within normal range in both the groups.

Conclusion

We conclude that, during spinal anesthesia, IV supplementation of loading dose of dexmedetomidine (1 μ/kg), followed by infusion at 0.5 μ/kg/h is more effective than midazolam (0.04 μ/kg) loading, followed by 0.04 μ/kg/h infusion, as it provides longer duration of sensory and motor blockade and postoperative analgesia with minimal and similar side effects. Both provide satisfactory arousable sedation without respiratory depression.

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