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Original Research Article

Sedation during spinal anaesthesia: A comparison between Dexmedetomidine and midazolam infusion

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Abstract

Objective: To study the effects of intravenous dexmedetomidine infusion and compare it with intravenous midazolam infusion during spinal anaesthesia (S/A) with regards to effect on psychomotor performance, memory and any side effect.
Materials Methods: A prospective randomized double blind study was conducted on 60 patients of ASA I to III, scheduled for lower abdominal or lower limb surgery under S/A. All patients were randomly divided into two groups of 30 each; randomization was done by computer generated random numbers. In Group D, dexmedetomidine 1 µg/kg and In Group M, midazolam 0.04 mg/kg basal infusion for 10 min then S/A was given with hyperbaric bupivacaine (0.5%). After achieving required level of S/A; position given and then infusion of inj. Dexmedetomidine 0.5µg/kg/hr in group D and Inj. Midazolam 0.04mg/kg/hr by infusion started. Both psychomotor and memory test were performed before study drug infusion and after 1 and 4 hour of stoppage of infusion.
Results: Thus, in both the groups, psychomotor performance was not significantly changed as compared to baseline at 1 hour and 4 hour after stoppage of infusion. There was significantly decreased in recall of picture, after 1 hour of study drug infusion in both the groups (anterograde amnesia); which was regained at 1 hour after stoppage of infusion. The mean time required to achieved sedation score (RSS) of 3 were statistically significant shorter in group D as compared to in group M ($P < 0.05$). At the end of surgery, after stoppage of infusion of study drug, patients of group D achieved RSS score of 2 and that of group M which was comparable ($p > 0.05$).
Conclusion: Thus, we conclude that, Dexmedetomidine provide rapid onset of arousable sedation without causing respiratory and cardiovascular depression. It provides anterograde amnesia with rapid recovery of psychomotor function.
Keywords: Spinal anaesthesia, dexmetomidine, midazolam.

1. Introduction

Positioning for surgery can be uncomfortable and spontaneous movements by an inadequately sedated patient can cause interference with the surgical procedure. On the other hand, vigilance during surgery may increase concerns including being aware of surgical intervention and pain. Patients may hence experience intense stress and anxiety, which is unfavorable for patient, anesthesia and surgical team. All these points may be alleviated by sedating the patient during surgery. There are some constraints on the choice of these supplemental medications as long acting amnesia is also undesirable. The ambulatory day case surgical patient is expected to remember all the postanaesthetic and post surgical discharge instructions given to him or her. Hence these drugs should be carefully selected. [1-3]

Midazolam, a short acting water soluble benzodiazepine, has a fast onset and short recovery time, so it is one of the most widely used sedative in spinal anesthesia. With a low context sensitive half time, it can be easily titrated as per the need of the user, making its use well suited for ambulatory conscious sedation techniques.

Alpha-2 adrenoceptor agonists have been recently used for their sedative, analgesic and perioperative sympatholytic and cardiovascular stabilizing effects with reduced anesthetic requirements. Because of more selective alpha-2 adrenoreceptor and properties like sedation, analgesia, and respiratory-sparing, dexmedetomidine might prove useful for sedation during regional anesthesia. 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.[3]

So, we evaluated and compared the efficacy of intravenous infusion of dexmedetomidine with midazolam on haemodynamic parameters, Psychomotor performance and amnesia during spinal anesthesia with 0.5% bupivacaine.

2. Methods

After obtaining approval from the institutional ethics committee a prospective randomized double blind study was conducted on 60 patients of 20 to 65 years, belonging to ASA class I to III, weighing 40-75kg & BMI<30 scheduled for lower abdominal or lower limb surgery under spinal anaesthesia at Govt. Medical college and New Civil Hospital, Surat. The procedure to be performed explained to patient and relative and written informed consent was taken. Patients with 2^{nd} or 3^{rd} degree heart block, Patient under antihypertensive treatment, H/O sleep apnea, Obesity; BMI>30, Hepatic and Renal dysfunction, History of allergy to study drugs and Current history of psychiatric illness were excluded. Patients were randomly and equally divided into 2 groups dexmedetomidine group (group D) and midazolam group (group M) using computer-generated numbers.

On the day of surgery, in the recovery room pulse rate, blood pressure and respiratory rate were recorded. Both psychomotor test and memory test were performed to obtain baseline data. Intravenous line was secured and all the patients were preloaded with Inj. Ringer lactate 10 ml/kg. They were premedicated with Inj. Glycopyrolate 0.004 mg/kg i.v. 30 minutes prior to induction.

Group D patients received a loading dose of 1 µg/kg of dexmedetomidine IV and in group M received a loading dose of Inj. Midazolam 0.04mg/kg iv infusion over 10 minute by infusion pump. The time of initiation of loading dose was noted. Pulse rate, blood pressure, SpO_2, respiratory rate and sedation score were recorded at 5 minute and 10 minute after loading dose. Spinal anaesthesia was given with Inj. Bupivacaine (0.5%) 3 ml Under strict aseptic precaution. When required level of spinal anaesthesia was achieved and position had been given, maintenance dose of dexmedetomidine at 0.5 µg/kg/h IV in group D and midazolam at 0.04mg/kg/hr IV in group M by infusion pump till the end of surgery. Pulse rate, ECG & SPO_2 were monitored continuously. Pulse rate, systolic blood pressure, SpO_2, respiratory rate, were recorded every 5 minutes up to 30 minutes and then every 15 minutes till end of surgery. MEM test was performed after 1 hour of starting infusion. Than both psychomotor tests and memory test were performed 1 hour after stoppage of infusion and 4 hour of stoppage of infusion. Oxygen was delivered by oxygen mask 4 L/min to all patient throughout procedure. Patients were observed for any adverse effects and treated accordingly.

Psychomotor performance tests were based upon Peg-board test (post box test) designed by Vickers (1965) and P-deletion test described by Dixon and Thornton (1973). Post box test was to involve the use of a Kiddicraft post box toy. Eighteen shapes, three each of six different types, available for "posting" through corresponding holes in the lid of the toy. The numbers of shapes posted in 20 seconds are noted after the patient has practiced to consistent result. In our study prenursery education toy was used for post box test with twenty four different shapes available for posting. At preoperative visit after familiarization with the apparatus and test, all patients practiced using psychomotor test apparatus to attain stable level of performance. The number of shapes, patient was able to post in corresponding holes in one minute was noted.[4-7]

In P-deletion test, patients were presented with foolscap sheet containing 58 lines of 36 close-spaced letters and ask to delete as many letters P as possible without omission or error in 3 minutes. As many patients coming in our hospital were illiterate or may not be able to recognize letter P, in this study we were used 0-deletion test, in which patients were presented with foolscap sheet containing 41 lines of 24 close-spaced numbers i.e. 0, 8, 9, 6, 4 and were asked to delete as many "0" as possible without omission in 3 minutes.[8-10]

For memory of the patient, we used MEM test is used in which series of 16 unrelated words were listened to the patients and ask patients to reciting them as many as possible. But in our test, we have used 10 words, and ask patients to reciting them as many as possible. At the 4-h after stoppage of infusion, subjects performed a comprehensive memory test (CMEM). Rather than listening

to a new word list, the CMEM test required them to recall as many of the words as possible from the three previous lists. The total number recalled was tallied.

2.1 Statistical considerations

Data was analyzed using computer statistical software system SPSS® 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 $p < 0.05$ were considered significant and $p < 0.001$ were considered highly significant.

3. Results

Table 1: Demographic data and duration of surgery were comparable in both the groups

	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		

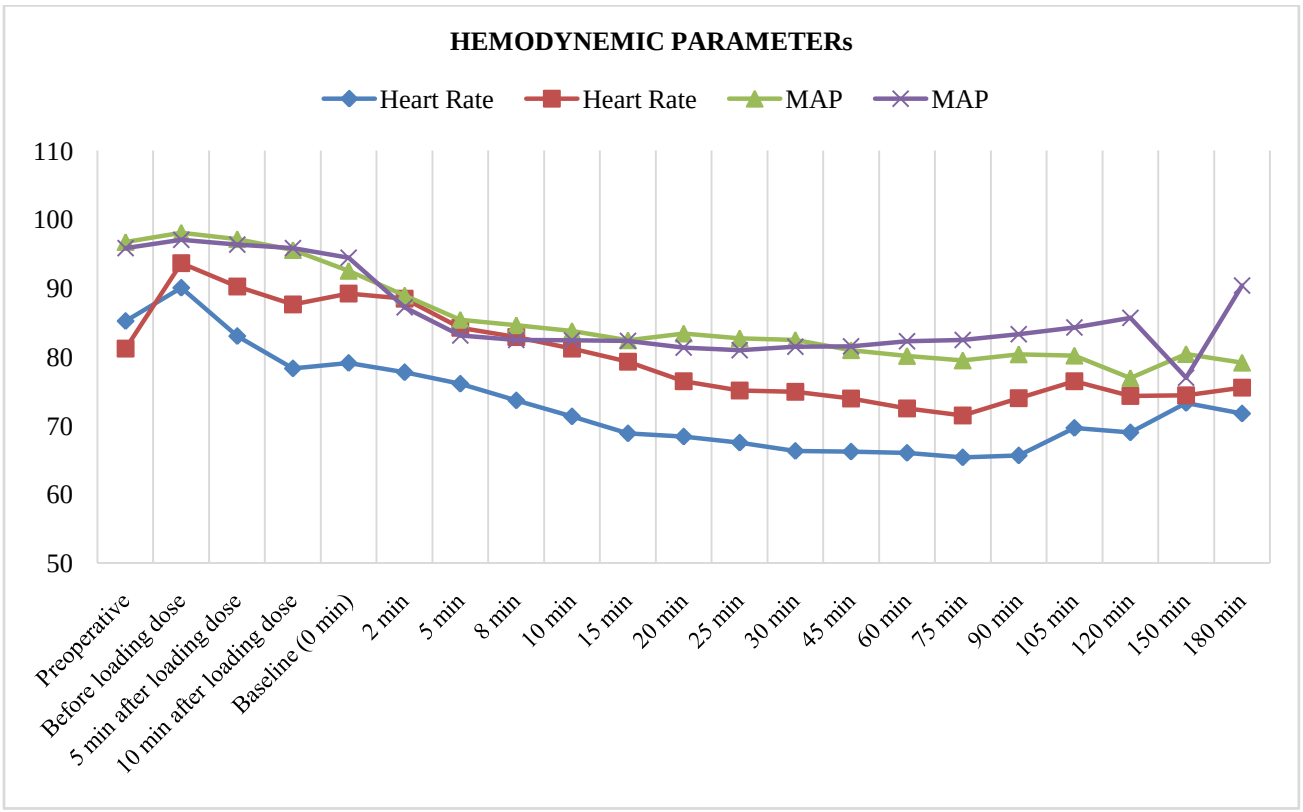

Figure 1: Comparison of intraoperative hemodynamic parameter

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

3.1 Psychomotor functions

Table 2: Deletion Test (Number of 0 deleted out of 272)[4]

Time interval	Group D (n=30)			Group M (n=30)		
	Mean	SD	P value	Mean	SD	P value
Baseline	137.8	51.32		133.83	58.31	
1 hour after stoppage of infusion	139.3	52.39	>0.05	135.8	58.25	>0.05
4 hour after stoppage of infusion	144.93	53.18	>0.05	143.3	56.04	>0.05

In group D, the mean value for number of 0 deleted in 3 minutes at baseline was 137.8 ± 51.32 and in group M, was 133.83 ± 58.31. Thus, the mean value for number of 0 deleted in 3 minutes at 1 hour(139.3 ± 52.39 vs 135.8 ± 58.25) and 4 hour(144.93 ± 53.18 vs 143.3 ± 56.04) after stoppage of infusion were comparable to baseline in both the groups (P>0.05).

Table 3: Kiddicraft toy method (Number of correctly placed picture out of 16)[4]

Time interval	Group D (n=30)			Group M (n=30)		
	Mean	SD	P value	Mean	SD	P value
Baseline	12.53	3.6		11.97	3.63	
1 hour after stoppage of infusion	12.37	3.65	>0.05	11.97	3.71	>0.05
4 hour after stoppage of infusion	13.23	3.27	>0.05	12.8	3.24	>0.05

Thus, in both the groups, the mean value for number of correctly placed in Kiddicraft toy at 1 hour(12.37 ± 3.65 vs 11.97 ± 3.71) and 4 hour(13.23 ± 3.27 vs 12.8 ± 3.24) after stoppage of infusion were comparable to baseline (P>0.05).

Thus, in both the groups, psychomotor performance was not significantly changed as compared to baseline at 1 hour and 4 hour after stoppage of infusion.

Table 4: Memory test [4]

Time interval	Group D (n=30)			Midazolam (n=30)		
	Mean	SD	P value	Mean	SD	P value
Baseline	6.47 (64.7%)	1.59		6.07 (60.7%)	1.68	
After 1 hour of infusion started	5.2 (52.0%)	1.54	<0.001	4.83 (48.3%)	1.44	<0.05
1 hour after stoppage of infusion	6.3 (63.0%)	1.68	>0.05	5.8 (58.0%)	1.56	>0.05
4 hour after stoppage of infusion	10.97 (36.56%)	3.33		9.33 (31.1%)	2.64	

Thus, there was significantly decreased in recall of picture, after 1 hour of study drug infusion in both the groups (anterograde amnesia); which was regained at 1 hour after stoppage of infusion.

At 4 hour after stoppage of infusion, in group D, patients recalled 36.56% of pictures, while in group M, they recalled 31.56% of pictures out of 30 pictures.

But, we had not observed that how many pictures were recalled from baseline list. So, we can say that patients of both the groups developed anterograde amnesia but cannot comment on retrograde amnesia.

4. Discussion

In our study we found that, psychomotor performance was not significantly changed as compared to baseline at 1 hour and 4 hour after stoppage of infusion in both the groups. Psychomotor performance was checked by 0 Deletion Test (/272) and Kiddicraft toy method (/16).

Hall *et al*[4] had used The DSST (Digital Symbol Substitution Test) and MEM test to assess psychomotor performance. It was clear that, even though the dexmedetomidine-treated volunteers could be easily awakened to perform the testing, their performance was impaired. This persisted for at least one hour after terminating the dexmedetomidine infusions, but was restored to baseline at the four-hour post infusion testing period. There were no differences in the degree of performance impairment or the time course of impairment of either the DSST or CMEM tests between the two infusion doses of dexmedetomidine.

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).[11-13]

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. Many studies

have noted bradycardia as a prominent side effect following dexmedetomidine infusion. However, we did not note any incidence of bradycardia in our study. Incidence of hypotension was comparable with other studies.[14-19]

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 catecholamine caused by dexmedetomidine. Respiratory rate and oxygen saturation were maintained within normal range in both the groups.

5. Conclusion

Dexmedetomidine administered as 1 µg/kg loading dose followed by 0.5 µg/kg/hr continuous infusion and compared with midazolam given as 0.04 mg/kg as loading dose followed by 0.04 mg/kg/hr continuous infusion during spinal anaesthesia both caused no impairment of psychomotor function at 1 hour after stoppage of infusion and provides intraoperative (Anterograde) amnesia, which is more intense with dexmedetomidine with minimal and similar side effects.

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