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Original Research Article

Comparison of Intravenous Midazolam and Dexmedetomidine Effects

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Abstract

Introduction: Spinal anesthesia is a very commonly used procedure in modern day anesthesia practice. Today most of the lower limb and infraumblical surgeries are performed under spinal anaesthesia. Midazolam and dexmedetomidine are common intravenous adjuvants used during anaesthesia to alley anxiety and sedation. The aim of this study was to compare the effects if intravenous midazolam and dexmedetomidine in terms of analgesic characteristics, sedation and adverse effects.

Material and Methods: This is a randomised prospective study which included 30 patients in two groups, posted for lower limb orthopaedic surgery. Intravenous midazolam and dexmedetomidine was administered after subarachnoid block. Data for block characteristics, sedation, hemodynamic parameter and adverse effects were recorded.

Results: Both the groups were comparable in terms of age, weight and ASA grade. The mean age for dexmedetomidine was 38.83 +13.69 years and for Midazolam group was 35.76 + 13.54 and 110 +8.61 minutes for midazolam group. The two dermatomal sensory regression was 137.6 + 10.40 minutes and 110 + 8.61 minutes for midazolam group. This difference was statistically significant with p value <0.001, with 95% CL [22.73-32.60].

Conclusion: In conclusion intravenous dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine in spinal anesthesia compared to midazolam. Intravenous dexmedetomidine supplementation during SAB provides intraoperative sedation equivalent to midazolam without causing respiratory depression. However, there were incidences of bradycardia and hypotension in dexmedetomine group.

Introduction

Spinal anesthesia is a very commonly used procedure in modern day anesthesia practice. Spinal anesthesia or subarachnoid block is a type of central neuraxial anesthesia requiring the injection of a

small volume of local anesthetic agent directly into the cerebrospinal fluid (CSF) [1].

These neuraxial techniques result in a combination of sympathetic, sensory and motor blockade depending on the dose, concentration, or volume of local anesthetic drug used [2]. The technique of spinal anesthesia is primarily used for lower abdominal and lower limb surgeries [3]. It offers many advantages over general anesthesia, key advantages being more cardiovascular and respiratory stability, preservation of protective airway reflexes and rapid postoperative recovery [4]. From the patient's point of view, it offers the advantage of the patient having control over respiration, early family contact, and early food intake [5].

Few drawbacks associated with these regional techniques include: pain, fear and anxiety associated with the procedure and needles, recall of surgical procedures and awareness during the surgical procedure. [6-9] These factors thus, stress the importance of sedation in spinal anesthesia, thus improving patient compliance during the procedure [10].

Sedation in spinal anesthesia is used routinely as a part of the general management of the patient, providing anxiolysis, sedation and amnesia [11].

Sedation has been shown to improve patient satisfaction during regional anesthesia techniques and thus, may be considered as a means to increase the patient's acceptance of procedures under spinal anaesthesia [12].

The drugs used for sedation include benzodiazepines such as midazolam; alpha agonists such as dexmedetomidine and clonidine; anaesthetic drugs like propofol and ketamine in subanaesthetic doses; and opioids such as fentanyl, remifentanil and pentazocine [13].

Commonly used drug in our institute for sedation are midazolam and dexmedetomidine. Midazolam, a short acting benzodiazepine is a frequently used drug during procedures under spinal anesthesia [14]. The α2-adrenergic agonist class of drugs is found to have sedative, anxiolytic, hypnotic, analgesia and sympatholytic effects [15-17]. Due to its action on the locus coeruleus situated in pons, it is associated with modulation of sleep and respiration, leading to a sedative effect with minimal respiratory depression. Previous clinical studies have found that the injection of intravenous dexmedetomidine results in a significant opioid-sparing effect in post-surgical cases, decrease in inhalational anesthetic requirements during general anesthesia and prolongation of motor and sensory block during spinal anesthesia [18-22]. However, because of its sympatholytic effects, dexmedetomidine can result in hypotension and bradycardia. A number of studies have been carried out to ascertain the effect of various doses ranging from 0.25 -1μg/kg of iv dexmedetomidine in spinal anesthesia in the form of a single bolus dose or bolus dose followed by infusion rate of 0.5 μg/kg/hr.

Sedation during spinal anesthesia is necessary to allay patient anxiety during surgery and improve quality in lower limb orthopedic procedures as immediate postoperative pain relief is extremely important. Dexmedetomidine and midazolam are commonly used perioperative sedative drugs. In addition to sedation these drugs may have benefit of prolonging the action of spinal anesthesia. It also providing post-operative analgesia which is an effective and safe method.

The aim of our study was to compare intravenous dexmedetomidine and midazolam on duration of action of spinal anesthesia (subarachnoid block) in patients undergoing lower limb orthopedic surgery under spinal anesthesia. They are compared mainly with respect to effect on duration of action of spinal anesthesia. We also studied and compared the level of

patient's satisfaction, sedation score and pain score in the elective lower limb orthopedic under spinal anesthesia.

Materials & Methods

The study was initiated after obtaining permission from the Institutional Ethics and Research Committee from our institute. Written informed valid consent was taken from all patients. The study adhered to the declaration of Helsinki 2013 and conducted as per the updated CONSORT statement 2010 [23-24]. Study group comprised of patients admitted for routine elective lower limb orthopaedic surgery under spinal anaesthesia in a tertiary care teaching public hospital. The study spanned over a period of 9 months from February 2018 to October 2018. All the patients continued to receive standard routine management in the Operating Room as per the attending anaesthesiologist's discretion. Identity of all the patients was kept confidential. At the end of study, Ramsay Sedation Scores, visual analogue scale (VAS score) of all patients, along with time required for two-dermatomal regression, total duration of spinal anaesthesia, rescue analgesia time and patient satisfaction score which were noted and analyzed with appropriate statistical techniques.

Aim of the study is to compare effect of intravenous dexmedetomidine and midazolam on duration of action of spinal anesthesia in patients undergoing lower limb orthopedic surgery under spinal anesthesia. The secondary objectives are to compare the duration of spinal anesthesia, the level of patient's satisfaction and pain score (Visual Analogue scale), duration of postoperative analgesia and the time required for rescue analgesia, perioperative sedation level using sedation score (Ramsay sedation score) and incidence of any complication.

Details of study procedure involved

This was Prospective randomized double-blind study. The data was collected from patient's case record forms during the surgical procedure and post-operatively in the Recovery room. The standard, routine procedure for spinal anaesthesia in elective surgeries is as follows:

After application of standard monitoring and adequate pre-loading of the patient, standard balanced spinal anaesthesia using 0.5% hyperbaric Bupivacaine is given according to the weight and height of the patient and the surgical requirement. Duration of spinal anaesthesia is usually 90-120 minutes and is administered for surgeries lasting 90-120 minutes. Occurrence of any complications such as hypotension and bradycardia, shivering nausea and vomiting were noted and treated accordingly.

The patients were randomly divided into two groups by computerised randomisation. Two syringes of 20 cc were prepared, one syringe containing midazolam and another containing dexmedetomidine as both are clear colourless solutions. All solutions were prepared by an anaesthesiologist not participating in the study. The patient and observer were blind to the sedation drug used. One group (Group D) was received 0.5ug/kg dexmedetomidine over 10 minutes, followed by 0.2ug/kg/hr. with infusion pump. Another group (Group M) was received midazolam 0.6ug/kg bolus over 10 minutes followed by normal saline infusion. Both the infusions were stopped just before the end of the surgery Vital parameters (Baseline heart rate, NIBP and SPO2) was noted at the time of spinal anaesthesia and at the time of sedation. Then every 5min for 20 min then 10 minutes for 1 hour and every 20 minutes till the end of surgery.

The following data was collected from each patient:

Age, gender, ASA grading, sedation drug used, surgery performed, duration of surgery, spinal level achieved, time of sedation administration, Ramsay sedation

score, two dermatomal regression of spinal level, total duration of spinal anaesthesia, any complication such as hypotension, bradycardia, nausea, vomiting, shivering occurring both intraoperatively and post operatively, as shown in table 1 and figure 1.

Table 1: Modified Ramsay sedation scale

Sedation Score	Clinical Response
0	Unable to evaluate
1	Awake
2	Lightly Sedated
3	Moderately sedated, follows simple commands.
4	Deeply sedated, responds to non-painful stimulus.
5	Deeply sedated, responds only to painful stimulus.
6	Deeply sedated, unresponsive to painful stimulus.

Figure 1: Visual analogue scale.

Any of the above complication was treated immediately using interventions like Inj. Atropine iv. for bradycardia., Inj. Ephedrine iv. for hypotension and inj. ondansetron for nausea, vomiting. At the end of procedure, the patients were asked to assess their level of satisfaction on scale 1to 10. (1: completely dissatisfied to 10: completely satisfied)

In the postoperative period they were observed in post anaesthesia care unit (PACU). the duration of postoperative analgesia was noted and the time of first request for analgesia was noted. And inj. diclofenac sodium 75 mg was given as a rescue analgesic to the patient.

Assessment parameters:

Vital parameters (heart rate, NIBP, SPO2):

Baseline heart rate, MAP, RR and SPO2 noted and then every 5min for 20 min then 10 minutes for 1 hour and 20 minutes till 120 minutes. Ramsey sedation score: Ramsey sedation score will be recorded every 5 minutes for 20 min then 10 minutes for 1 hour and 20 minutes till 120 minutes. Visual analogue scale: Visual analogue scale will be recorded every 5 minutes for 20 min then every 30 minutes till 210 minutes. Time for two segment regression, Total duration of spinal anesthesia, that is time to complete regression of motor block, Time required for rescue analgesia, Patients satisfaction score

Study population:

Study group comprised of patients undergoing elective lower limbs

orthopaedic surgeries under spinal anaesthesia.

Inclusion criteria:

Patient undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia. (Knee arthroscopy, Tibia nailing, K wire fixation, Implant removal, Ligament tear repair, Tarsal metatarsal injuries etc.)

- Duration of surgery: Approximately 60-120 minutes duration.
- American society of anaesthesiologist (ASA) grade 1 and 2.
- Age:18-60 years.
- Sex: male and female

Exclusion criteria:

- Pregnant women.
- Refusal for spinal anaesthesia or any other contraindication to spinal anaesthesia
- Patients on sedative medications, opioids, antidepressants
- Patients with anticipated difficult airway (Mallampatti class 3 and 4)

Sample Size:

With α of 0.05, β of 0.20 (power of 80%), with mean± SD of Pain score of 2.1 ± 0.6 (n= 25) among Dexmedetomidine case as compared to 2.8 ± 0.5 (n= 25) among Midazolam cases, with allowable difference of 0.7 and Population variance of 0.3 (based on SD of both groups), using below mentioned formula, the sample size calculated was 10 per group. Sample size calculation was done based on study by Fatma Nur Kaya et al on Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anaesthesia [25]. However, sample size of 10 is not sufficient for most statistical analysis, and since resources like patients, investigative tools, time for research exist in sufficient quantity, it is planned to enrol minimum of 30 cases per group for the present study.

Z: Value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

α: The probability of type I error (significance level) is the probability of rejecting the true null hypothesis.

β: The probability of type II error (1 - power of the test) is the probability of failing to reject the false null hypothesis.

μ2 - μ1: The value of allowable difference is the true mean difference between a test drugs (μ2) and a placebo control or active control agent (μ1).

Statistical Analysis:

Study population was selected by non-probability convenience sampling method. During the study period all the patients fulfilling inclusion criteria were included in the study. 60 patients who were posted for elective lower limb orthopaedic surgeries under spinal anaesthesia were included in the study.

After data collection, data entry was done in an Excel sheet Graphical representation done in MS Excel 2010. Quantitative data (i.e. Age, Ramsay sedation score, time for two dermatomal sensory level regression, time for rescue analgesia, patient satisfaction score) was presented with the help of Mean, Standard deviation, Median and Interquartile range. Qualitative data (i.e. sex, ASA grade, sedation drug used, any complications) was presented with the help of frequency and percentage table. Epi Info 7.2 software was used for statistical analysis. Results were presented in the form of charts and graphs. Percentages were calculated. Chi square test and unpaired t test were applied wherever required. 95% confidence interval was taken and p value less than 0.05 was considered for tests of significance.

Results

The mean age of patients in Dexmedetomidine group was

38.83 +13.69 years the mean age of patients in Midazolam group was 35.76 + 13.54 years. The minimum and maximum age for the both the group was 18 year and 60 years respectively. Above results have been summarised in table *2*.

Table 2: Age wise distribution

Groups	Total Frequency(N)	Minimum	Maximum	Mean	SD
1. Group D	30	18	60	36.833	13.69
2. Group M	30	18	60	35.767	13.54

Gender

Distribution of study subjects according to gender in both the groups was as follows. Out of the 60 cases selected, 46 (76.7%) were males and 14 (23.3%) were females. A total no of 30 cases received dexmedetomidine, including 24 males (80%) and 6 females (20%). 30 patients were given midazolam, including 22 males (73.3%) and 8 females (26.7%), as shown in table *3*.

Table 3: sex wise distribution.

Groups	Male	Female	Total Frequency(N)
1. Group D	24 (80%)	6 (20%)	30
2. Group M	22(73.3%)	8 (26.7%)	30

ASA grading: Distribution of patients according to ASA grades.

In our study out of 30 patients in dexmedetomidine group, 19 patients (63.3%) were ASA 1and 11(36.7%) were ASA 2. Out of 30 patients in midazolam group, 17 (56.7%) were ASA 1and 13 (43.3%) were ASA 2. Above results have been summarised in table *4*.

Table 4: ASA Grade of the study participants

	ASA Grade	Frequency	Percentage
Group D	I	19	63.3%
	II	11	36.7%
	Total	30	100
Group M	I	17	56.7%
	II	13	43.3%
	Total	30	100

Surgery performed:

Out of 30 patients who received dexmedetomidine, surgery performed was debridement 4(13.3%), femur nailing 4 (13.3%), implant removal 5 (16.7%), knee arthroscopy 6 (20%), patella K wiring 1(3.3%), tibia nailing 6 (20%), tibia plating 4(13.3%) .Out of 30 patients who received midazolam, surgery performed was debridement 7(23.3%), femur nailing 1 (3.3%), implant removal 1(3.3%), knee arthroscopy 15 (50%), tibia nailing 3 (10%), tibia plating 3(10%). Above result have been summarised in table no 5.

Table 5: types of surgery performed.

	Surgery	Frequency	Percentage
Group D	Debridement	4	13.3%
	Femur nailing	4	13.3%
	Implant removal	5	16.7%
	Knee Arthroscopy	6	20%
	Patella K wiring	1	3.3%

	Tibia Nailing	6	20%
	Tibia plating	4	13.3%
	Total	30	100
Group M	Debridement	7	23.3%
	Femur nailing	1	3.3%
	Implant removal	1	3.3%
	Knee Arthroscopy	15	50%
	Tibia Nailing	3	10%
	Tibia plating	3	10%
	Total	30	100

Two-dermatomal sensory level regression

In Dexmedetomidine group, two-dermatomal sensory levels regression was noted in 137.6 + 10.40 minutes. In midazolam group, two-dermatomal sensory levels regression was noted in 110 + 8.61 minutes. This difference was statistically significant with p value <0.001, with 95% confidence interval having lower limit of 22.73 and upper limit of 32.60. The above data has been summarized in table *6*.

Table 6: Comparison of mean time for two dermatomal sensory level regression.

Duration of time for two dermatomal sensory level regression	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean (minutes)	137.6	110	22.73	32.60	<0.001
SD	10.40	8.61			

Mean duration of spinal anesthesia.

In dexmedetomidine group Mean duration of spinal anesthesia was 201.37+10.40 mins and in midazolam group mean duration of spinal anaesthesia was 173.3 +11.01 mins. This difference was statistically significant with p<0.001 and with 95% confidence interval having lower limit of 22.49 and upper limit of 33.59. The above data has been summarised in table *7*.

Table 7: Mean duration of spinal anesthesia

Duration of SA	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean	201.37	173.3	22.49	33.59	<0.001
SD	10.40	11.01			

Mean time for rescue analgesia.

In dexmedetomidine group mean time for rescue analgesia requirement was 249.16+10.09 minutes.
In midazolam group mean time for rescue analgesia requirement was 207+15.58 minutes. This difference was statistically significant with p value <0.001, with 95% confidence interval having lower limit of 34.61 and upper limit of 48.28. The above data has been summarized in table *8*.

Table 8: Comparison of mean time for rescue analgesia in minutes

Duration of time for rescue analgesia	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean	249.16	207.67	34.61	48.28	<0.001
SD	10.09	15.58			

Patient satisfaction score:

Patient satisfaction score in Dexmedetomidine group was 7.13 + 0.78 minutes and in Midazolam group was 6.63 + 0.88 minutes. This difference was statistically significant with p Value of 0.024, with 95% confidence interval having lower limit of 0.0685 and upper limit of 0.9315. The above data has been summarised in table *9*.

Table 9: Patient Satisfaction Score between drugs used for sedation

Patient Satisfaction Score	Group D	Group M	95%Confidence Interval		P value
			Lower	Upper	
Mean	7.133	6.633	0.0685	0.9315	0.024
SD	0.776	0.889			

Hemodynamics

Heart rate:

Minimum heart rate in patients of dexmedetomidine group was 48 bpm and maximum heart rate was 96 bpm. Minimum heart rate in patients of midazolam group was 60 bpm and maximum heart rate was 100 bpm.

Following loading dose administration fall in heart rate was noted in Group D, comparing to Group M, which was statistically significant.

Mean heart rate for Dexmedetomidine group was 68.34 bpm (+/-3.75) and for Midazolam group was 73.35 bpm (+/-3.49). This value was statistically significant with p<0.001, with 95% confidence interval having lower limit of -6.88314 and upper limit of -3.13738. This data has been summarised in table 10.

Table 10: Comparison of intraoperative mean heart rate between drugs used for sedation

Mean Heart Rate	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean	68.34	73.3564	-6.88314	-3.13738	<0.001
SD	3.754	3.487			

Mean arterial pressure

The mean of mean arterial pressure for Dexmedetomidine group was 83.3 + 2.52 mmHg (mean + SD) and for Midazolam group was 84.17 + 3.16 mmHg (mean + SD) This value was statistically not significant with p value of 0.239 (p value >0.05), with 95% confidence interval having lower limit of - 2.36 and upper limit of 0.599. The above data has been summarised in table 11.

Table 11: Comparison of intraoperative mean arterial pressure amongst sedation drugs

Mean MAP	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean	83.3	84.1795	-2.35764	0.59867	0.239
SD	2.521	3.162			

Respiratory rate:

Minimum respiratory rate in patients of dexmedetomidine group was 12 per min and maximum respiratory rate was 22 per min. Minimum respiratory rate in patients of midazolam group was 11 per min and maximum heart rate was 20 per min.

Mean respiratory rate for Dexmedetomidine group was 15.10 per min (+/-0.71) and for Midazolam group was 14.09 per min (+/-0.46). This value was statistically not significant with p=0.156, with 95% confidence interval having lower limit of 0.708 and upper limit of 1.327. This data has been summarised in table 12.

Table 12: Comparison of intraoperative mean respiratory rate between both the group

Mean RR	Group D	Group M	95%Confidence Interval		P value
			Lower	Upper	
Mean	15.107	14.0897	0.70808	1.32782	0.156
SD	0.712	0.459			

Mean VAS score

Mean VAS score after sedation in study po pulation was 1.10 + 0.28 in the dexmedetomidine group and 1.4 + 0.26 in midazolam group the difference in this value was statistically significant with p value <0.001, with 95% confidence interval having lower limit of - 0.44 and upper limit of -0.15. The above data has been summarised and presented in table 13.

Table 13: Drug used and mean VAS score.

Mean VAS	Group D	Group M	95% Confidence Interval		P value
			Lower	Upper	
Mean	1.10	1.4	-0.44	-0.15	<0.001
SD	0.28	0.26			

Mean Ramsay sedation score

Mean RSS after sedation in dexmedetomidine group was 2.9 (+/-0.18). mean RSS after sedation in midazolam group was 2.6(+/-0.16). the difference in this value was statistically significant with p value <0.001, with 95% confidence interval having lower limit of 0.16 and upper limit of 0.34. The above data has been summarised and presented in table 14.

Table 14: Mean Ramsay sedation score

Mean RSS	Group D	Group M	95%Confidence Interval		P value
			Lower	Upper	
Mean	2.9	2.6	0.16	0.34	<0.001
SD	0.18	0.16			

Complications

In the study population 2 (6.7%) patients in dexmedetomidine group developed bradycardia and 2 (6.7%) patients developed hypotension. There was no event of shivering, nausea & vomiting noted in dexmedetomidine group.

Three (10%) of the patients in midazolam group developed shivering. There was no event of hypotension, bradycardia, nausea, and vomiting noted in midazolam group. Above data has been summarised and presented in table 15.

Table 15: incidence of complications.

Complications	Dexmedetomidine (N= 30)	Midazolam (N=30)
Hypotension	2 (6.7%)	0
Bradycardia	2 (6.7%)	0
Shivering	0	3 (10%)
Nausea & vomiting	0	0
Total	4	3

Discussion

Dexmedetomidine and midazolam are not new drugs for anaesthesia. They have been studied in several routes in perioperative medicine. Both these drugs can be used as sole anaesthetic agents or as an adjuvants. We studied midazolam and dexmedetomidine as an intravenous adjuvant for subarachnoid block in lower limb surgeries.

The demographic profile of the two groups in our study were similar. Like other studies such as by Kaya et al and Rekhi BK et al have similar demographic profile [25-27].

In the current study we observed that the mean time required for regression of two dermatomal sensory levels after spinal anesthesia was prolonged in Dexmedetomidine group, 137.6 + 10.40 minutes compared to midazolam group 110 + 8.61 minutes with p value <0.001. In the study by Kaya et al two dermatomal sensory regression was found to be 145+26 mins in dexmedetomidine group and 106+39 mins in midazolam group, thus concluding that intravenous Dexmedetomidine and not Midazolam prolongs the duration of spinal anaesthesia [25]. Harsoor et al in their study with similar dosage of Dexmedetomidine reported a two-dermatomal sensory level regression time of (111.52 + 30.9) min in comparison with the control group receiving an equal volume of normal saline reporting a time of (53.6 + 18.22) min [22].

Similarly, Gupta et al in their study found that the time required for two segment regression was significantly prolonged in dexmedetomidine group (124.35 ± 30.7) mins, when compared with control group receiving an equal volume of normal saline (98.54 ± 23.2) min ($p < 0.05$)28. However, Talakoub et al in their study on the action of Midazolam on spinal anesthesia found no statistically significant effect of Midazolam on duration of sensory block [28]. In study by Dinesh et al the effect of dexmedetomidine on spinal anesthesia reported the two dermatomal regression of sensory blockade in dexmedetomidine group was 137.4 + 10.9 mins compared to 102.8 + 14.8 mins in the normal saline group [13]. Majority of these findings in other studies were comparable to our study, with significant prolongation of sensory anaesthesia in patients given Dexmedetomidine, as compared with Midazolam.

In our study mean duration of spinal anesthesia that is time to complete regression of motor block was significantly longer in de xmedetomidine group 201.37+10.40 mins, when compared to midazolam group 173.3 +11.01 mins (mean +SD). With p<0.001.

In the study by Rekhi BK et al found that the time for complete regression of motor blockade in dexmedetomidine group (190.25±13.81min) was significantly much longer than that in midazolam group (136.50±17.54 min) (p<0.001) [26]. Al-Mustafa et al in their study found that the

duration of motor block was longer with Dexmedetomidine than with normal saline (199 ± 42.8 min versus 138.4 ± 31.3 min, P < 0.05) [29]. They concluded that intravenous dexmedetomidine prolongs the sensory and motor blocks of bupivacaine spinal analgesia with good sedation and associated hemodynamic stability.

Tekin et al in their study found that the time required for complete abolishment of motor blockade was also significantly longer with dexmedetomidine as compare to normal saline (215.16 versus 190.83 minutes; P < 0.001) [30].

The current study showed that the mean time for rescue analgesia requirement significantly prolonged in dexmedetomidine group (249.16 +10.09 minutes) compared to midazolam group (207+15.58 minutes). with p value <0.001.

Kaya et al in their study found that the time to first request for postoperative analgesia was significantly prolonged with Dexmedetomidine group than with Midazolam and saline groups [216 ± 43 mins vs 136 ± 25 mins vs122 ±34 mins, P<0 .001] [25]. Harsoor et al in their study found that duration of analgesia was significantly prolonged with dexmedetomidine up to 228 ±123.4 mins, as compared with normal saline which reported analgesia for up to 138 ± 21.62mins (p<0.01)[22]. In study by Dinesh et al they reported the duration of sensory block (269.8 ± 20.7 min versus 169.2 ± 12.1 min) were significantly prolonged with dexmedetomidine than normal saline (P < 0.001) [13]. All these findings are consistent with our findings of prolonged post-operative analgesia with patients of Dexmedetomidine group in comparison with Midazolam group. In our study, mean Ramsey sedation score after sedation was greater in dexmedetomidine group as compared to midazolam group [2.9 +0.18; 2.6 + 0.16 , p<0.001].

Rekhi et al in their study found that, deeper sedation was induced in dexmedetomidine and midazolam group than in normal saline Group from which they concluded that dexmedetomidine has the advantage of eliminating the need for extra sedative agents [26]. Liang et al in their study comparing dexmedetomidine with midazolam in gynecological procedures under epidural anaesthesia, found that RSS of 3 and above was achieved in 100% patients receiving dexmedetomidine and 97% patients receiving midazolam (p=0.162) [31]. Kaya et al in their study concluded that the Ramsay sedation score was greater in the dexmedetomidine and midazolam groups than in the normal saline group with the median (range) of the highest Ramsay sedation score was 2 (2-5) in the dexmedetomidine group, 3 (2-5) in the midazolam group, and 1 (1-2) in the saline group (P<001) [25]. Our study thus showed contradictory results as those shown by Kaya et al with the RSS values being higher in the Dexmedetomidine group as compared with midazolam.

In our study mean VAS score after sedation was lower in dexmedetomidine group
(1.10 + 0.28) compared to midazolam grou p (1.4 + 0.26.) (p value <0.001) patients of midazolam group attained VAS score of 4 earlier than dexmedetomidine group.

Rekhi et al in their study found that, the patients of midazolam group and saline group attained a VAS score of 4 earlier than the patients of dexmedetomidine group. These findings were thus consistent with the findings of our study [26].

In our study patient's satisfaction score was greater in dexmedetomidine group (7.13 + 0.78) compared to midazolam group (6.63 + 0.88) P= 0.024. Liang et al found similar patient satisfaction scores (8 vs 9, p value 0.779) in their study comparing midazolam and dexmedetomidine for epidural anaesthesia and stated that most would opt for the same intravenous sedation for a similar

procedure in the future32. In our study the heart rate significantly decreased in dexmedetomidine group compared to midazolam group for first 15 minutes and the mean heart rate was significantly decreased in Dexmedetomidine group 68.34 + 3.75 bpm compared to Midazolam group 73.35 + 3.49 bpm with p<0.001.

The MAP was statistically insignificant. Respiratory rate was comparable and lower in midazolam group 14.09 + 0.46 per min compared to Dexmedetomidine group 15.10 + 0.71 per min there was no incidence ofrespiratory depression (RR <10) or desaturation (SpO2 <90%) noted in any of the group. Rekhi et al in their study found that there was significant reduction in heart rate in dexmedetomidine group for the first 15 minutes compared with midazolam and normal saline group [26]. They also conclude that mean arterial pressures were significantly lower in midazolam and saline group than in dexmedetomidine group at 15th minutes, whereas the fall in MAP in dexmedetomidine group occurred at 40th minute, showing gradual fall in blood pressure in dexmedetomidine group. in their study, respiratory depression was noted in any of the patients.

In the study by Liang et al they found that heart rate decreased significantly during dexmedetomidine administration than with midazolam, the reduction in MAP was however statistically insignificant in the two groups [31].

In the study population 2 (6.7%) of patients in dexmedetomidine group developed bradycardia and 2 (6.7%) patients developed hypotension. There was no event of shivering, nausea & vomiting noted in dexmedetomidine group. three (10%) of the patients in midazolam group developed shivering. There was no event of hypotension, bradycardia, nausea, and vomiting noted in midazolam group. These complications were however not clinically significant and were given adequate treatment and had no effect on the clinical outcome of the patients. Kaya at al in their study found that 2(8%) patient in the dexmedetomidine group had bradycardia and hypotension needing treatment while there was no incidence of bradycardia or hypotension in any of the patients [25].

Harsoor et al in his study of a similar dosage of Dexmedetomidine, recorded Bradycardia requiring treatment in 4 patients (out of 25) in Dexmedetomidine group compared with none in normal saline group (P=0.055) [22]. Hypotension was observed in 2 patients (out of 25) receiving Dexmedetomidine and in 1 patient (out of 25) receiving normal saline (P=0.5).

There were certain limitations of our study. Firstly it was a single center study with small sample size. Multicenter study with larger sample size would give a better perspective and validity. Geriatric age group (>60 years) and patients of ASA 3 and 4 have been excluded from the study so the result cannot be generalized in this patient population. Lastly, level of spinal anaesthesia and amount of drug administered were not fixed, which could act as confounding factors for the interpretation of the study.

Conclusions

We derived certain conclusion from our study and correlated with existing evidences. First of all intravenous dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine in spinal anesthesia compared to midazolam. Intravenous dexmedetomidine supplementation during SAB provides intraoperative sedation equivalent to midazolam without causing respiratory depression. Dexmedetomidine provides significant postoperative analgesia as compared to midazolam. VAS score and patient satisfaction score were better with dexmedetomidine as compared to midazolam. Incidence of bradycardia and hypotension are significantly higher

when intravenous dexmedetomidine is used as an adjuvant to bupivacaine spinal anesthesia as compared to midazolam and incidence of perioperative shivering is less in dexmedetomidine than midazolam. Therefore, to establish these findings a larger multi centric superiority trials are required.

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