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COMPARATIVE STUDY OF INTRAVENOUS DEXMEDETOMIDINE AND MIDAZOLAM AS A PREOPERATIVE SEDATION UNDER SPINAL ANESTHESIA

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ABSTRACT **INTRODUCTION:** Preoperative anxiety is a frequent condition. Comfortable anesthesia induction and maintenance can be achieved by controlling anxiety. Various agents are used to relieve anxiety and provide sedation. We conducted this study to compare the sedative effects of dexmedetomidine versus midazolam for patients undergoing spinal anesthesia.

AIMS AND OBJECTIVES : To compare the sedative effect of both drugs and observe intraoperative and postoperative comfort level, cardiovascular and respiratory changes and side effects of both drugs.

MATERIALS AND METHODS: Sixty patients between 18-65 years of age requiring spinal anaesthesia for their procedures were selected randomly and division was done in 2 groups (Each group having 30 patients). Group D was given Inj. Dexmedetomidine at the dose of 1 mcg/kg within 10 mins in 100 ml NS and group M was given Inj Midazolam at the dose of 0.04 mg/kg in 100 ml NS within 10 mins.

DISCUSSION: Anxiety is more common among young patients, women, and people with negative experience of anesthesia or fear that arises just before the operation and anesthesia my lead to psychological trauma. Various agents such as phenothiazines, bezodiazepines, barbiturates, opioids, propofol, ketamine, dexmedetomidine or clonidine and antihistamines are used to relieve anxiety and provide sedation. Midazolam is a benzodiazepine,commonly used as an intravenous sedative agent for pre-operative sedation. Dexmedetomidine is an alpha-2 agonist which acts on adrenoreceptors in many tissues including the nervous, cardiovascular and respiratory systems. Unlike midazolam, dexmedetomidine does not affect the ventilatory response to carbon dioxide, it also produces analgesia which could potentially alleviate pain.

KEYWORDS : dexmedetomidine, midazolam, preoperative sedation.

INTRODUCTION

Preoperative anxiety is a frequent condition. Generally, it starts two days before the surgery and reaches its peak just prior to induction of anesthesia. Anxiety is more common among younger patients, women and people with negative experience of anesthesia or fear of death. Anxiety, stress, and fear that arise just before the surgery and anesthesia may lead to psychological trauma and increase the level of stress hormones, resulting in undesirable metabolic responses before anesthesia. High catecholamine levels increase arterial blood pressure, heart rate and oxygen consumption. Controlling this metabolic reaction is a necessity for modern anesthesia. Comfortable anesthesia induction and maintenance can be achieved by controlling anxiety.

Various agents such as phenothiazines, benzodiazepines, barbiturates, opioids, propofol, ketamine, dexmedetomidine or clonidine and antihistamines are used to relieve anxiety and provide sedation. Various agents and routes have been used for preoperative sedation, all have their own merits and demerits. Today, the most frequently used drugs are benzodiazepines. Midazolam is a most common drug from this group with rapid onset and short-lasting effect but after repeated administration, it will result in prolongation of sedation and hangover effects due to relatively long half-life of midazolam and its metabolites. Moreover, it depresses the ventilatory response to carbon dioxide and results in respiratory depression. Dexmedetomidine is an alpha-2 agonist which acts on adrenoreceptors in many tissues including the nervous, cardiovascular and respiratory systems. Unlike midazolam, dexmedetomidine does not affect the ventilatory response to carbondioxide, it also produces analgesia which could potentially alleviate pain. Such a pharmacodynamics profile may have an advantage over midazolam. Therefore, we conducted this study to compare the sedative effects of dexmedetomidine versus midazolam for patients undergoing spinal anesthesia.

In a prospective, randomized controlled study, we tried to assess the comparison between dexmedetomidine and midazolam for preoperative sedation in patients undergoing spinal anaesthesia. We also assessed the intraoperative and postoperative comfort level, cardiovascular and respiratory changes and side effects of both drugs.

MATERIALS AND METHODS

It was a prospective study in which 60 patients were selected who were posted for lower limb surgery and randomly divided into two groups. First group received dexmedetomidine and second group received midazolam. Group D was given Inj. Dexmedetomidine at the dose of 1 mcg/kg within 10 mins in 100 ml NS and group M was given Inj Midazolam at the dose of 0.04 mg/kg in 100 ml NS within 10 mins.

The patient who were selected and posted for lower limb surgeries were assessed. They randomly divided in to two groups, using random number chart. Both were comparable with respect to age, height and ASA grading.

Patients with overnight fasting for 8-10 hours, with no intravenous fluid was given till arrival to operating theatre. Patients received no premedication before arrival in the operation theatre. On arrival in the operating room an IV access was secured using 18g cannula before spinal anesthesia, each patient received an infusion 10-15ml/kg of ringer's solution. Standard monitoring in the form of continuous ECG, pulse oximeter, non invasive automated blood pressure measurements and visual assessment of respiration with body temperature done and baseline values were noted.

Group D – Inj DEXMEDETOMIDINE [1µg.kg-1.was given within 10 min in 100ml NS]

Group M – Inj MIDAZOLAM [dose 0.04mg.kg-1 infused within 10 in in 100ml NS]

Sedation was monitored by Ramsay sedation score. The infusion of sedative agent was taken a minute 0, patients were monitored till they reach ramsay sedation score of 4 then regional anesthesia was performed after obtaining appropriate position and aseptic precautions. Surgery started after achieving desired level of anesthesia. And all the patients were given inj diclofenac before shifting out of operation theatre.

RESULTS

The prospective study was carried out in 60 ASA risk 1&2 patients,

posted for elective lower limb surgeries. The study population was randomly allocated to two groups. Demographic data was analysed using two-tailed student's t-test assuming equal variance for both the study groups.

All the patients in both groups were comparable with respect to their age, sex and ASA status and there is no statistical difference between them(p value > 0.05)

		GROUP D (n=30) (Mean ± SD)	GROUP M (n=30)(Mean ± SD)
AGE (YEAR)		46.8±21.2	41.8±15.8
SEX	M	24	24
	F	6	6

Comparison of PULSE RATE between group D & M

	GROUP D (n=30)	GROUP M (n=30)
ASA 1	1	7
ASA 2	29	23

	GROUP D(n=30)		GROUP M(n=30)	
	Mean	SD	Mean	SD
0 min	87.8	12.79	99.68	17.09
5 min	87.3	11.56	99.06	19.82
10 min	89.7	11.93	98.98	18.83
15 min	80.3	9.95	98.96	21.08
20 min	76.6	9.90	98.72	19.07
25 min	73.9	9.31	98.98	19.00
30 min	72	9.83	98.80	18.18
45 min	71	8.90	99.54	17.97
60 min	71.2	7.86	99.53	16.85
90 min	74.3	9.48	98.96	14.38
120 min	77.4	6.83	99.48	15.34
150 min	79.8	7.09	99.40	14.73

The mean pulse rate was less in GROUP D s compared to GROUP M, and the two difference between the two groups was statistically significant.($p<0.05$).

Comparison of systolic blood pressure and diastolic blood pressure between D &M groups

	SYSTOLIC BLOOD PRESSURE				DIASTOLIC BLOOD PRESSURE			
	GROUP D (n=30)		GROUP M (n=30)		GROUP D (n=30)		GROUP M (n=30)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
0 min	127.41	12.79	137.67	17.09	82.2	7.79	84.27	7.09
5 min	128.8	11.56	138.80	19.82	84.90	8.56	83.67	9.82
10 min	112.2	11.93	136.87	18.83	85.00	9.93	83.20	8.83
15 min	111.5	9.95	130.93	21.08	73.24	9.95	79.67	10.08
20 min	106.4	9.90	124.67	19.07	71.4	9.90	76.00	9.07
25 min	103.9	9.31	120.20	19.00	71.4	9.31	73.80	9.00
30 min	102.4	9.83	119.60	18.18	70.0	9.83	72.27	8.18
45 min	103.7	8.90	122.23	17.97	68.2	8.90	75.00	7.97
60 min	102.00	7.86	123.93	16.85	66.80	7.86	75.93	6.85
90 min	102.90	9.48	126.87	14.38	66.30	9.48	77.33	12.38
120 min	108.20	6.83	129.73	15.34	69.80	6.83	79.73	10.34
150 min	110.40	7.0	131.33	14.73	71.20	7.09	80.80	10.73
180 min	114.40	8.36	132.93	13.21	72.80	8.36	81.07	11.21

The mean systolic pressure and diastolic pressure were less in GROUP D as compared to GROUP M and the difference between the groups was statistically significant ($p<0.05$)

Comparison of RESPIRATORY RATE between D &M groups

	GROUP D(n=30)		GROUP M(n=30)	
	Mean	SD	Mean	SD
0 min	14.53	1.02	13.72	1.06
5 min	13.88	1.53	13.23	1.49
10 min	13.37	1.03	12.41	1.35
15 min	12.41	0.83	12.37	1.46
20 min	12.43	0.88	11.87	0.51
25 min	12.45	1.37	11.87	0.90
30 min	12.56	1.18	12.13	1.26
45 min	12.25	0.66	13.59	0.95
60 min	12.20	0.61	13.74	1.46
90 min	12.57	0.88	13.09	1.00
120 min	13.33	1.37	13.20	1.00
150 min	12.24	0.74	14.05	1.29
180 min	12.40	0.81	13.64	1.38

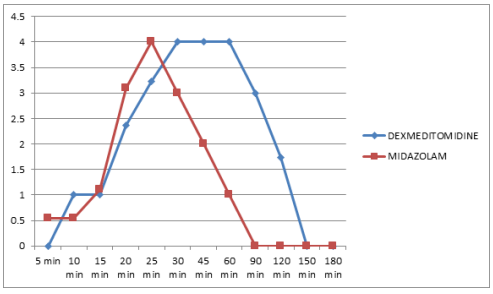
Respiratory rate in group d and group m caused significant decreases in RR as compared to the levels at the onset of administration. The difference in the respiratory rate between the 2 groups was not statistically significant

Comparison of RAMSAY SEDATION SCORE between D &M groups

	GROUP D(n=30)		GROUP M(n=30)	
	Mean	SD	Mean	SD
0 min	0	0	0	0
5 min	0	0	0.54	O.23
10 min	1.00	0	0.54	0.23
15 min	1.00	0	1.10	0.31
20 min	2.37	0.49	3.10	0.31
25 min	3.23	0.43	4	0
30 min	4.00	0	3	0
45 min	4.00	0	2	0
60 min	4.00	0	1	0
90 min	3.00	0	0	0
120 min	1.73	0.45	0	0
150 min	0	0	0	0
180 min	0	0	0	0

RAMSAY SCORE of group M were significantly higher in 20th and 30th min as compared to group D. Ramsay scores of group D were significantly higher than those of groups M at the 30th,45th, 60th,and the 90th minutes($p<0.05$). Signifying early onset and early offset in the group M and late onset and prolonged effect in group D.

Patients were observed for side effects like hypotension , bradycardia, respiratory depression, nausea, vomiting. There were no significant side effects were noted in patients of either group. Only 3 patients underwent hypotension(SBP<80) and bradycardia (HR<60). Intraoperative hypotension was treated by mephentermine and bradycardia was treated with glycopyrrolate in group D patients.



DISCUSSSION

Preoperative anxiety is a frequent condition. Generally, it starts two days before the surgery and reaches its peak just prior to induction of anesthesia. Anxiety is more common among young patients, women, and people with negative experience of anesthesia or fear that arises just before the surgery and anesthesia my lead to psychological trauma and increase the level of stress hormones, result in undesirable metabolic responses before anesthesia. High catecholamine level increases the blood pressure, heart rate, and oxygen consumption. Controlling these metabolic reaction is a necessity for modern anesthesia.

During surgical procedure, both under- and over- sedation carry inherent risk, former increases the likelihood of recall and agitation induced sympathetic activation , and the latter, excessive depression of vital physiological functions. It is important to distinguish sedation scales used to assess the sedation during surgical procedures rather than in patients in intensive care units, because the aim of intraoperative sedation is to provide calmness more than decrease in the level of consciousness.

In our study we have used dexmedetomidine 1mcg/kg dose. Potential side effect of dexmedetomidine, an alpha 2 receptor agonist ,such as hypotension , bradycardia, hypertension, and tachycardia were considered at the planning stage. Hypotension and bradycardia have

been observed in studies earlier. These effects are known to be related to dose, route of administration, and infusion rate. Reports of its use state that alpha 2 agonist effect is observed , but not alpha 1 effect , on administration of low and moderate doses and slow rate of infusion. Consequently , peripheral vasoconstriction and hypertension would not be expected in these instances. Taking these data into account , we elected to use in the dose of 1μg/kg, so as to avoid effects associated with high infusion rates.

In our study we have MIDAZOLAM in dose of 0.04mg/kg. And we found no significant side effects or any significant effect on respiratory system at use of this dose of midazolam(0.04mg/kg). As use of higher doses (0.06) can lead to decrease in respiratory rate and a significant decrease (0.04/0.02) of spo2 s compared to lower doses. And the sedative action of doses (0.04/0.06) are compared to lower doses. And the sedative action of doses (0.04/0.06) are comparable so opted to use 0.04mg/kg .

Dexmedetomidine (1mcg/kg) significantly decreased MAP and HR levels following its sedative effect compared to other groups or pre-sedation levels. The sedative effect of midazolam (0.04mg/kg) decreased after 45 minutes according to Ramsay, MAP levels slightly increased at the 45 and 60 minutes. However, the sedative effect of dexmedetomidine (1mcg/kg) continued at the 45 and 60 minutes, but MAP and HR measurements was not to a level that could compromise hemodynamics of the patients in both groups. These effects were present in both groups with similar sedative characteristics but were more evident on the dexmedetomidine group. In two patients who received dexmedetomidine (1mcg/kg), HR decreased below 60 bpm, and 0.2mg of glycopyrrolate was administered and the heart rate returned to normal within 1 mins. Dexmedetomidine-induced bradycardia was not statistically significant and was not found to be clinically challenging.

When RR and SpO2 values were evaluated, dexmedetomidine (1mcg/kg) caused significant decreases in RR as compared to the levels at the onset of administration. The decrease in SpO2 levels was more evident and resultant hypoxemia was more frequent in group M. The effects of dexmedetomidine (1mcg/kg) on respiratory parameters were reported to be minimal in a number of studies performed with similar doses. We enrolled ASA I-II patients for the study, as they are not much compromised. The average age of the patients in the study groups was approximately 47 years. This can be considered as a limitation of the study as geriatric and more compromised patients may possibly develop respiratory depression and altered hemodynamics.

When sedative effects were compared, Dexmedetomidine (1mcg/kg) causes an evident sedative effect at 25th min and Midazolam (0.04mg/kg) caused an evident sedative effect after 15 minutes according to Ramsay score 4. While the efficacy of Dexmedet omidine(1mcg/kg) persisted after 60 minutes nd then started to decline, the sedative effect of midazolam (0.04mg/kg) decreased. This decrease was suggested to be due to shorter half-life of midazolam (0.04mg/kg).

In our study there are no significant side effects in any patient with dexmedetomidine (1mcg/kg) and Midazolam (0.04mg/kg). Three patients required inj glycopyrrolate for bradycardia in group D. The variations in SpO2 and respiratory rate were negligible in both groups.

CONCLUSION

This study was conducted to compare the efficacy and effects of dexmedetomidine (1mncg/kg) and Midazolam (0.04mg/kg) as preoperative sedation. Ramsay score for sedation, mean arterial pressure, heart rate, and SpO2 measurement including respiratory rates were recorded, every 5 minutes for 30 minutes following infusion then every 15 mins for next 30 mins, then every 30 mins for next 2 hours continuing in the perioperative phase.

Our results indicate that dexmedetomidine is an effective agent for preoperative sedation and its administration results with longer duration of sedation compared to Midazolam which produced comparable sedation but duration of sedation is shorter than dexmedetomidine. We concluded in our study that dexmedetomidine (1mcg/kg) is a safe drug s preoperative sedative in non-compromised patient. With longer duration of sedation, as compared to Midazolam, with better hemodynamic stability, with no respiratory depression and negligible side effects.

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