Original Research Paper

Volume-9 | Issue-12 | December - 2019 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

A COMPARISON OF IV DEXMEDETOMIDINE AND MIDAZOLAM FOR SEDATION IN PATIENTS UNDER NEURAXIAL ANAESTHESIA

Dr. Ajaykumar Anandan MD, Professor, Department Of Anesthesiology, Pain Medicine And Critical Care, Sree Balaji Medical College And Hospital, Biher, Chennai.

Dr. Juvairiya Banu* Junior Resident, Department Of Anesthesiology, Pain Medicine And Critical Care, Sree Balaji Medical College And Hospital, Biher, Chennai. *Corresponding Authour

ABSTRACT

BACKGROUND: Spinal anesthesia is the most widely practiced method of anesthetizing a patient for majority of the infraumbilical surgeries. Several drugs have been used as an adjuvant to prolong the intrathecal block which can be given either intrathecally or intravenously. This study aims at comparing the efficacy of iv dexmedetomidine and midazolam for sedation for patients under neuraxial anesthesia.

MATERIALS AND METHODS: It was a randomized study. 60 patients were enrolled in this study of either sex age group between and American society of Anesthesiology(ASA) physical satus I, II&III Study was conducted after getting informed and written consent. Patients were divided into two groups GROUP D(iv dexmedetomidine) and GROUP M(iv midazolam). Various parameters like HR, MAP, were recorded. Sedation score was recoded using ramsay sedation score 10 minutes, 15 minutes, 20 minutes, 35 minutes, 50 minutes, 65 minutes & 80 minutes.

RESULTS: Among the cases, with respect to the Ramsay Sedation Score, both the groups were statistically comparable and were statistically significant ($P < 0.05$) after 10 minutes, 15 minutes, 20 minutes, 35 minutes, 50 minutes, 65 minutes & 80 minutes. Throughout the mentioned time frame, group D had faster onset of sedation than Group M.

Ramsay's Sedation score in patients who received Dexmedetomidine was of higher grade than those who received Midazolam.

CONCLUSION: Dexmedetomidine had a better satisfactory sedation compared to Midazolam. Midazolam provided a lesser haemodynamic fluctuation compared to Dexmedetomidine throughout the intraoperative period.

KEYWORDS : Dexmedetomidine, Midazolam, Spinal Anesthesia, Sedation

INTRODUCTION:

Surgical exposure is one of the most serious stresses experienced by humans, anxiety and fear tend to influence the morbidity by increasing the neuroendocrine stress response. Neuraxial anaesthesia offers advantages such as being awake during surgery, preservation of spontaneous breathing and preservation of protective airway reflexes such as swallowing and coughing. In addition to this, extended postoperative analgesia, minimised pulmonary complications, early mobilization in post-operative period and shortened duration of hospitalisation are other benefits. On the other hand, wakefulness during surgery may increase concerns including awareness of surgical intervention and pain. Needle fear and recall of procedures are the other undesired concerns regarding regional anaesthesia. Hence, patients may experience intense stress and anxiety, which is unfavourable for the patient, from the anaesthetic and surgical aspect. These issues may be alleviated by sedating the patient during surgery[1]. .Nowadays, anaesthetists are fortunate enough to have agents that can be used either intrathecally or intravenously to enhance the efficacy and duration of the block. They are named **Adjuvants.** Some of the Adjuvants that were previously used are Epinephrine, Magnesium Sulphate, Fentanyl, Midazolam, Clonidine, nowadays Dexmedet omidine is trending.[2,3]

Dexmedetomidine activates the central nervous system and decreases plasma catecholamine level with stimulation of alpha2 adrenoceptors in post-synaptic site, resulting in decrease in heart rate and blood pressure, in addition to sedation and anxiolysis. It was demonstrated to decrease pain and catecholamine response in healthy volunteers.[4,5] This study is to compare the hemodynamic parameters, and sedative effect of Intravenous Dexmedetomidine and Intravenous Midazolam.

RAMSAY SEDATION SCORE

AWAKE LEVELS	Patient anxious or agitated or both	1
	Patient cooperative or tranquil and oriented	2
	Patient responds to commands only	3
ASLEEP LEVELS	A brisk response to a light glabellar tap	4
	A sluggish to a light glabellar tap	5
	No response	6

MATERIALS AND METHODS:

This study was done to compare intravenous Dexmedetomidine and intravenous Midazolam for sedation in patients under Neuraxial Anaesthesia. It was a randomized study. This study was approved by the Institutional Ethical Committee. 60 patients were posted for surgeries at Sree Balaji Medical College and Hospital, Chennai, and were studied .

INCLUSION CRITERIA:

ASA I, II & III patients, Age between 25-65 yrs,Weighing 40-90 kg of both Genders, Patients undergoing elective surgeries with Neuraxial. Anaesthesia with duration of 1 to 2 hrs.

EXCLUSION CRITERIA:

ASA IV Patients, Morbidly obese patients, Chronic alcoholic patients, Pregnant women ,Patients with hepatic diseases

PREANAESTHETIC EVALUATION AND PREPARATION:

1. History and clinical examination.
2. Relevant investigations: Hemoglobin %, urinalysis, renal function test, liver function test random blood sugars, bleeding time, clotting time, Electrocardiograph(ECG) and Chest X ray. Written informed consent was obtained from the patients and their relatives. All patients were maintained nil per oral for 6 hours prior to surgery.

PREPARATION AND PROCEDURE:

Monitors (Non-invasive blood pressure, Pulse Oximetry, ECG, temperature) were connected to the patient.Baseline values of heart rate, systolic and diastolic blood pressure and oxygen saturation was noted. Intravenous cannula inserted and 15-20ml/kg .Crystalloids were started prior to surgery. In patients requiring Epidural 18 GGauge Tuohy's epidural needle was used and confirmed using LOR technique.Epidural catheter was threaded into epidural space and kept in situ for sensory and motor blockade with local anaesthetic agents for the purpose of intraoperative and postoperative pain relief.. Under strict aseptic precautions, after infiltration of skin with 2% lignocaine, subarachnoid block was performed in the sitting position in L3-L4 intervertebral space with 25gauge quincke's spinal needle. After ensuing free flow of CSF, the drug was injected. After injection, the patient was positioned in supine position. The patients were randomly divided into two groups as per computer generated random number.

GROUP D and GROUP M. The patients of GROUP D were given IV Inj. Dexmedetomidine loading dose: 1 mcg/kg over 10 minutes,

followed by infusion of 0.2 to 1 mcg/kg/hour. Any reaction to drug administration was evaluated.

GROUP M patients were given IV 0.01 to 0.1 mg/kg of Midazolam followed by dose of 1mg/hour infusion titrated to achieve desired clinical effect.

PARAMETERS RECORDED:
Heart rate, non-invasive blood pressure and oxygen saturation was monitored every 5 minutes for the first 20 minutes and every 15 minutes till the end of the surgery. Any decrease in mean arterial blood pressure 20% from baseline or less than 90mm systolic blood pressure, was treated with a bolus of Inj. Ephedrine 6mg. Any decrease in pulse rate less than 60% was treated with Inj. Atropine 0.6 mg.

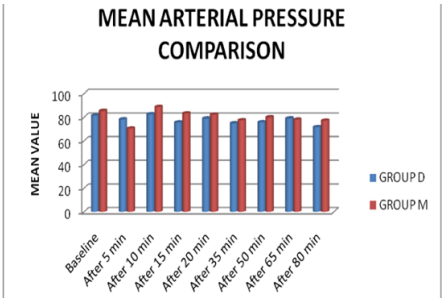
RESULTS

AGE (IN YEARS)	GROUP D	%	GROUP M	%	P-VALUE
21 – 30	11	37	12	40	0.421
31 – 40	7	23	4	13	
41 – 50	12	40	14	47	
TOTAL	30	100	30	100	

Among the total cases, In Group D, 37 % belong to 21 – 30 years, 23 % belong to 31 – 40 years and 40 % belong to 41 – 50 years. In Group M, 40 % belong to the age group 21 – 30 years, 13 % belong to the age group 31 – 40 years and 47 % belong to 41 – 50 years. It is significant from the above table that in both the groups the majority of the age group lies between 41 – 50 years. There was no statistically significant difference found in age between the two groups. (paired t test applied, P Value ≥ 0.05).

HEART RATE
Both the Groups D and M were statistically comparable with regard to the mean heart rate where it was statistically insignificant ($P > 0.05$) during the baseline and after 5 minutes. However, it was statistically significant ($P < 0.05$) in all the other timeframes. Group M showed a higher heart rate during the significance.

MEAN ARTERIAL PRESUURE
Both the Groups D and M were statistically comparable with regard to the mean arterial blood pressure where it was statistically insignificant ($P > 0.05$) during the baseline. However, it was statistically significant ($P < 0.05$) in all the other time frames. Group M showed a higher mean arterial pressure during the significance.

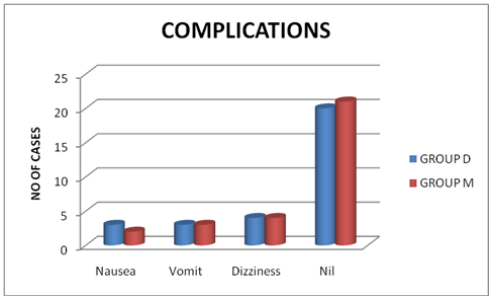


RAMSAY SEDATION SCORE
Among the cases, with respect to the Ramsay Sedation Score, both the groups were statistically comparable and were statistically significant ($P < 0.05$) after 10 minutes, 15 minutes, 20 minutes, 35 minutes, 50 minutes, 65 minutes & 80 minutes. Throughout the mentioned time frame, group D had faster onset of sedation than Group M.

Ramsay's Sedation score in patients who received Dexmedetomidine was of higher grade than those who received Midazolam.

V ATTTIME	GROUP D		GROUP M		p-value
	MEAN	SD	MEAN	SD	
After 10 min	1.72	0.67	1.17	0.41	0.0074
After 15 min	2.76	0.62	2.03	0.59	0.0010
After 20 min	2.41	0.51	1.62	0.42	0.0012
After 35 min	2.39	0.43	1.63	0.51	0.0002
After 50 min	1.94	0.59	1.17	0.32	0.0001
After 65 min	1.42	0.47	1.04	0.07	0.0004
After 80 min	1.39	0.43	1.09	0.02	0.0120

COMPLICATIONS



Among the cases, 67 % did not have major complications, 13 % had dizziness, 10 %had vomit and another 10 % had nausea in the Group D. In the Group M, 70 % had no complications, 7 % had nausea, 10 % had vomit and 13 % had dizziness.

DISCUSSION
Sedation is a patient's reduction of responsiveness to external stimulation. during regional anaesthesia and has different indications. Either an initial bolus or continuous infusion of sedative drugs can be used to provide anxiolysis. Sedation reduces the postoperative recall of intra operative events. Moreover, sedation increases the comfort level during uncomfortable positioning. The drugs used for sedation and analgesia act on the nervous system. One such drug is Dexmedetomidine. This versatile drug is used in general anaesthesia widely, since approved by FDA IN 1986.

Dexmedetomidine is the pharmacologically active dextroisomer of Medetomidine, has an imidazoline structure and is a potent and selective agonist of the alpha-2 adrenoceptor. Dexmedetomidine shows 8 times greater selectivity for alpha-2 than alpha-1 receptors compared with Clonidine. A high density of alpha-2 receptors exists in the locus-ceruleus, a small brainstem structure that is important in modulating vigilance. The locus-ceruleus is part of an endogenous sleep-promoting pathway. These neurons have an inhibitory control over gamma amino butyric acid containing neurons in the ventero-lateral preoptic-nucleus of the anterior hypothalamus and in turn affect the higher centres in the brain associated with the loss of wakefulness. The clinical sedative response of alpha-2 adrenergic agonists is similar to natural sleep and patients are easily arousable and able to follow commands after minimal stimulation. Present evidence suggest that there are 3 major receptors for Dexmedetomidine- alpha-2a, alpha2b and alpha2c predominate in the CNS and is responsible for the sedative, analgesic and sympatholytic components of agonist action.

Midazolam enhances the affinity of the receptors for GABA, as a result of which there is enhanced opening of chloride gated channels resulting in increased chloride conductance. The subsequent enhanced opening of the chloride channels leads to hyperpolarisation of the neurons and resistance to stimulation. Midazolam also acts directly by activation of alpha-1 subunit of GABA receptors whereas anxiolytic effect is due to alpha-2 subunit activity.Alpha1 containing GABA-a receptors are the most numerous accounting for 60%.Alpha-2 subtypes are less common and present in hippocampus and amygdala. GABA receptors are large macromolecules and provide separate attachment sites for GABA, Benzodiazepines, Barbiturates, Etomidate, Propofol, Neurosteroids and Alcohol.

Normal psychological responses to anxiety and fear are usually not harmful; however in a medically compromised patient they may present a risk to the patient. patient's health. Epilepsy, asthma, hypertension and angina are examples of systemic diseases that may be exacerbated by stress. Anxious patients with these medical conditions can often be benefitted from receiving sedation. Anxiety and pain can cause over activity of the sympathetic nervous system leading to hypertension, tachycardia and arrhythmias. Sedation reduces psychological responses to anxiety and fear. Patients who have involuntary movements due to neuromuscular disease (Cerebral Palsy, Parkinson's disease) may wish to but are unable to cooperate. It is often difficult to treat patients with movement disorders safely; and sedation facilitates management in this group of patients also. Various studies have been mentioned in the review of literature that have studied the effects of sedation in patients undergoing surgeries under neuraxial blockade. In the present study, total of 60 cases were included; of which 30 were in group D for whom sedation with inj.

Dexmedetomidine was given intravenously after neuraxial blockade, and 30 in group M for whom inj. Midazolam was given as intravenous sedation. Patients belonging to ASA I, II and III PATIENTS were chosen to avoid the life-threatening complications of the disease which may also influence the observation.

In our study, demographic profile(age, gender) of patients, were statistically insignificant and is comparable in both groups.Patients undergoing elective surgeries like hernioplasty, fistulectomy, haemorrhoidectomy, incision and drainage of perianal abscess, split skin grafting and eversion of sac of hydrocele were included in the study. Patients posted for emergency surgeries were excluded. Haemodynamic effects- heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, oxygen saturation and Ramsay's sedation score were monitored. A significant decrease in pulse rate and mean arterial blood pressure (MAP) were observed when compared with baseline in both groups throughout the surgery but the fall in pulse rate and MAP was greater with Dexmedetomidine infusion upto 45 minutes after spinal anaesthesia when compared with Midazolam which is attributed to decreased sympathetic outflow and circulating catecholamine levels. Intravenous sedation with inj. Dexmedetomidine in Group D showed a better grade of Ramsay's Sedation score compared to inj. Midazolam in Group M.

In a recent study, **Dere et al**[6] concluded that Dexmedetomidine provided better sedation scores and hemodynamic stability. Similarly**, Nirmala B, Chikkahanumanthappa** et al[7] concluded in their study that Dexmedetomidine provided better quality of sedation during regional anaesthesia resulting in superior patient satisfaction than Midazolam. **Y ongxin Liang, Miaoning Gu** et al,[8] also concluded in their study that Dexmedetomidine for sedation was safe and feasible compared to Midazolam.

In contrast to our studies, **Riker** et al[9] performed a study and compared the efficacy and safety of prolonged sedation with Dexmedetomidine and Midazolam for mechanically ventilated patients and concluded that Dexmedetomidine and Midazolam showed no difference in sedation level. The most notable adverse effect of Dexmedetmidine was bradycardia which was the adverse effect noted in our present study.

Kuzucuoglu T et al[10] studied the sedative and hemodynamic effects of Dexmedetomidine and Midazolam and concluded that both Midazolam and Dexmedetomidine provided good sedation and stable hemodynamics, but Midazolam was considered first due to its cost effectiveness.

Changes in pulse rate (bradycardia) and blood pressure(hypotension) observed in our present study was also observed in a study by **Eren** et al[11] who observed significant decrease in blood pressure and heart rate, but it probably normalised increased levels caused by preoperative stress.

CONCLUSION

Dexmedetomidine had a better satisfactory sedation compared to Midazolam. Midazolam provided a lesser haemodynamic fluctuation compared to Dexmedetomidine throughout the intraoperative period. In addition to this, Midazolam has an additional advantage of cost-effectiveness.

REFERENCES

1. WuCL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anaesthesia and analgesia: a systematic review, RegAnesth Pain. Med, 2001, vol 26 (pg 196-208).
2. Liu J,Singh H, White P: Electroencephalographic Bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. AnesthAnalg 1997; 84; 185-9 Liu, J Singh, H White.P .
3. SS Nethra, M Sathestha et al. Intrathecal Dexmedetomidine as adjuvant for Spinal Anesthesia for perianal ambulatory surgeries: A Randomised double blind controlled study. (Indian Journal of Anaesthesia, Year 2015, volume 59, issue:3, page: 177-181.)
4. Kamibayashi T, Maze M. Clinical uses of alpha2- adrenergic agonists. Anesthesiology. 2000; 93 :1345- 1349.
5. ISSA FG Effect of clonidine in obstructive sleep apnea. Am Rev Respir Dis. 1992; 45: 435-438.
6. Macario A, Weinger M, Carney S, Kim A. Which clinical Anaesthesia attempts are important to avoid? The perspective of patients, Anesth Analg,1999 vol.89(pg. 652-8).
7. Kohrs R, Dureaux ME, Ketamine, teaching an old drug new tricks. Anesthanalg, 1998,87: 1186-1193.
8. Lepage C, DroletP, Girard M, et al. Music decreases sedative requirements. Anesthanalg, 2001; 93 : 912:916.
9. Eilers H. Intravenous anaesthetics. In Miller RD & Pardo MC.(eds) Basics of Anesthesia 6th ed. Philadelphia: Elsevier Saunders; 2011. P 99-114.
10. Asehnoune K, Albaladejo P, Smail N, et al. Information and Anesthesia: what does the patient desire? ANN Fr Anesth Reanim, 2000, vol.19 (pg 577-81).
11. KochME, Kain ZN, Ayoub C, Rosenbaum SH, The sedative and analgesic sparing effect of music, anaesthesiology, 1998,89, 300-306.