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INTRAMUSCULAR DEXMEDITOMIDINE AND MIDAZOLAM AS A PREMEDICATION IN PAEDIATRIC SURGICAL PATIENTS, A DOUBLE BLIND RANDOMIZED CONTROL STUDY

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ABSTRACT

Aims and Objective-

- To compare between intramuscular Dexmeditomidine and Midazolam as premedication in paediatric surgical an aesthesia.
- To compare anxiolysis produced by Dexmeditomidine and Midazolam perioperatively.
- To study the post operative recovery by analgesic requirement in patients receiving Dexmeditomidine compared with Midazolam.

Materials and Methods: A prospective randomized, double blind study involving 60 children undergoing short procedures was conducted. The patients were divided in to 2 groups each involving 30 patients. One group received Dexmeditomidine 1.5 mg/kg and other received Midazolam 0.05mg/kg IM 45 min preoperatively. The efficacy of sedation was assessed using Ramsay Sedation Score. **Results:** Hemodynamic parameters between the 2 groups were comparable. All sedation scores were comparable in the Dexmeditomidine and Midazolam group. Only 3 children required postoperative analgesia in Dexmeditomidine group, while 7 children in Midazolam group required postoperative analgesia. **Conclusion:** Dexmeditomidine facilitates adequate sedation as premedication as compared to Midazolam.

KEYWORDS: Dexmeditomidine and Midazolam.

INTRODUCTION

The problem with paediatric patients is anxiety, apprehension with restlessness during separation from the parents, crying and agitation. This perioperative anxiety is shown to delay the induction of anaesthesia[1] and provoke release of stress hormones which hinders recovery. For perioperative sedation and anxiolysis, Midazolam (Benzodiazepine) is used intramuscular since decades. When given preoperatively Midazolam relieves anxiety, provides sedation and anterograde amnesia of perioperative events. Midazolam has been administered as a hypnotic for the short term management of amnesia.

Dexmeditomidine is a potent and highly selective Alpha2 adrenorecptor agonist providing sedation and analgesia. Intramuscular Dexmeditomidine is considered as a premedication to produce anxiolysis, sedation and it does not produce respiratory depression. It also decreases the opioid requirement in the perioperative period. In the last few years it has emerged as a promising therapeutic drug in wide range of anaesthetic management for perioperative period. This study analyses and compares the efficacy of Midazolam and Dexmeditomidine used intramuscularly as a premedication in paediatric surgical procedures.

MATERIALS AND METHODS

After the approval of the institutional ethical committee of KIMS and informed consent from the parents, this study was conducted in the department of Anaesthesiology, KIMS, Karad.
This randomised, double blind, comparative parallel group study involving 60 paediatric surgical patients was done by distributing these patients into two equal groups having 30 patients each.

This study was carried out as a part of our routine anaesthetic services in paediatric patients
Inclusion Criteria:

- Age group between 3-14 years
- ASA grade I & II
- Short surgical procedures lasting for 90 minutes or less.

Exclusion Criteria

- ASA grade III and higher
- Surgery lasting for more than 90 minutes
- Congenital disorders predicted difficult airway
- Pre-existing psychiatric diseases

Anaesthesia Technique

On arrival in the preoperative room after assessing the hemodynamic parameters, intramuscular premedication was given as per randomization. In the preoperative room before shifting the patient to operation theatre sedation level was assessed using Ramsay Sedation Score every 10 minutes with 6 points for maximum 45 minutes and then the patient was shifted to operation theatre.

Premedication was administered to each patient as per dose chart

Table No-1 Dose Chart

	Route	**Dose**	**Time Before Induction**
Group I Midazolam	Intramuscular	0.05mg/kg	45Min
Group II Dexmeditomidine	Intramuscular	1.5mcg/kg	45Min

Table No- 2 Ramsay Sedation Score

Score Response	**Anxious or Restless or both**	**Co-operative, oriented and tranquil**	**Responding to commands**	**Brisk response to stimulus**	**Sluggish response to stimulus**	**No response to stimulus**
Score	1	2	3	4	5	6

Satisfactory sedation score: 4-6.

Standard technique for delivering anaesthesia was maintained for all patients.

After placement of standard monitoring each child received an intravenous canula and was given 1 microgram/kg Fentanyl and anaesthesia was induced with inhalation Sevoflurane 2.5% in oxygen by modified Jackson Rees anaesthesia system via face mask gently kept on face. Endotracheal intubation was performed in all cases without muscle relaxant, thereafter maintained with Sevoflurane (2-4%) in nitrous oxide (60%) and oxygen (40%) at normocapnia as judged by continuous end tidal CO2 monitoring. Intravenous infusion was started using Ringers Lactate solution at the rate of 4ml/Kg/hr. Extubation was done at the end of the surgery when awake. Behaviour at teh awakening was evaluated with 4 points wake up score.

Table No-3 Wake up Score

Score Response	Calm And Cooperative	Not Calm But Easily Calmed	Not Easily Calmed, Moderately Agitated And Restless	Combative, Excited And Disoriented
SCORE	1	2	3	4

Satisfactory wake up score: 1-2.

Postoperative pain was assessed every hour for 6 hours. The recovery time was assessed and observed for 6 hours.

Analgesia dose of Fentanyl 0.5 microgram/kg was given when patient was in pain and demanding analgesia. The time at which the patient required first analgesia was recorded and supplemental analgesia administered. The study ended 6 hours post operatively. The results obtained were subsequently entered in the statistical analysis after completion of the entire study and decoding of the study.

OBSERVATION AND RESULTS

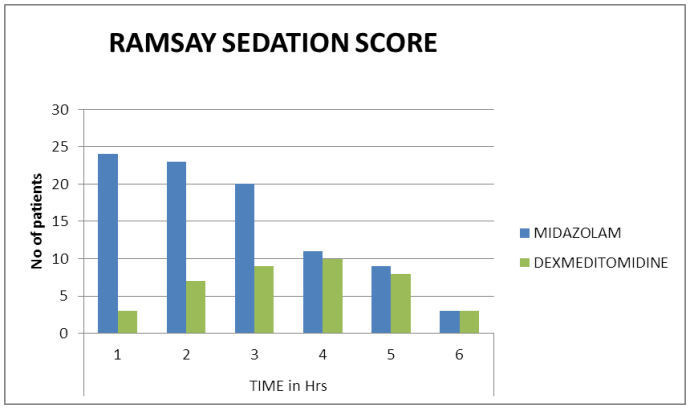
The demographic data of two groups was comparable. There was no statistical difference in type and duration of surgery.

There was no statistical as well as clinically significant difference in the hemodynamic parameters of the two groups.

Table No-4 Ramsay Sedation Score

Sedation Score at 45 minutes	Group 1 (Midazolam)	Group II (Dexmeditomidine)	P value
1	0	0	
2	5(16.6%)	0	
3	8(26.6%)	3(10%)	
4	15(50%)	7(23.3%)	
5	2(6.6%)	14(46.6%)	
6	0	6(20%)	
Acceptable levels4-6	17(56.6%)	27(90%)	0.0074

Statistical test- Fisher's exact Test statistical software graph pad Instat version 3.06



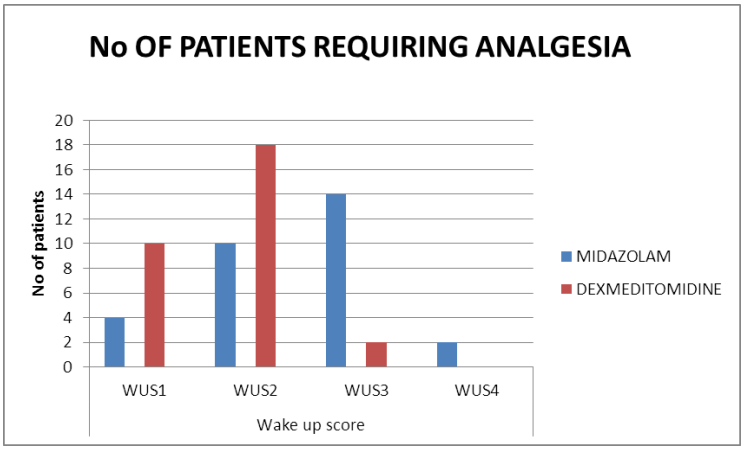
Graph No 1- Ramsay Sedation Score

- 7 out 30 patients in the Midazolam Group achieved adequate sedation, while in Dexmeditomidine group 27 out 30 patients achieved adequate sedation.
- Dexmeditomidine group achieved satisfactory sedation than the Midazolam group.
- Sedation Scores were statistically significant in Dexmeditomidine group compared to Midazolam group.
- P value 0.0074.

Table No- 5 Wakeup Score

Wakeup Score	Group I	Group II	P value
1	4(13.3%)	10(33.3%)	
2	10(33.3%)	18(60%)	
3	14(46.6%)	2(6.6%)	
4	2(6.6%)	0	
Acceptable level (1,2)	14(46.6%)	28(93.3%)	0.0001

Premedication with Dexmeditomidine not only reduces the opioid requirement but it also reduces the dose requirement of analgesic agents.



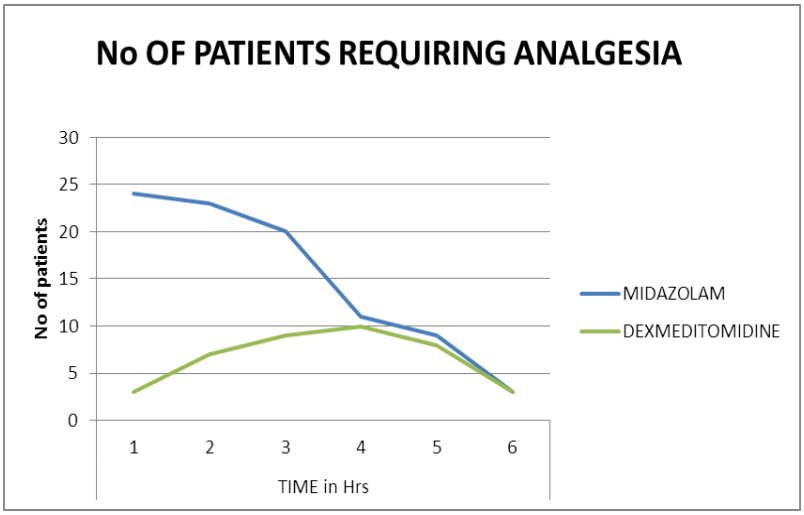
Graph No-2 Wake up Score Graph

- 14 patients out 30 in Midazolam Group achieved satisfactory wakeup score.
- 28 out of 30 patients in Dexmeditomidine group achieved satisfactory wakeup score.
- Good number of children in the Dexmeditomidine group achieved satisfactory wakeup score of 1or 2 as compared to Midazolam group.

Number of patients requiring Postoperative Analgesia.

Table No-6 FPS-R Face pain scale- Revised

Post Op Pain Scale	Group I Midazolam	Group II Dexmeditomidine	P Value	95% confidence Interval
1	24	3	<0.0001	2.694 to 23.761
2	23	7	<0.0001	1.994 to 7.460
3	20	9	0.0092	1.217 to 4.059
4	11	10	1.000	0.5512 to 2.195
5	9	8	1.000	0.5020 to 2.521
6	3	3	1.0000	0.2190 to 4.566



Graph No-3 FPS Graph

DISCUSSION

In children the most commonly used analgesic is Midazolam. It increases Gamma amino butyric Acid (GABA) receptor mediated chloride conductance, which has an inhibitory effect on neurons in the cerebral cortex. Midazolam is used intravenous, intramuscular and by intranasal route.[3]

Nowadays Dexmeditomidine, an alpha 2 receptor agonist is found to be useful for premedication in children. It acts on central alpha 2 receptors which are located at the presynaptic terminal where they inhibit the release of nor adrenaline.[4, 5] The site of action of

this drug is the locus Coerulus where it causes EEG activity similar to normal slip. This results in anxiolytic effects, sedation and analgesia without excessive drowsiness.[6] As there is no need of deep preoperative sedation[7] many studies have used a low dose intramuscular Midazolam 0.05mg/kg.[8,9,10,11]

Low dose of Dexmeditomidine 1.5microgram/kg was used to prevent unwanted hemodynamic changes and other side effects.[12]

We have chosen the doses as per previous studies to prevent unwanted side effects.[7]

Most commonly used drug for premedication is Midazolam. When used intranasally or orally it causes unpleasant burning sensation and irritation in the nasal cavity and throat. Dexmeditomidine was used intramuscularly only. Sedative effect of IM Dexmeditomidine is observed at 45- 60 minutes.[13, 14]

The parameters were found to be identical in the 2 groups. All the scores were used for comparison in this study were standard. Sedation scores were compared using Ramsay Sedation score.[15, 16]

Post operative pain was evaluated by Free Pain Scale Revised.[17]

Sedation and anxiolysis effects of intra muscular Midazolam and Dexmeditomidine were compared. Dexmeditomidine and Midazolam induced comparable pre-operative sedation and anxiolysis. It suggests that pre-treatment with a single intramuscular injection of Dexmeditomidine is effective than Midazolam.

Our results were also similar and comparable concluding Dexmeditomidine is better than Midazolam as a premedication with respect to sedation, anxiolysis.

Dexmeditomidine when used in high doses causes bradycardia and hypertension occasionally. Most studies using high dose of Dexmeditomidine were predominantly adopted with the dose finding study performed by Erkola, AhoM and colleagues,[14] who reported that 2.5 microgram/kg dose of intramuscular Dexmeditomidine is comparably sedative and anxiolytic to 0.08mg/kg Midazolam.

However few investigations have addressed the clinical effects of low dose Dexmeditomidine as premedication.

Jaakola M conducted a study to evaluate the use of intramuscular Dexmeditomidine as premedication and alternative to Midazolam- Fentanyl combination.[13]

Kamal K[x] evaluated the effects of oral Dexmeditomidine with Midazolam and found that Dexmeditomidine is better than Midazolam in post operative recovery profile in children. This is comparable with our study.[18]

CONCLUSION

Dexmeditomidine facilitates adequate sedation, anxiolysis as compared to Midazolam and hence Dexmeditomidine is a superior drug as compared to Midazolam as intramuscular premedication in paediatric age group.

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