Original Research Article

A comparative study to evaluate the efficacy of intranasal dexmedetomidine versus intranasal midazolam as premedicant in children

Jayashree[1], Asrar Hussain[2*], Humaira[3]

[1]Associate Professor, [2]Assistant Professor, [3]Post Graduate of Anesthesia
Deccan College of Medical Sciences, Hyderabad, India
*Corresponding author email: **asrar.king@gmail.com**

International Archives of Integrated Medicine, Vol. 7, Issue 2, February, 2020.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 03-02-2020 **Accepted on:** 09-02-2020
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Jayashree, Asrar Hussain, Humaira. A comparative study to evaluate the efficacy of intranasal dexmedetomidine versus intranasal midazolam as premedicant in children. IAIM, 2020; 7(2): 94-100.

Abstract

Background: Pediatric surgery amounts for enormous stress due to anesthesia and surgery for the children. This study was mainly undertaken to assess the efficacy and safety of Midazolam and dexmedetomidine as premedicants in children.

Material and methods: A randomized controlled trial was undertaken in 100 children belonging to ASA Grades I and II posted for surgery in a Institute of Medical sciences hospital were divided equally in to two groups. One group received Dexmedetomidine and other received Midazolam. A baseline heart rate, respiratory rate, systolic blood pressure and activity of the child were noted in the pre-operative room. The premedicant was administered and after 30 minutes, a standard general anesthesia procedure was administered.

Results: About 36.7% of children in Dexmedetomidine group and 10% in Midazolam group had their eyes closed but verbally arousable, 33.3% of dexmedetomidine and 40% of the Midazolam group had their eyes closed but arousable with light physical stimulation. About 43.3% of the Dexmedetomidine group children and 46.7% of the Midazolam children had moderate fear of mask, co-operative reassurance and 36.7% of the children in Dexmedetomidine group and 30% in Midazolam group were combative, crying.

Conclusion: Dexmedetomidine was shown to be effective than Midazolam in Parental separation, pre induction and sedation.

Key words

Dexmedetomidine, Midazolam, Premedicant, Pre induction score, Parental separation, Pain score.

Introduction

Pediatric surgery amounts for enormous stress due to anesthesia and surgery for the children. The stress can be due to separation from the parents, strange surroundings, painful procedures, frightening procedures and also survival [1]. This warrants for the effective predication for pediatric patients posted for surgery. Pediatric patients are more uncooperative during securing IV line, IV/IM drug administration, separation from parents and induction of anesthesia [2, 3].

The literature available has shown that about 50 - 75% of the children shows signs of significant preoperative fear and anxiety [4]. It has also been reported that there are correlations between the heart rate, blood pressure and behavioral ratings of anxiety [5]. In order to alleviate physiological and psychological effects of preoperative anxiety in children, most anesthesiologists use either parental presence or sedative premedication, since separation from parents and induction of anesthesia are considered the most perioperative stress inducing phases. Both approaches are considered appropriate choice of interventions. Anesthesiologists who allow parental presence during induction of anesthesia, use sedative premedication least frequently, and vice versa [6].

The drugs which are commonly used for sedation and anxiolysis are midazolam, keatmine, clonidine and dexmedetomidine. Route of administration of these drugs is mainly parenteral, which make it more invasive and painful [7].

The ideal premedication in children should be readily acceptable and should have a rapid and reliable onset with minimal side effects. Midazolam is a water soluble benzodiazepine and most commonly used sedative premedicant in children. The advantages of midazolam include rapid onset, effective sedation, anterograde amnesia, anxiolysis and reduction in post-operative vomiting. However, the undesirable effect such as restlessness, hiccups and paradoxical hyperactive reaction, that accompany the use of midazolam render this drug a less than ideal sedative [8].

Dexmedetomidine is a highly selective alpha – 2 agonist with both analgesic and sedative effects. It produces a type of sedation recognized as cooperative or arousable which is different from the clouding of consciousness sedation included by drugs acting on the GABA system. These characteristics make it potentially useful for anesthesia premedication in children [15]. This study was mainly undertaken to assess the efficacy and safety of Midazolam and dexmedetomidine as premedicants in children.

Materials and methods

A randomized controlled trial was undertaken in 100 children belonging American Society of Anesthesiologists (ASA) Grades I and II of both sexes, aged between 2 and 7 years who posted for surgery in a Institute of Medical sciences hospital. An informed consent, written and bilingual consent was obtained from the parents of the children before they were included in to study. Ethical clearance was obtained from the institutional ethical committee. Children without other co morbidities, Children undergoing elective surgeries only, American Society of Anesthesiologists (ASA) physical status I and II, No Known history of allergy, sensitivity or any other form of reaction to the drugs used and parents willing to sign informed accent were included in the study. Children with chronic pain and central nervous system disorders, Nasal deformity, rhinitis, nasal polyps and other nasal diseases, Previous reactions to dexmedetomidine or benzodiazepines, Patients with ASA grade $\leq$ 2, Patient scheduled to undergo emergency surgery were excluded from the study.

The patients thus selected were randomly divided into two groups Group D and Group M, each comprising of 50 children by using a computer generated random numbers.

Group D children received dexmedetomidine, 1 µg/kg intranasally 40-45 min prior to anesthesia induction. Group M children received midazolam 0.2 mg/kg intranasally 40-45 min prior to anesthesia induction.

The child's condition was evaluated just before induction by the surgeons with a scale assigning score of 1 to 4 to quality of sedation, anxiolysis and behavior at parental separation, while side effects were assessed by the anesthetist conducting the case. A thorough pre anesthetic examination was conducted on all children before surgery. All observers including anesthesiologists, surgeons and nurse were blinded about the contents of the premedicant. A baseline heart rate, respiratory rate, systolic blood pressure and activity of the child were noted in the pre-operative room. The pre medicant was administered and after 30 minutes, a standard general anesthesia procedure was administered.

The data thus obtained was collected in a predesigned proforma and entered in to a spread sheet. The data was transferred to Statistical Package for Social Services (vs 20). The data analysis was performed by unpaired Student's t test and Chi Square test. A P value of < 0.05 was considered as statistically significant and $P < 0.0001$ was considered as highly significant.

Results

The mean (± SD) age of the Dexmedetomidine group was 4.32 (± 1.6) years and Midazolam group was 4.2 (± 1.57) years. There was no statistically significant difference between the age of the Dexmedetomidine group and Midazolam groups. About 26.7% of the dexmedetomidine and 36.7% of the Midazolam group were aged 4 years. About 60% of the dexmedetomidine and 50% of the Midazolam group were males. About 40% of the Dexmedetomidine and 50% of the Midazolam group were females. The mean weight of the dexmedetomidine group was 9.1 (± 3.2) kg and Midazolam group was 10.2 (± 2.67) kg. About 96.0% of the subjects in both the groups were categorized as ASA grade I and 4.0% of the subjects in both the groups were categorized as ASA grade II. The mean duration of surgery in Dexmedetomidine group was 65.0 (± 16.07) minutes and 60.1 (± 12.4) minutes in Midazolam group. This difference in duration of surgery was not statistically significant (**Table – 1**).

Table – 1: Distribution of the study group according to age.

		Group	
		Group D [N (%)]	**Group M [N (%)]**
Age group	**2**	9 (18.0)	11 (22.0)
	3	5 (10.0)	2 (4.0)
	4	15 (30.0)	20 (40.0)
	5	10 (20.0)	7 (14.0)
	6	4 (8.0)	4 (8.0)
	7	7 (14.0)	3 (10.0)
Sex	**Male**	30 (60.0)	22 (44.0)
	Female	20 (40.0)	28 (50.0)
Weight in kg	**Mean ± SD**	9.71 ± 2.79	10.2 ± 2.67
ASA Grade	**I**	48 (96.0)	49 (98.0)
	II	2 (4.0)	1 (2.0)
Duration of surgery in min	**Mean ± SD**	65.0 ± 16.07	60.1 ± 12.4

Table – 2: Distribution of the study group according to behavior at parental separation.

Behavior at parental separation	Group	
	Group D [N (%)]	Group M [N (%)]
Completely awake & oriented	0	0
Sleepy and drowsy, eyes open	3 (10.0)	9 (30.0)
Eyes closed but verbally arousable	11(36.7)	3 (10.0)
Eyes closed but arousable with light physical stimulation	10 (33.3)	12 (40.0)
Eye closed bout not arousable with physical stimulation	6 (20.0)	6 (20.0)
Total	30 (100)	30 (100)

χ^2 value= 7.753 df=3 P value= 0.051, NS

Table – 3: Distribution of the study group according to Pre-induction scores.

Pre induction sedation scores	Group	
	Group D [N (%)]	Group M [N (%)]
Calm, cooperative or asleep	6 (20.0)	7 (23.3)
Moderate fear of mask, cooperative reassurance	13 (43.3)	14 (46.7)
Combative , crying	11 (36.7)	9 (30.0)
Total	30 (100)	30 (100)

χ^2 value= 0.314 df=2 P value= 0.855, NS

Table – 4: Distribution of the study group according to modified objective pain score.

Modified objective pain score	Group	
	Group D [N (%)]	Group M [N (%)]
0 – 3	4 (13.3)	10 (33.3)
4 – 6	10 (33.3)	14 (46.7)
7 – 9	16 (53.3)	6 (20.0)
Total	30 (100)	30 (100)

χ^2 value= 7.784 df=2 P value= 0.02, Sig

Table – 2 shows that about 10% of children in Dexmedetomidine group and 30% of the children in Midazolam group were sleepy and drowsy, eyes open, 36.7% of children in Dexmedetomidine group and 10% in Midazolam group had their eyes closed but verbally arousable, 33.3% of dexmedetomidine and 40% of the Midazolam group had their eyes closed but arousable with light physical stimulation and 20% in both the groups had eyes closed but not arousable with physical stimulation. This difference in behavior at parental separation was statistically not significant between both the groups.

The pre induction scores have shown that, about 20.0% of the Dexmedetomidine group children and 23.3% of the Midazolam group children were calm, cooperative or asleep, 43.3% of the Dexmedetomidine group children and 46.7% of the Midazolam children had moderate fear of mask, cooperative reassurance and 36.7% of the children in Dexmedetomidine group and 30% in Midazolam group were combative, crying. There was no statistically significant difference between the Pre-induction sedation scores between the two groups (**Table – 3**).

Table - 4 shows the distribution of study groups according to Modified objective pain score. About 53.3% of the study subjects had a score of 7 – 9, 33.3% had a score of 4 – 6 and 13.3% had a score of 0 – 3. In the Midazolam group, 46.7% had score of 4 – 6, 33.3% had a score of 0 – 3 and 20% had a score of 7 – 9. This difference was statistically significant.

Discussion

Anesthesia and surgery represent a huge time of stress for the kid. The ideal premedication in children should be readily acceptable and will have a rapid and reliable onset with minimal side effects. The drugs which have been tried as premedication is ketamine, it is an easily administered parenteral anesthetic that produces profound analgesia in sub anesthetic doses and lacks the cardio-respiratory depression seen with most other general anesthetics, but it produces excessive salivation and hallucination [8].

The difficulty in securing IV line, excessive cry and apprehension, intranasal (Dexmedetomidine and Midazolam) help us to get rid of apprehension, several unwanted pricks to secure IV line, excessive crying and achieve the goal, i.e. pediatric patients free from anxiety, inapprehensive about separation from parents and uncooperative during induction of anesthesia.

The mean (± SD) age of the Dexmedetomidine group was 4.32 (± 1.6) years and Midazolam group was 4.2 (± 1.57) years. About 26.7% of the dexmedetomidine and 36.7% of the Midazolam group were aged 4 years. About 60% of the dexmedetomidine and 50% of the Midazolam group were males. Yuen, et al., have also noticed similar results in their study [9].

About 96.7% of the subjects in both the groups were categorized as ASA grade in this study. The mean duration of surgery in Dexmedetomidine group was 65.1 (± 16.07) minutes and 60.1 (± 12.4) minutes in Midazolam group which was not statistically significant. Yuen, et al. have noticed that the mean duration of the surgery was 27.7 min in midazolam group, 29.5 min in 0.5 µg/kg of dexmedetomidine and 33.4 min in 1 µg/kg of dexmedetomidine group [9]. In a study by Ghali, et al., the mean duration of surgery in dexmedetomidine group was 38.23 min and in midazolam group was 36.65 min [10]. In a similar study by Mostafa, et al., the mean duration of surgery in midazolam group was 18.52 minutes and Dexmedetomidine group was 19.02 minutes [11]. Sundaram, et al., have noticed that the mean duration of surgery in midazolam group was 34.5 minutes and 43.6 minutes in Dexmedetomidine group [12].

About 10% of children in Dexmedetomidine group and 30% of the children in Midazolam group were sleepy and drowsy, eyes open, 36.7% of children in Dexmedetomidine group and 10% in Midazolam group had their eyes closed but verbally arousable, 33.3% of dexmedetomidine and 40% of the Midazolam group had their eyes closed but arousable with light physical stimulation and 20% in both the groups had eyes closed but not arousable with physical stimulation. In a study by Yuen, et al., the successful parental separation was found in 96.9% of the midazolam group, 93.7% in 0.5 µg/kg of dexmedetomidine and 100% in 1 µg/kg of dexmedetomidine group [9]. In a study by Mostafa, et al., about 87.5% of the midazolam group and 93.75% of the dexmedetomidine group had child parent separation score grade I [11]. In a study by Sivrikaya, et al., the mean parental separation score was 3 in dexmedetomidine group and 3 in midazolam group [14]. In a study by Sundaram, et al., the successful separation was present in 95% in midazolam group and all the patients in dexmeditomidine group [12].

The pre induction scores have shown that, about 20.0% of the Dexmedetomidine group children and 23.3% of the Midazolam group children were calm, cooperative or asleep, 43.3% of the Dexmedetomidine group children and 46.7% of the Midazolam children had moderate fear of mask, cooperative reassurance and 36.7% of the children in Dexmedetomidine group and 30% in Midazolam group were combative, crying. Yuen, et al. have noticed that the sedation at induction was satisfactory in 18.8% of the midazolam group, 40.6% in 0.5 µg/kg of dexmedetomidine and 53.1% in 1 µg/kg of dexmedetomidine group [9]. In a study by Faritus, et al., the behavior at anesthesia induction time revealed that more children receiving dexmedetomidine are calm

and cooperative well in terms of mask acceptance while number of patients with mask acceptance behaviors, anxious but without resistance, was higher in midazolam group [13]. In a study by Sivirkaya, et al., the mean mask acceptance score was 4 in dexmedetomidine group and 3 in midazolam group [14]. In a study by Sundaram, et al., the induction was satisfactory in 62.5% of the midazolam group and 65% of the dexmedetomidine group [12].

About 53.3% of the study subjects had a score of 7 – 9, 33.3% had a score of 4 – 6 and 13.3% had a score of 0 – 3. In the Midazolam group, 46.7% had score of 4 – 6, 33.3% had a score of 0 – 3 and 20% had a score of 7 – 9. In a study by Ghali, et al., children in dexmedetomidine group had significantly lower levels of pain in the first two hours postoperatively compares with the same values in midazolam group [10].

All the children in Dexmedetomidine group had no post-operative nausea and vomiting. About 10% of children in Midazolam group had nausea/ vomiting and 90% had no nausea/vomiting. Mostafa, et al., have noticed that there was no significant nausea or vomiting [11]. In a study by Faritus, et al., no case reported to have nausea and vomiting in Midazolam and dexmedetomidine group [13].

Conclusion

This study was mainly undertaken to compare the effectiveness and efficacy of Dexmedetomidine and Midazolam group as premedicants in children undergoing surgery. In this study, dexmedetomidine was shown to be effective than Midazolam in Parental separation, pre induction and sedation.

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