



EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AND EMERGENCE DELIRIUM AMONG CHILDREN UNDERGOING INGUINAL HERNIA REPAIR UNDER GENERAL ANESTHESIA

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ABSTRACT

Introduction: Addressing child anxiety during medical procedures is a growing trend and dental treatment is not an exception. In today's dentistry, parents and caregivers may not be contented with some non-pharmacological behavior management techniques. The present study is designed to assess the magnitude of emergence delirium and parental separation anxiety among children. Thereby some strategies could be devised to overcome this morbidity and to improve quality of life of these children.

Objective: To determine the effect of preoperative oral midazolam sedation on separation anxiety and emergence delirium among children undergoing inguinal hernia repair under general anesthesia

Setting: Mayo Hospital Lahore, from February 2020 to January 2021.

Design: Descriptive cross sectional study

Subject and Methods: A total of 82 children undergoing inguinal hernia repair were included in this study. Children age, weight, height measured and pre medicated with 0.5 mg/kg (maximum total dose was 20 mg) of oral Midazolam in 20 ml of 10% sodium citrate solution, 30 min prior to induction. Premedication was done 10–15 min prior to separation from parents and 20–25 min prior to intubation. ALL information was noted in the Performa attached as annexure.

Results: - The average age of the patients was 44.44±19.12 years. Effectiveness of preoperative oral midazolam sedation on separation anxiety and emergence delirium among children undergoing inguinal hernia repair was 60.98% and 74.39% respectively.

Conclusion: - Oral Preoperative Midazolam in a dose of 0.5 mg/kg might be a useful treatment adjunct in reducing parental separation anxiety, and for ease of anesthesia induction. Preoperative

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Midazolam sedation has no reducing effect on postoperative ED in children undergoing dental treatment under general anesthesia.

Key Words: - Oral midazolam, Anxiety and emergence delirium, Inguinal hernia repair.

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INTRODUCTION

Addressing child anxiety during medical procedures is a growing trend and dental treatment is not an exception.^[1] In today's dentistry, parents and caregivers may not be contented with some non-pharmacological behavior management techniques such as voice control, hand over mouth, and intimidation.^[2] When treating a child with limited cooperation margin due to fear or anxiety, the use of physical restraining might not result in a satisfactory outcome, especially if the child is in need of comprehensive dental treatment which may necessitate the use of general anesthesia. Physical restraining in the dental office affects the image of the pediatric dentist and may harm the self-respect of the child at a very young stage of psychological development not to mention the legal implications of harming a vulnerable human being.^[3] Dental General Anesthesia (DGA) might save the child from the psychic trauma he/she might get in the dental office and may help deliver better quality of dental treatment; however, when a pediatric dentist decides to expose his/her patient to the calculated risk of general anesthesia, the decision should not substitute psychic trauma in the dental office with another psychic trauma in the operating theater in the form of parental separation anxiety with the added psychic trauma of physical restraining during induction of anesthesia. A survey conducted by Homer and Bass in 2010^[4] showed that up to 60% of anesthetists frequently use physical restraints on resistant and fearful children. In 2009, Sheta and AlSarheed^[5] studied the anxiolytic effect of different doses of Midazolam on 60 children aged 2–6 years undergoing DGA. They reported that satisfactory anxiolytic effect can be achieved with higher doses which raised the potential risk of some adverse effects. In 2011, Mountain *et al.*^[6] conducted a study to compare the effects of Midazolam versus Dexmedetomidine premedication on

preoperative anxiety and postoperative emergence delirium (ED) on 41 children aged 1–6 years and concluded that the latter has an advantage of reducing the incidence of postoperative ED. The parental separation anxiety and emergence delirium was found in 33.33% and 30.77% in children respectively sedated with preoperative midazolam.^[7]

There is dearth of literature locally on this topic therefore the present study is designed to assess the magnitude of emergence delirium and parental separation anxiety among children. Thereby some strategies could be devised to overcome this morbidity and to improve quality of life of these children.

MATERIAL & METHODS

Study Design: Descriptive cross sectional study

Setting: Department of Anaesthesia, Abbasi Shaheed Hospital, Karachi

Duration: 06 months, from.....to.....

Sample size:

Proportion of emergence delirium: 0.308 [7]

Confidence level: 95%

Absolute precision: 0.1%

Sample size: 82 children undergoing inguinal hernia repair

Sampling Technique: NonProbability Consecutive

Sample Selection:

▪ **Inclusion Criteria**

❖ Healthy, American Society of Anesthesiology (ASA) I children

❖ Age range 2 to 7 years

❖ Undergoing inguinal hernia repair

▪ **Exclusion Criteria:**

❖ Children with history of allergy to Midazolam

❖ History of post-anesthesia ED

❖ Children with ASA scores greater than I

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- ❖ Mental retardation, physical developmental delay, preoperative agitation

DATA COLLECTION PROCEDURE

Prior to the conduct of the study approval from the institutional ethical committee and College of Physicians and surgeons Pakistan was obtained. Children matching the inclusion criteria, attending, outpatient Department of Paediatric Surgery Abbasi Shaheed hospital, Karachi was enrolled in the study. The purpose procedure, risk and benefits of the study was explained, confidentiality was ensured and informed consent was obtained from their parents. Children age, weight, height was measured and pre medicated with 0.5 mg/kg (maximum total dose was 20 mg) of oral Midazolam in 20 ml of 10% sodium citrate solution, 30 min prior to induction. Premedication was done 10–15 min prior to separation from parents and 20–25 min prior to intubation, by an anesthesia assistant.

Children were not allowed to eat or drink for at least 6 h before the procedure. Induction was carried out via a facemask with 8% Sevoflurane (Abbott Co. North Chicago, Illinois, USA) in 100% oxygen. After loss of consciousness, an intravenous line was established through which Propofol (Diprivan®; AstraZeneca Co. London, UK.) was administered to allow nasotracheal intubation. Anesthesia was maintained with 2–3% Sevoflurane® in a mixture of oxygen and nitrous oxide.

Parental Separation Anxiety Scale (PSAS) was used to assess parental separation anxiety. A score of 3–4 was considered as Parental Separation Anxiety. Paediatric Anaesthesia Emergence Delirium Scale (PAEDS) was used to assess ED. Out of 20 points, a score greater than 10 was counted as ED. Scoring for PAEDS was done at the peak of the ED episode. This information along with demographics like age, weight, gender and duration of anaesthesia was noted in the proforma attached as annexure.

DATA ANALYSIS PROCEDURE

SPSS version 17 for windows was used for data analysis. Age, weight of the children,

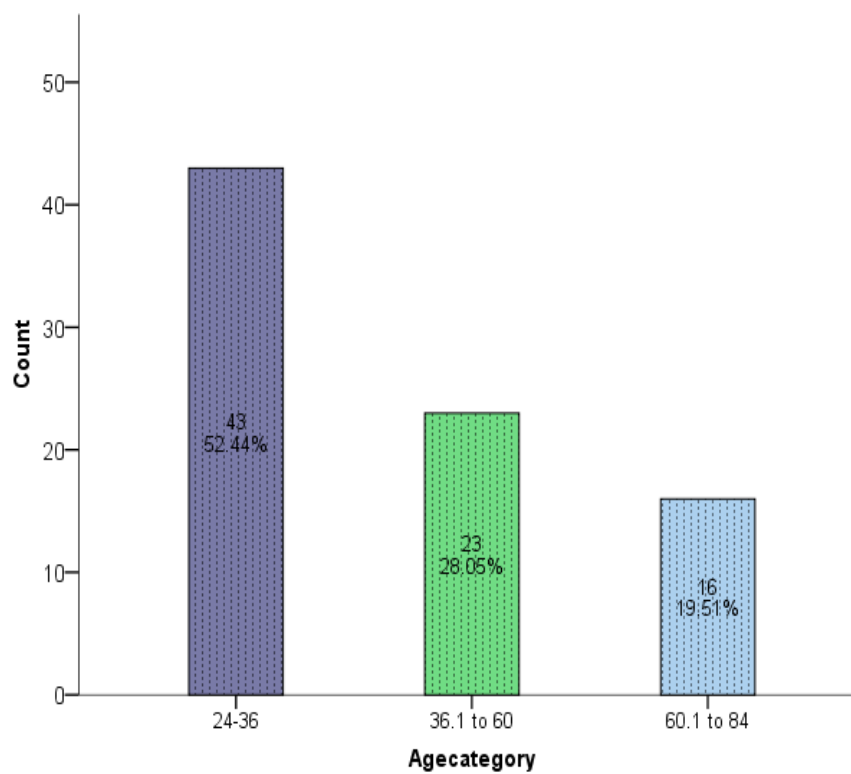
duration of anaesthesia, parental separation anxiety score and anaesthesia emergence delirium scale score was computed as Mean \pm SD. Qualitative data like gender, residential status, parental separation anxiety and emergence delirium was computed as frequencies and percentages. Effect modifiers like age, weight, gender, residential status and duration of anaesthesia was dealt through stratification to see the effect of these on outcome (parental separation anxiety and emergence delirium). Post stratification Chi square test was applied and significance level was set at 0.05.

RESULTS

A total of 82 children undergoing inguinal hernia repair were included in this study. Age distribution of the patients is shown in figure 1. The average age was 44.44 ± 19.12 years. Similarly average weight, duration of anaesthesia, parental separation anxiety score and pediatric emergency delirium score is reported in table 3. There were 76(92.68%) male and 6(7.32%) female (figure 2). Residential status of the patients is presented in figure 3.

Rate of parental separation anxiety and emergence delirium was 39.02% and 25.61% as shown in figure 4 and 5 respectively. Effectiveness of preoperative oral midazolam sedation on separation anxiety and emergence delirium among children undergoing inguinal hernia repair was 60.98% and 74.39% respectively. Rate of parental separation anxiety was high in lower age group (24-36 months) so effective was significantly high in above 36 years of age children ($p=0.004$) as shown in table 4. Effectiveness was preoperative oral midazolam sedation was insignificant in gender, residential status, weight of the patients and anaesthesia time a tabulated in table 5 to 8 respectively. Rate of emergence delirium was also observed after controlling effect of confounder but not statistically significant difference was observed and effectiveness was similar in all stratified variables as shown in table 9 to 13.

FIGURE 1
 AGE DISTRIBUTION OF THE PATIENTS
 n=82



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TABLE 3
 DESCRIPTIVE STATISTICS OF PATIENTS

Variables	Mean \pm SD	95% Confidence Interval for Mean	
		Lower Bound	Upper Bound
Age (Years)	44.44 \pm 19.12	40.24	48.64
Weight (kg)	16.56 \pm 5.34	15.39	17.74
Duration of anaesthesia (Min)	61.90 \pm 20.34	57.43	66.37
parental separation anxiety Score	2.22 \pm 1.01	2.00	2.44
Pediatric emergence delirium scale	9.40 \pm 3.20	8.70	10.11



FIGURE 2
GENDER DISTRIBUTION OF THE PATIENTS
n=82

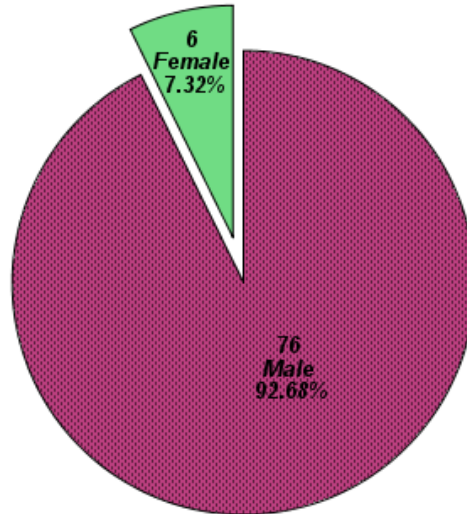


FIGURE 3
RESIDENTIAL STATUS OF THE PATIENTS
n=82

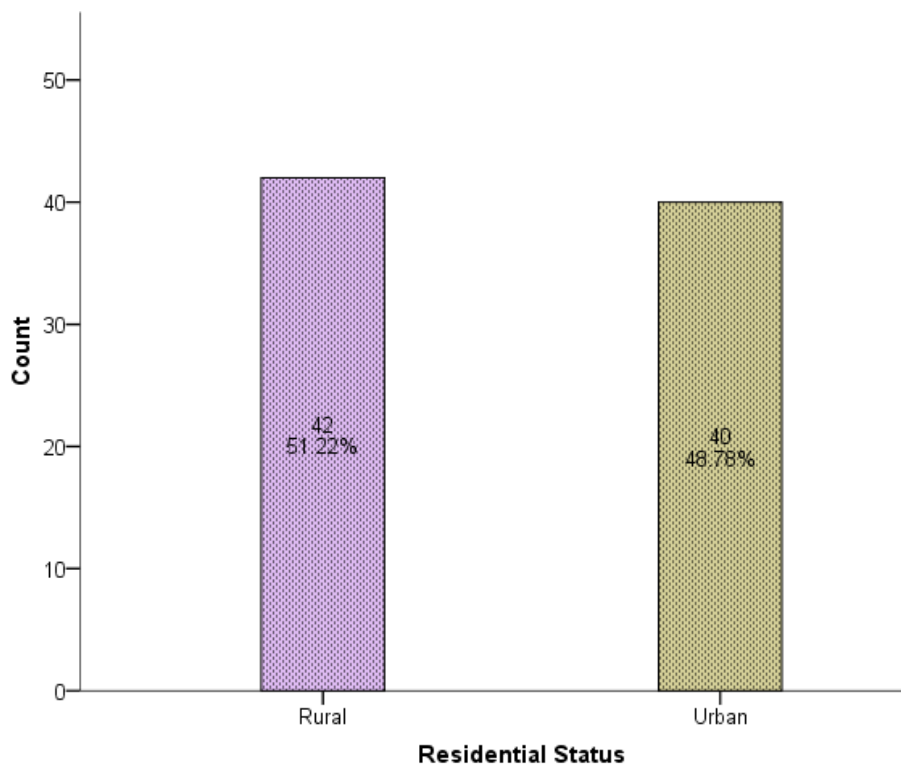


FIGURE 4
EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG
CHILDREN UNDERGOING INGUINAL HERNIA REPAIR
n=82

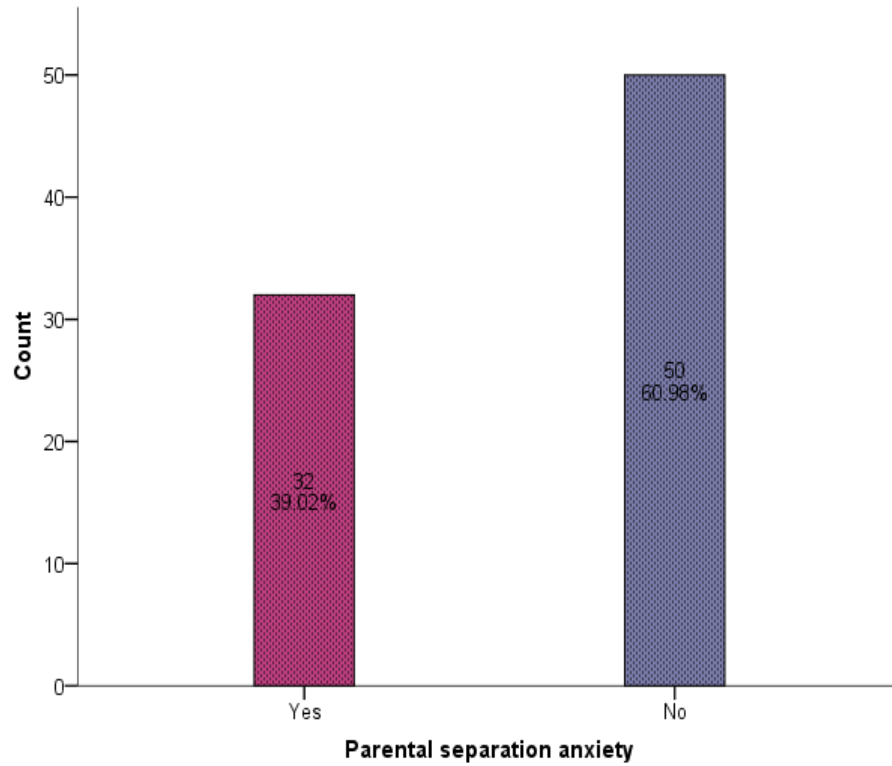
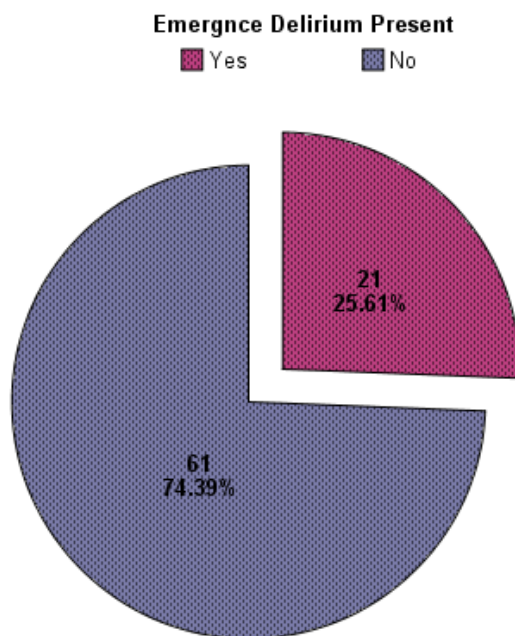


FIGURE 5
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG CHILDREN UNDERGOING INGUINAL HERNIA REPAIR
 n=82



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TABLE 4
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY AGE GROUPS
 n=82

Age Groups (months)	Parental Separation Anxiety		Total	P-Value
	Yes	No		
24-36	24(55.8%)	19(44.2%)	43	0.004
36.1-60	4(17.4%)	19(82.6%)	23	



60.1-84	4(25%)	12(75%)	16	
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TABLE 5
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY SEX
 n=82

Sex	Parental Separation Anxiety		Total	P-Value
	Yes	No		
Male	28(36.8%)	48(63.2%)	76	0.149
Female	4(66.7%)	2(33.3%)	6	

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TABLE 6
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY RESIDENTIAL STATUS
 n=82

Residential Status	Parental Separation Anxiety		Total	P-Value
	Yes	No		
Rural	17(40.5%)	25(58.5%)	42	0.782



Urban	15(37.5%)	25(62.5%)	40	
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TABLE 7
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY WEIGHT
 n=82

Weight	Parental Separation Anxiety		Total	P-Value
	Yes	No		
≤12 kg	15(62.5%)	9(37.5%)	24	0.018
12.1-20kg	11(27.5%)	29(72.5%)	40	
>20	6(33.3%)	12(66.7%)	18	

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TABLE 8
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON SEPARATION ANXIETY AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY ANAESTHESIA TIME
 n=82

Anaesthesia Time	Parental Separation Anxiety		Total	P-Value
	Yes	No		



≤60 min	15(34.9%)	28(65.1%)	43	0.420
>60 min	17(43.6%)	22(56.4%)	39	

TABLE 9
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY AGE GROUPS
 n=82

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Age Groups (months)	EMERGENCE DELIRIUM		Total	P-Value
	Yes	No		
24-36	11(25.6%)	32(74.4%)	43	0.713
36.1-60	7(30.4%)	16(69.6%)	23	
60.1-84	3(18.8%)	13(81.3%)	16	



TABLE 10
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY SEX
 n=82

Sex	EMERGENCE DELIRIUM		Total	P-Value
	Yes	No		
Male	18(23.7%)	58(76.3%)	76	0.713
Female	3(50%)	3(50%)	6	

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TABLE 11
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY RESIDENTIAL STATUS
 n=82

Residential Status	EMERGENCE DELIRIUM		Total	P-Value
	Yes	No		
Rural	9(21.4%)	33(78.6%)	42	0.374
Urban	12(30%)	28(70%)	40	



TABLE 12
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY WIRGHT
 n=82

Weight	EMERGENCE DELIRIUM		Total	P-Value
	Yes	No		
≤12 kg	8(33.3%)	16(66.7%)	24	0.588
12.1-20kg	9(22.5%)	31(77.5%)	40	
>20	4(22.2%)	14(77.8%)	14	

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TABLE 13
 EFFECT OF PREOPERATIVE ORAL MIDAZOLAM SEDATION ON EMERGENCE DELIRIUM AMONG
 CHILDREN UNDERGOING INGUINAL HERNIA REPAIR BY ANAESTHESIA TIME
 n=82

Anaesthesia Time	EMERGENCE DELIRIUM		Total	P-Value
	Yes	No		
≤60 min	10(23.3%)	33(76.7%)	43	0.608
>60 min	11(28.2%)	28(71.8%)	39	



DISCUSSION

The perioperative period is a stressful time for most patients undergoing surgery, especially children. It is estimated that 50%-75% of children undergoing surgery experience significant anguish and anxiety throughout the entire perioperative period.^[84] Anxiety can lead to negative behavior manifestations postoperatively, with 54% of children exhibiting negative behavior manifestations 2 weeks postsurgery and 20% continuing to show them for 6 months.^[85] Numerous studies have examined the effects of various factors on postoperative anxiety and negative behavior manifestations. These factors include the child's and parents' preoperative anxiety, the child's temperament, previous hospitalization for surgery, length of hospitalization, preoperative preparation and medications, the kind of anesthetic drugs used, the presence of parents during the induction of anesthesia, and the child's experience in the postanesthetic care unit (PACU).^[86-90]

The most common medication for reducing preoperative anxiety in children is midazolam, which has a rapid onset and limited duration of action.^[91] MID is a common and routinely used drug for oral premedication in children at a dose of 0.5 mg/kg.¹¹ MID has a rapid onset and short duration of action and provides reliable sedation and anxiolysis. Beyond these advantages, there are some disadvantages such as bitter taste, cognitive impairment, long-term behavioral disturbances, paradoxical reactions, hiccups, and respiratory depression.⁵ The bioavailability of oral MID varies from 15% to 27% in children.²⁴ Fabre et al²⁵ reported that the maximum concentration (C_{max}) of 0.6 mg/kg of MID rectally was calculated as 147±58 µg/L, median t_{max} was 31.5 min (range: 18–38 min), and the half-life was 1.3±0.3 h in a pediatric population. In Keles and Kocaturk et al study^[92] the mean age of the patients was 5.2±1.9 years, In Du et al study^[93] age was 7.6 years however in this study the average age was 44.44±19.12 months.

The time spent in the operating room holding area prior to surgery is often traumatic to children's psychology,^[94] especially for children who already suffer surgery fear. This may contribute to extreme anxiety during the induction of anesthesia. In our study rate of parental separation anxiety and emergence delirium was 39.02% and 25.61%. Effectiveness of preoperative oral midazolam sedation on separation anxiety and emergence delirium among children undergoing inguinal hernia repair was 60.98% and 74.39% respectively. It is also reported in El Batawi et al study^[7] twenty-six children (66.67%) in midazolam group showed acceptable separation from parents, compared to 3 children (7.9%) in group B ($P < 0.01$). Acceptance of anesthesia mask was significantly observed in group A as well ($P < 0.05$). However, there was a lower score for postoperative ED in group A, but the difference was not of statistical significance ($P > 0.05$).

A meta-analysis of RCTs concluded that dexmedetomidine effectively decreased separation anxiety and postoperative agitation, and provided more effective postoperative analgesia than midazolam.^[95] This hypothesis of this study was based on the fact that dexmedetomidine has a half-life of 2-3 hours^[96] so its analgesic effects are likely to persist into the recovery period,^[97] thereby reducing the postoperative anxiety of children undergoing surgeries that take a relatively short amount of time.

In the El Batawi et al study^[7], the time selected to separate the child from his/her parents was 10–15 min after Midazolam administration. This was guided by Levine et al.^[98] who reported that 10 min after premedication was the minimum time needed for smooth separation from parents. The same authors reported that the peak sedative effect of Midazolam was achieved 20–30 min after administration;

In 2009, Sheta and AlSarheed^[99] studied the anxiolytic effect of different doses of Midazolam on 60 children aged 2–6 years undergoing DGA. They reported that satisfactory anxiolytic effect can be achieved

with higher doses which raised the potential risk of some adverse effects. In 2011, Mountain *et al.* [100] conducted a study to compare the effects of Midazolam versus Dexmedetomidine premedication on preoperative anxiety and postoperative emergence delirium (ED) on 41 children aged 1–6 years and concluded that the latter has an advantage of reducing the incidence of postoperative ED.

Reducing preoperative anxiety is important, not only to improve preoperative cooperation for patients and families but also for immediate postoperative outcomes. Aono *et al.* [101] found that high levels of preoperative anxiety were associated with an increased incidence of ED. The incidence of ED was 60% in preschool children undergoing anesthesia with sevoflurane without premedication. [102]36 Özcengiz *et al.* [103] showed that ED of children premedicated orally 45 min preoperatively with 2.5 mg/kg of DEX, 0.5 mg/kg of MID, and 0.1 mg/kg of melatonin was significantly lower than that of a placebo group. In this study, the overall incidences of ED were 0% and 19.2% in the DEX and MID groups, respectively. Jannu *et al.* [104] reported that 4 µg/kg of oral DEX vs 0.75 mg/kg of oral MID as premedication provided a lower incidence of ED in children aged 1–7 years. Prabhu and Mehandale [105] compared the effect of 4 µg/kg of oral DEX vs 0.5 mg/kg of oral MID as premedication and concluded that oral DEX is superior to oral MID for reducing the incidence (from 40% to 4.4%) and severity of ED. Similar to their study, the incidence of ED in the DEX group was significantly lower than that in the MID group.

CONCLUSION

Oral preoperative Midazolam in a dose of 0.5 mg/kg might be a useful treatment adjunct in reducing parental separation anxiety, and for ease of anesthesia induction. Preoperative Midazolam sedation has no reducing effect on postoperative ED in children undergoing dental treatment under general anesthesia. Effective management of preoperative dental anxiety is an essential part of pediatric dental treatment under general anesthesia.

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