Journal Homepage: - www.journalijar.com
INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)
Article DOI: 10.21474/IJAR01/6537
DOI URL: http://dx.doi.org/10.21474/IJAR01/6537

*RESEARCH ARTICLE*

# TO STUDY THE EFFICACY OF ORAL MIDAZOLAM AS A PRE-MEDICATION FOR CHILDREN POSTED FOR GENERAL ANAESTHESIA.

**Dr. Karuna Taksande[1] and Dr. Pallavi Deulkar[2].**
1. Professor, Department of Anesthesia, Datta Meghe Institute of Medical Science, Sawangi (Meghe), Wardha.
2. PG student, Department of Anesthesia, Datta Meghe Institute of Medical Science, Sawangi (Meghe), Wardha.

## Manuscript Info

***Manuscript History***

Received: 14 December 2017
Final Accepted: 16 January 2018
Published: February 2018

***Key words:-***
oral Midazolam, pre-medication, children, General Anaesthesia.

## Abstract

**Introduction:** The major objectives of preanesthetic medication are to decrease the stress response with preservation of hemodynamic parameters, facilitate anaesthesia induction and produce amnesia. Preoperative anxiety is a common phenomenon in children. Midazolam is commonly used in children and has been demonstrated to be a very good sedative, anxiolytic and amnesic premedicant. Midazolam is absorbed rapidly and completely after oral administration.

**Methods:** Aim of the study was to study the effectiveness of oral Midazolam as premedication of paediatric patients undergoing surgery under general anaesthesia with respect to: Ease of separation from parents, degree of sedation achieved (sedation score) preoperatively and postoperatively and patient's co-operation for venipuncture.

**Material and method**: The study was carried out in department of anaesthesiology JNMC and AVBRH Savangi,Meghe,Wardha,during 2016-2018 after taking prior permission from institutional ethical committee. It comprised of 60 subjects. They were randomly allocated to 2 groups. Group A - patients received 0.5mg/kg body weight oral Midazolam, Group B – patients received 1.0mg/kg body weight oral Midazolam

**Results:** 1 mg/kg body weight dose gave better results than 0.5mg/kg body weight dose in terms of ease of separation from parents and co-operation for venepuncture.

**Conclusion:** 0.5mg/kg and 1mg/kg body weight doses of oral Midazolam can be safely administered as premedication to paediatric patients but 1 mg/kg body weight dose is more effective as a pre medication for children posted for General Anaesthesia



## Introduction:-

The major objectives of preanesthetic medication are to decrease the stress response with preservation of hemodynamic parameters, facilitate anaesthesia induction and produce amnesia. Factors to be taken into consideration prior to administration of premedication are the child's age, body weight, drug history, allergic history and any medical or surgical history . Medications administered without a needle are more pleasant for children as well as the family of the child.

**Corresponding Author:- Dr. Pallavi Deulkar.**
Address:- PG student, Department of Anesthesia, Datta Meghe Institute of Medical Science, Sawangi (Meghe), Wardha.

Preoperative anxiety is a common phenomenon in children. Increased preoperative anxiety have been associated with difficulty in anesthetic induction, emergence agitation and also the development of negative postoperative behavioural changes.

Children to undergo surgery are uncooperative due to parental separation, unfamiliar environment, fear of pain or a previous unpleasant experience. This lack of cooperation and preoperative anxiety is shown to be associated with release of stress hormones which affect the haemodynamics of the patients intra-operatively and postoperatively[1,2]. Pharmacological sedation and anxiolysis are commonly practised techniques to reduce the anxiety and achieve best co-operation in the paediatric patients.[3,4]

An effective premedication will allow smooth induction of general anaesthesia with reduced hemodynamic disturbances. Many drugs have been used for effective premedication in paediatric patients such as Benzodiazepines, Antihistamines, α-2 agonists , Ketamine and opioids .[5] Out of all the benzodiazepines studied, extensive research has been carried out on Midazolam as a premedicant in paediatric age group.[5]

Midazolam is commonly used in children and has been demonstrated to be a very good sedative, anxiolytic and amnesic premedicant . Due to its rapid onset and relatively short duration of action , it has been proven to be a useful premedication to facilitate easy separation from parents with very few side effects as compared to other drugs.

Midazolam is available in many formulations and can be administered by different routes like intravenous, intramuscular, rectal, oral and intranasal. There are advantages and disadvantages of all these routes of administration. Intramuscular & intravenous routes are associated with pain and patient discomfort. Both intranasal and rectal routes are associated with local irritation, erratic absorption etc.[3]

An oral preparation is well absorbed due to acidic gastric pH, painless and easily acceptable by a child, more so if it is mixed with a sweetner [3] . Oral preparation of Midazolam is not readily ava ilable in all places. Therefore intravenous preparation of Midazolam has been used by oral route after mixing with a sweetner (clear fluid) . In this study the iv preparation was used by oral route after mixing it with a clear sweetner.

Midazolam is absorbed rapidly and completely after oral administration. The drug can produce highly water-soluble salts (pH less than 4) or exist in lipophilic diazepine ring-closed form (pH greater than 4). This characteristic contributes to rapid onset of action and to good local tolerance after parenteral administration. After both oral and parenteral administration, Midazolam has a fast absorption rate and is rapidly excreted, with a half-life of only about 2 hours . Two different doses was compared to assess ease of separation from parents, co-operation for venepuncture, pre and post operative sedation scores and the intra-operative hemodynamic parameters.

**Aims and Objectives:** To study the effectiveness of oral Midazolam as premedication of paediatric patients undergoing surgery under general anaesthesia and to compare efficacy of two different doses of oral Midazolam – 0.5mg/kg body weight and 1.0mg/kg body weight with respect to:

a. Ease of separation from parents.
b. Degree of sedation achieved (sedation score) preoperatively and postoperatively.
c. Patient's co-operation for venipuncture.

## Materials and Methods:-

After obtaining approval from institutional ethical committee, the study was carried out in 60 patients undergoing different type of elective surgeries under general anaesthesia.
Procedure was explained to the patients and written ,informed and valid consent was obtained from each patient.

The patients were randomly divided into 2 groups of 30 patients each:

a. Group A - patients received 0.5mg/kg body weight oral Midazolam
b. Group B – patients received 1.0mg/kg body weight oral Midazolam

The maximum dose that was administered to any patient was 20mg .
Preparation of the Drug: Commercially available intravenous Midazolam (5mg/ml ampoule) was used to prepare the required oral formulation to be administered to the patients.

Proper preanaesthetic evaluation of the patients was done prior to the surgery and the patients satisfying the inclusion criteria were selected.

Preoperative vitals of the patients, Heart rate, SBP, DBP, Respiratory Rate and SpO2 were recorded. Then the dose of prepared formulation was given orally 40 mins prior to the induction according to the group. Patient's vitals were again recorded at 10 mins, 20 mins, 30 mins and at 40 mins after administration of the drug.

The following parameters were noted:
a. Ease of separation from parents after 40 mins of Midazolam administration
b. Level of sedation achieved at the above mentioned time intervals and
c. Cooperation of patient for venipuncture after 40 mins of Midazolam administration

The response of the children when taken away from their parents (separation from parents) were graded as:
Grade 1 - inconsolable cry
Grade 2 - complaining
Grade 3 - quiet but awake
Grade 4 - sleepy

The degree of sedation, in the operating room (OR) at 0 mins, 10 mins, 20 mins, 30 mins and 40 mins of drug administration and postoperatively were noted, based upon the 5 points sedation score(Modified Ramsay Sedation Score ) as follows:

| MODIFIED RAMSAY SEDATION SCORE | |
|---|---|
| 1 | Patient agitated and anxious or restless or both |
| 2 | Patient cooperative, oriented and tranquil |
| 3 | Patient responds to commands only |
| 4 | Brisk response to a light glabellar tap or auditory stimulus |
| 5 | Sluggish response to light glabellar tap or auditory stimulus |
| 6 | No response |

Cooperation of patient for venipuncture was graded depending upon the individual child's response in the operation room:
i) Poor (1)
ii) Fair (2)
iii) Good (3)
iv) Excellent (4)
Patients' vitals were recorded at induction, at intubation, at 5 mins interval till 20 mins.
All children were given general anaesthesia. Either Sevoflurane or Inj. Propofol(2mg/kg body wt) was used for induction of the patients. Thereafter 2mcg/kg of Inj. Fentanyl and 0.5mg/kg of Inj. Atracurium was administered for endotracheal intubation. Sevoflurane, the inhalational anaesthetic was used for maintenance of anaesthesia. Patients were put on controlled ventilation to maintain normocapnea. Patients' ECG, SBP, DBP, saturation and heart rate were monitored intra-operatively as a part of standard General Anaesthesia procedure. Extubation of patient was done after return of spontaneous ventilation and after regaining of gag or cough reflex.

## Results:-

The prospective randomized study was done to assess the effectiveness of oral Midazolam as premedication of paediatric patients undergoing surgery under General Anaesthesia with respect to
a. Ease of separation from parents after oral Midazolam
b. Degree of sedation achieved (sedation score) preoperatively and postoperatively
c. Patients' co-operation for venepuncture.

60 ASA Grade I and II patients (age 2-12 years) were equally divided into two Groups viz. Group A and Group B
Group A – received 0.5mg/kg body weight oral Midazolam
Group B– received 1.0 mg/kg body weight oral Midazolam.
Haemodynamic parameters viz. HR, SBP, DBP, MAP, RR and $SpO_2$ were also monitored.

The two groups were comparable with respect to age, weight, gender, ASA Grade and duration of surgery.

The haemodynamic parameters viz. HR, SBP, DBP, MAP, $SpO_2$ and respiratory rate were compared.

Ease of separation from parents and co-operation for venepuncture after 40 minutes of administration of drug were also compared between the two study groups.

The HR, SBP, DBP, MAP and $SpO_2$ were statistically comparable between the two groups throughout the study at all time intervals.

On assessment of the pre-operative sedation scores:
10 minutes after the administration of the drug, sedation scores were similar between the two groups.
At 20 minutes after drug administration, sedation score was 2 in Group A in all patients and sedation score was 3 in 76.67% of patients in Group B.
At 30 minutes after drug administration, sedation score was 2 in Group A in all the patients and sedation score was 3 in 86.67% of patients in Group B.
At 40 minutes after drug administration, Sedation score was 2 in Group A in all the patients and the sedation score was 3 in 86.67% of patients in Group B. However the sedation score was 4, in 10% of patients in Group B. Thus patients who received 1mg/kg oral Midazolam were highly sedated at the time taking them to operating room.

On assessment of ease of separation from parents:
In Group A – 53.33% of the patients were comfortable on separation
In Group B– 100% of the patient were comfortable on separation. Thus all patients in Group B were comfortable while separation from parents.

On assessment of co-operation for venepuncture:
In group A – co-operation in most patients (22) was fair and good in 8 patients.
In group B – co-operation was good in 9 patients and excellent in 21 patients.
Thus in Group B, co-operation for venepuncture was excellent in majority of the patients.

## Discussion:-

Benzodiazepines have been widely used in all age groups to achieve sedation, anxiolysis and amnesia. It has been used as preanaesthetic medication as it facilitates smooth induction of anaesthesia. Amongst the various drugs of this group, Midazolam has been the choice of drug as it has short duration of action and show less side effects.

The present study was conducted to compare the efficacy of two different doses of oral Midazolam in 60 ASA Grade I and II paediatric patients aged 2-12 years. The patients were divided into two groups comprising 30 patients each:

a. Group A: received 0.5mg/kg body weight Midazolam
b. Group B: received 1 mg/kg body weight Midazolam

Haemodynamic parameters were monitored throughout the study. Pre-operative sedation score, ease of separation from parents and co-operation for venepuncture were studied.

In 2009, Saad A. Sheta et al [3] studied 60 patients who were randomly divided into three groups and received 0.5mg/kg, 0.75mg/kg or 1mg/kg Midazolam orally. The patients were assessed for acceptance of the drug preparation, reaction to separation from parents, sedation score, co-operation for venepuncture and recovery conditions.

In 2012, Somri et al [6] compared the effect of three doses of oral Midazolam (0.5. 0.75 and 1mg/kg) on sedative state and co-operative behaviour of 90 children during dental treatment who initially were unable to tolerate treatment under behavioural management and local anaesthesia or in combination with nitrous oxide.

Comparison of demographic data:
The median age in Group A and Group B was 4.563 years and 4.697 years respectively. The median weight in Group A and Group B was 12.49 kgs and 13.022 kgs respectively. The male:female ratio in Group A and Group B

was 25:5and 24:6 respectively . The demographic data was statistically comparable.The ASA I:II ratio in Group A and Group B was 22:8and 23:7 respectively and were statistically comparable.

Comparison of Haemodynamic parameters:
Comparison of mean HR:
HR reduced from the baseline to induction in both the groups, which can be attributed to the effect of induction agents used for general anaesthesia viz. Propofol or Sevoflurane.

Comparison of mean MAP:
There was a drop in mean MAP from the baseline to induction in both the groups. This change in the mean MAP was due to the induction agents used for general anaesthesia viz. Propofol or Sevoflurane.. [7]

Comparison of pre-operative sedation scores:
The sedation score was 2 in all the patients in Group A and Group B at the end of 10 minutes of drug administration. The sedation score was 2 in all the patients in Group A and in 7 patients (23.33%) in Group B at the end of 20 minutes. However the sedation score was 3 in 23 patients (76.67%) in Group B.

At the end of 30 minutes of drug administration, sedation score was 2 in all the patients in Group A and in 4 patients (13.33%) in Group B. However the sedation score was 3 in 26 patients (86.67%) in Group B.

The sedation score was 2 in all the patients in Group A and 1 patient (3.33%) in Group B at the end of 40 minutes after drug administration. However the sedation score was 3 in 26 patients (86.67%) in Group B. The sedation score was 4 in 3(10%) patients in Group B.

Thus it was seen that the sedation score gradually increased after administering Midazolam. The increase was more in Group B than in Group A.

Saad A. Sheta et al [3] studied 60 patients in 2-6 years age group for assessing various parameters using 0.5mg/kg, 0.75mg/kg and 1 mg/kg oral Midazolam as premedication. The number of children who had desirable sedation was similar in the 0.75mg/kg and 1.0mg/kg dose groups.

Comparison of ease of separation from parents:[3]
The ease of separation from parents was assessed at 40 minutes from the administration of the respective doses in Group A and Group B. While comparing the ease of separation from parents, the children were categorized into 4 grades. Grade 1 – inconsolable cry, Grade 2 – complaining, Grade 3 – quiet but awake and Grade 4 – sleepy.

In Group A, 14 patients (46.67%) were Grade 2 and 16 patients (53.33%) patients were Grade 3. In Group B, 22 patients (73.33%) were Grade 3 and 8 patients (26.67%) were Grade 4.

Since the assessment of separation from parents is more subjective, to make it more objective and to simplify, Grade 1 and Grade 2 were clubbed together and named as ‘Uncomfortable’ and Grade 3 and Grade 4 as ‘Comfortable’.
In Group A, 46.67% and in Group B 0% of the children were uncomfortable. In Group A 53.33%; Group B 100% of children were comfortable which suggests that higher the dose of Midazolam, better the grade of ease of separation from parents.

Saad A. Sheta et al [3] studied 60 patients in 2-6 years age group for assessing various parameters using 0.5mg/kg, 0.75mg/kg and 1 mg/kg oral Midazolam as premdication. 45% of patients who received 0.5mg/kg Midazolam were uncomfortable, whereas 75% of patients who received 0.75mg/kg and 90% of patients who received 1 mg/kg Midazolam were comfortable at the time of separation from parents.

Comparison of Co-operation for venepuncture:[3,7]
For comparison of co-operation for venepuncture among the groups, the patients were either categorized as poor, fair, good, or excellent.

At 40 minutes after administration of Midazolam, in Group A, 22 patients (73.33%) were in fair and 8 patients (26.67%) patients were good category. In Group B 9 patients (30%) were good and 21 patients (70%) were excellent category.

Thus, co-operation for venepuncture was excellent category in Group B. In Group A, the majority co-operation was in fair category. Thus, as the dose of sedation was increased, the level of co-operation for the venepuncture was also increased i.e. in the excellent category.

Saad A. Sheta et al [3] studied 60 patients in 2-6 years age group for assessing various parameters using 0.5mg/kg, 0.75mg/kg and 1 mg/kg oral Midazolam as premdication. 20 % of patients who received 1mg/kg had excellent result as compared to 10% of patients who received 0.75mg/kg. 25% of children who received 0.5mg/kg Midazolam had poor co-operation.

Mehrdad Shoroghi et al [7]] studied 90 children for skin laser treatment who received either orange juice or 0.5mg/kg or 1mg/kg oral Midazolam (with equal volume of orange juice) as premedication. The median scores of co-operation for venepuncture were better in Midazolam group who received 1mg/kg than those who received 0.5mg/kg, which was again better than the placebo group.

## Conclusion:-

From the study it was concluded that 0.5mg/kg and 1mg/kg body weight doses of oral Midazolam can be safely administered as premedication to paediatric patients but 1 mg/kg body weight dose is more effective as a pre medication for children posted for General Anaesthesia

1 mg/kg body weight dose gave better results than 0.5mg/kg body weight dose in terms of ease of separation from parents and co-operation for venepuncture. The patients with dose of 1mg/kg were deeply sedated than 0.5mg/kg group.

## References:-

1. Jawaid M, Mushtaq A, Mukhtar S, Khan Z. Preoperative anxiety before elective surgery.Neurosciences (Riyadh) 2007; 12(2):145-8
2. McCann ME,Kain ZN. The Management of Preoperative Anxiety in Children:An Update. AnesthAnalg 2001; 93:98–105.
3. Sheta SA, MahaAlSarheed. Oral Midazolam Premedication for Children Undergoing General Anaesthesia for Dental Care. International Journal of Pediatrics 2009; 22(3):56-62.
4. Hosey MT. Managing anxious children: the use of conscious sedation in paediatric dentistry. International Journal of Paediatric Dentistry 2002;12:359–72.
5. Abdallah C,Hannallah R. Premedication of The Child Undergoing Surgery. M.E.J. Anesth 2011; 21(2):26-9.
6. Optimising the dose of oral midazolam sedation for dental procedures in children: a prospective, randomised, and controlled study MOSTAFA SOMRI1 , CONSTANTINOS A. PARISINOS2 , JOHNY KHAROUBA3 , NAOMI CHERNI3 , AMI SMIDT 4 , ZACKARIYA ABU RAS4 , GEITH DARAWSHI3 & LUIS A. GAITINI1
7. Perioperative effects of oral midazolam premedication in children undergoing skin laser treatment. A double-blinded randomized placebo-controlled trial, Mehrdad Shoroghi[I]; Shahriyar Arbabi[II]; Farshid Farahbakhsh[III]; Mehrdad Sheikhvatan[IV]; Ali Abbasi.