

## **A RANDOMISED CONTROLLED STUDY TO EVALUATE THE EFFICACY OF ORAL MIDAZOLAM SYRUP AND INTRANASAL MIDAZOLAM SPRAY AS IDEAL PREMEDICANT IN CHILDREN UNDERGOING DIFFERENT TYPES OF SURGERIES**

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**INTRODUCTION:** Most of the preschool children suffer from severe anxiety and apprehension before surgery. This can largely affect the smooth conductance and emergence from anaesthesia, with complications such as bronchospasm at the time of induction and emergence phenomenon at the end. This can lead to the development of maladaptive behavioral responses or posttraumatic stress disorders in later part of life. Midazolam in current time has emerged as an ideal premedicant having all the desirable properties in this regard. It has been used by several routes for premedication which includes oral and intranasal administration as most frequently used route. Each has its own advantage and disadvantage. The search for an ideal route and dose still exists. So the current study was planned to find out the efficacy of midazolam intranasally & orally. Midazolam is a benzodiazepine. It is highly lipid soluble *in vivo*. Its lipid solubility is pH dependent, being more alkaline pH. It acts by binding to GABA-A receptors. It is metabolized by cyt P450 3A4. It has anxiolytic, amnesic, sedative, hypnotic, anticonvulsant & spinally mediated muscle relaxant property. Midazolam tastes bitter, so flavored midazolam syrup is available and its efficacy remains almost same and acceptability increases. The Midazolam nasal spray is also available.

**MATERIALS & METHODS:** Aim of study was to evaluate the efficacy of oral midazolam syrup (0.25mg/kg) vs intranasal midazolam spray (0.3mg/kg) as ideal premedicant in children (3-10 yrs) undergoing various types of surgeries. After obtaining institutional ethical committee approval, 50 children belonging to ASA grade I & II aged between 3-10 yrs posted for elective surgeries were randomly taken for the study. Informed & written consent was obtained from the parents regarding the study. These 50 children were randomly divided into 2 groups, each comprising 25. Group 1, OM group was given oral midazolam. Group 2, NM group was given nasal midazolam. Patients (ASA class I-II) scheduled for elective surgical procedures were candidates for study.

Exclusion criteria included gastrointestinal disorders that might affect absorption, nasal polyps, nasal trauma and any medical condition that could compromise the safety of the patient or interfere with the interpretation of the results. Because midazolam is a known substrate of the cytochrome P450 3A4 enzyme system, patients taking known cytochrome P450 3A4 inhibitors or inducers were excluded. The independent variable in the study was the choice of drug route (oral or intranasal). The dependent variables in assessment of the effectiveness of each route were the sedation level, respiratory & haemodynamic parameters.

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Student t test was used to analyze the data. The P value of  $<0.05$  was considered significant. All the children were allowed to take clear fluids up to 2hrs before surgery. Children belonging to OM group were given oral midazolam syrup (0.25mg/kg) 30-45min before anticipated surgery. Children belonging to the NM group were given an intranasal midazolam spray (0.3mg/kg) 15-30min before anticipated surgery. General anaesthesia was administered using similar drugs in both the groups.

In both the groups we have observed & compared for ease of separation from parents, acceptability of the child for shifting to the operation theatre, allowing for IV cannulation & application of a face mask. In all children RR, HR, SPO2 monitoring were done continuously, starting from the administration of drug to initiation of general anaesthesia, during intropertative & post operative period also.

**RESULTS:** There were no significant differences in sedation and anxiety levels among the 2 groups. Average sedation and anxiolysis increased with time, achieving a maximum at 30 min in group I and at 20 min in groups II. Patient mask acceptance was good for more than 75% of the children in both groups. Although the intranasal route provides a faster effect, it causes significant nasal irritation. 77% of the children from this group cried after drug administration. Most parents in all groups (67–73%) were satisfied with the level of sedative premedication. Parental separation is easy in both groups. Half of the children in both the groups were uncooperative during IV cannulation. Intranasal & oral, midazolam produces good levels of sedation and anxiolysis. Mask acceptance for inhalation induction was easy in the majority of children, irrespective of the route of drug administration. There was no incidence of respiratory depression, haemodynamic instability in any of the pts of both the groups.

**DISCUSSION:** Goals of sedation in pediatric patients, according to the American Academy of Paediatrics are to guard patient safety & welfare, Control anxiety, minimize psychological trauma, maximize the potential for amnesia, minimize physical discomfort & pain, Control behavior or movement to allow safe completion of the procedure. Return the patient to a state in which safe discharge from medical suspension is possible. These goals can be best achieved by selecting lowest dose with higher therapeutic index. We selected children in the age group of 3 - 10 years, because this age group is more susceptible to the separation anxiety, since their understanding is limited.

We selected this drug as more than 88% of anesthesiologists prescribe midazolam for premedication. There are numerous published reports documenting the safety & efficacy of oral midazolam premedication in children from 1-12 years of age. Some studies demonstrated that reduction in anxiety was better with oral midazolam than intranasal. Midazolam in the intranasal administration has got the limitation because of its irritation. So the acceptance rate was low. Even though the efficacy of oral & nasal midazolam are the same, oral is preferred because of easy administration, Palatable, due to the flavored syrups in which it is available, Easily accepted by the child without any incidence of crying or rejection or spitting. Good parental satisfaction.

Facilitation of smooth induction. Due to nasal discomfort & nasopharyngeal irritation, Majority of children cried after nasal spray with watering of eyes and bad taste. PT should be

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educated to take a deep breath when sprayed, which is cumbersome in this age group. It cannot be used in pts with nasal polyps, nasal trauma, nasal foreign body. Due to irritation pt sneezes & whole drug can be expelled.

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## PERI OP VITALS

PERI OP	ORAL M	INTRA NASAL M
HR/m	113+/- 30.67	116+/- 35.55
RR/m	22+/-2.29	23.33+/- 2.59
SP02	97+/-0.03	97+/-0.01

Vitals were recorded at 5,15, 30, 45 min after midazolam administration. Their mean & SD are displayed in the table. They are not statistically significant as their P value is >0.05

## DEMOGRAPHIC DATA

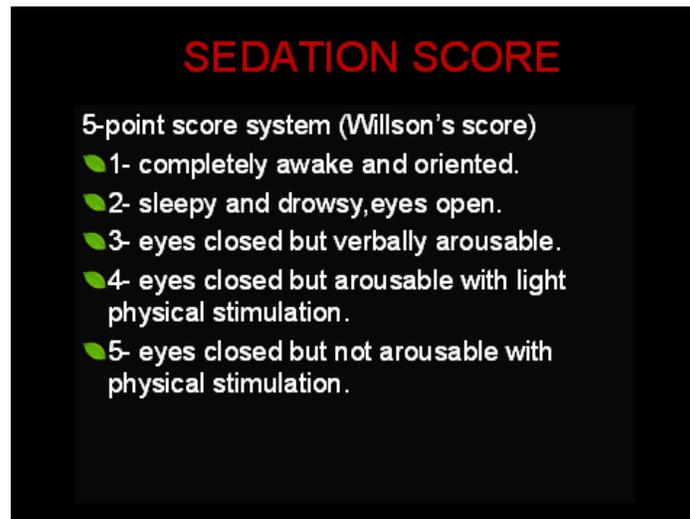
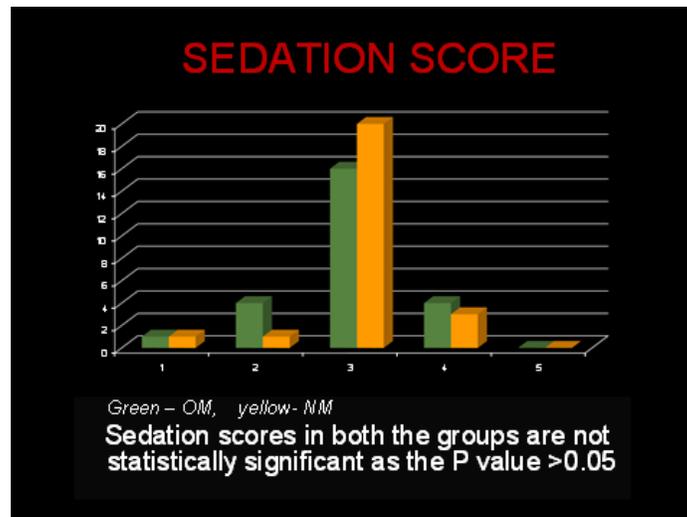
	ORAL M	INTRA NASAL M
AGE	4.35+/-1.24	4.92+/-0.87
SEX(M:F)	2:1	2:1
WEIGHT	12+/-2.03	12.93+/- 2.28

Demographic data was similar in both the groups

## SEDATION SCORE

SEDATION SCORE	ORAL M	INTRA NASAL M
1	1	1
2	4	1
3	16	20
4	4	3
5	0	0

Sedation scores in both the groups are not statistically significant as the P value >0.05



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