

## **(6) COMPARATIVE STUDY OF ORAL MIDAZOLAM AND ORAL KETAMINE AS PREMEDICATION IN CHILDREN.**

Dr. Rupal Kapadia, (assistant profesoor), Dr. Shruti Shah, (associate professor), Dr. Hetavi Contractor, (2nd year resident), Dr. Rajanikant Ribadiya. (2nd year resident) Department of Anaesthesia, Smt. N.H.L. Municipal Medical College. Ahmedabad 380006

### **Abstract:**

#### **Aims:**

To compare the effect of oral Midazolam and oral Ketamine on sedation and anxiety as premedication in children.

#### **Settings and Design:**

This is a randomized, controlled, prospective study conducted in 60 children undergoing surgery of more than 30 minutes duration.

#### **Methods and Material:**

60 children were divided in two groups. Group M received oral Midazolam 0.5 mg/kg and Group K received oral Ketamine 5 mg/kg as pre medication preoperatively 30 minutes before induction of anaesthesia. Standard general anaesthesia technique was used. Time of onset of sedation, anxiety level at the time of separation from parents and at the time of application of facemask was noted. Any side effect after ingestion of the drug until 6 hours in the post-operative period was looked for. Time of recovery from anaesthesia was noted.

#### **Results:**

It was observed that both the drugs were well accepted by the children. Sedation and anxiolysis was better in Ketamine group both during separation from parents and during facemask application. Recovery time in both groups was less than 20 minutes. Recovery is smooth in Ketamine group whereas recovery is associated with irritability and crying in Midazolam group. There were minimal side effects in both the groups. This study concludes that oral premedication with 5 mg/kg Ketamine is better than 0.5 mg/kg Midazolam.

#### **Conclusions:**

Preoperative Ketamine 5mg.kg<sup>-1</sup> is a better premedicant than Midazolam 0.5 mg.kg<sup>-1</sup> in pediatric patients. Optimum time interval for excellent anxiolysis and sedation from administration of oral premedication to parental separation is 30 minutes in both groups.

**Key-words:** Midazolam, Ketamine, Oral Premedication, Children

**Introduction:** Anaesthesia and surgery is stressful and traumatic experience for children. Children are especially vulnerable to long term psychological impairment due to many reasons. The aim of giving premedication to children is to relieve anxiety, reduce trauma associated with separation from their parents and facilitate induction of anaesthesia without prolonging recovery period.

Key features of good premedication are

- Rapid onset
- Short duration of action
- Smooth induction of anaesthesia
- Lack of significant side effects
- Rapid post-op recovery.

Oral Midazolam and Ketamine met these criterias with rapid onset, minimal side effects and rapid post-operative recovery. Feld and co-workers<sup>[1]</sup> suggested that oral Midazolam 0.5 mg.kg<sup>-1</sup> 30 mins prior to induction was as effective as Midazolam 0.2 mg.kg<sup>-1</sup> i.m. for preanesthetic medication. They also suggested that administration of small amounts of fluid to children prior to induction of anaesthesia does not pose a significant risk. Levine and co-workers<sup>[2]</sup> concluded that children may be separated from their parents as early as ten minutes after receiving oral Midazolam 0.5 mg.kg<sup>-1</sup>. Gutstein and co-workers<sup>[3]</sup> had found that Ketamine 5 mg.kg<sup>-1</sup> provides predictable, satisfactory premedication without significant side effects. We therefore designed this study to compare Midazolam and Ketamine as oral premedicants in paediatric anaesthesia.

The present study aims at comparing the efficacy of Ketamine and Midazolam as oral premedication in children with their advantages and disadvantages.

### **Subjects and Methods:**

Sixty children of age group between 1-10 years with ASA grade 1 or 2 undergoing surgery of more than 30 minutes duration were included in the study.

The exclusion criteria included children with neurological dysfunction, increased intracranial pressure, anomalies of cardiovascular system and long term therapy with hepatic enzyme inducing drugs.

The children were randomised in two groups of thirty each. In Group M commercial formulation of oral Midazolam syrup 2 mg/ml in a dose of 0.5 mg/kg and in Group K parenteral formulation of Ketamine 50 mg/ml in a dose of 5 mg/kg mixed with equal volume of sugar syrup were given to patients to swallow 30 minutes prior to induction. Injection Glycopyrolate 0.004 mg/kg intravenous given. Then it was followed by standard general anaesthesia technique in which induction was done by inj. Thiopentone sodium and inj. Succinylcholine, endotracheal intubation, maintenance by oxygen, nitrous oxide, sevoflurane and inj. atracurium and reversal

was done by inj. Neostigmine. Children were observed for the changes in mood, behaviour and appearance, onset of sleepiness, closure of eyes and side effects like nausea, vomiting, increased salivation, hallucination, nystagmus, and hiccup. Various observations were made in a blind manner by one person to avoid observer variation as follows

- a) Time of onset of sedation was noted (when the sedation score was 3 or less)
- b) Level of sedation at 30 minutes after premedication.
- c) Level of anxiety at the time of separation from their parents.
- d) Level of anxiety at the time of face masks application.
- e) Post-operative recovery time
- f) Side effects

**Level of sedation was noted on a five point scale as per table no.1**

Score	Sedation Level
1	Asleep, not readily arousable
2	Asleep but arousable
3	Calm and drowsy
4	Awake
5	Agitated

Level of anxiety was noted on a four point scale as per table no.2 (Emotional state scale).

Score	Anxiety level
1	Calm and sleepy
2	Apprehensive but withdrawn from surroundings
3	Crying
4	Agitated and difficult to control

**Results:**

Sixty children were randomised in two groups, Group K and Group M. Thirty patients in each group were observed.

**Table 1. Demographic data**

Age group	Group K	Group M
1-4 years	5	11
5-7 years	9	11
8-10 years	16	8

Sex	Group K	Group M
Male	22	22
Female	8	8

Age and sex do not show any significant relationship with our stud.( $P>0.05$ )

**Table 2. Details of sedation scores**

	Score	Number of patients	
		Time 30 min	
		Group K	Group M
Sedation	1	5	1
	2	13	1
	3	6	9
	4	5	14
	5	1	5

- Basal sedation score was comparable between both the groups after 30 min with median of 2 in group K and 4 in group M and mean of 2.46 in group K and 4.2 in group M. Table 2 shows that 80% children in group K (score 1=16.66%, score 2=43.33%, score 3=20%) and only 36.66% children in group M (score 1=3.33%, score 2=3.33, score 3=30) attained sedation score 3 or less within 30 minutes and rest remained awake. The difference was clinically significant.( $P<0.05$ )

**Table 3.Details of anxiety scores**

	Score	Number of patients at			
		Separation from parents		Application of facemask	
		Group K	Group M	Group K	Group M
Anxiety	1	11	4	9	3
	2	10	6	12	8
	3	7	14	8	12
	4	2	6	1	7

- Basal anxiolytic score was compared at two times, one at time of separation from parents and other at the time of application of facemask. Separation was successful in 70% of children in group K (score 1 =33.66%, score 2=33.33%) and 33.33 % in group M (score 1=13.33%, score 2= 20%). The values were statistically significant in both the groups. Application of face mask was excellent in 70 % in group K (score 1= 30%, score 2=40%) and 36.33 % in group M (score 1=10%, score 2=26.33%).It is statistically significant.( $P<0.05$ )

- In Midazolam group we observed side effects like nausea, vomiting in three patients, irritability in one patient, breath holding in one patient and low saturation (92%) in one patient. In Ketamine group only one patients experienced nausea, vomiting. We also compared post op recovery time. Average post-op recovery time in Ketamine group was 10 minutes and in Midazolam group was 13 minutes. Also post-op recovery was smooth in group K as compared to group M.

**Discussion:** The principal aim of sedative premedication used in children are to reduce anxiety, facilitate separation from parents and accomplish smooth induction of anaesthesia. The ideal premedication should be easily administered and acceptable, act rapidly, should not have prolong emergence from anaesthesia and have few side effects.

This can be overcome by orally acceptable premedication in addition to psychological preparation of children.

Many sedative analgesic agents and routes of delivery for facilitation of painful procedures have been studied, with varying degrees of patient acceptance, efficacy and safety<sup>[4]</sup>. The inhaled route appears effective primarily in children over eight years of age and requires specialized equipment and significant safety precautions<sup>[5]</sup>. The intravenous and intramuscular routes are traumatic. The intranasal route is similarly marked by variable absorption, may be irritating to nasal mucosa and drugs administered may traverse directly into the central nervous system through the cribriform plate by traveling along the olfactory nerves<sup>[6]</sup>. The oral route provokes the least anxiety in young children.

Our study evaluated the efficacy of oral Ketamine and oral Midazolam as premedicant in pediatric patients.

Baseline sedation and anxiolysis of children in both groups were comparable with median score of 2. The scores peaked at the time of parental separation. At 30 minutes the sedation and anxiolysis scores were better in Ketamine group compared to Midazolam group. In Ketamine Group 24 (80%) children achieved good sedation (sedation 3 or more), 21 (70%) were easily separated from parents (anxiolysis score 3 or 4) and 21(70%) have good mask acceptance score (anxiolysis score 3 or 4) while in Midazolam group it was 11 (36.66%) and 10 (33.33%) and 11(36.66%) respectively.

Gustein and co worker<sup>[3]</sup> observed that after oral Ketamine administration sedation occurred in 10-15 minutes which is comparable to other oral premedication regimen.

Gutstein and co-workers<sup>[3]</sup> and McMillan<sup>[8]</sup> also observed the benign effects of oral Ketamine and oral Midazolam on cardio respiratory system respectively. Lerman and co-workers<sup>[9]</sup> compared the clinical characteristics of oral Ketamine and oral Midazolam and found that no important side effects were attributable to either premedication. Gringrich<sup>[10]</sup> aborted his study after undesirable side effects, including increased secretions, laryngospasm, hallucination and

dysphoria from oral Ketamine  $6 \text{ mg.kg}^{-1}$ . Tobias<sup>[7]</sup> who used oral Ketamine  $10 \text{ mg.kg}^{-1}$  in 34 children found emergence phenomena in 9% of children, but none required any pharmacological intervention.

It can be concluded that oral premedication with Ketamine in the dose of  $5 \text{ mg/kg}$  provides better sedation and anxiolysis in children than oral premedication with Midazolam in the dose of  $0.5 \text{ mg/kg}$  and also Ketamine has minimal side effect and smooth post-op recovery than Midazolam.

## References

1. Feld LH, Negus JB, White PF. Oral Midazolam preanesthetic medication in paediatric outpatients. *Anesthesiology* 1990; 73(5):831-4.
2. Levine MF, Hartley EJ, Macpherson BA, Burrows FA, Lerman J. Oral Midazolam premedication for children with congenital cyanotic heart disease undergoing cardiac surgery: a comparative study. *Can J Anaesth* 1993; 40(10):934-8.
3. Gutstein HB, Johnson KL, Heard MB, Gregory GA. Oral Ketamine preanesthetic medication in children. *Anesthesiology* 1992; 76(1):28-33.
4. Cote CJ. Sedation for the pediatric patient. A review. *Pediatr Clin North Am* 1994; 41(1):31-58.
5. Gamis AS, Knapp JF, Glenski JA. Nitrous oxide analgesia in a pediatric emergency department. *Ann Emerg Med* 1989; 18(2):177-81.
6. Cote CJ. Preoperative preparation and premedication. *Br J Anaesth* 1999; 83(1):16-28.
7. Tobias JD, Phipps S, Smith B, Mulhern RK. Oral Ketamine premedication to alleviate the distress of invasive procedures in pediatric oncology patients. *Pediatrics* 1992; 90(4):537-41.
8. McMillan CO, Spahr-Schopfer IA, Sikich N, Hartley E, Lerman J. Premedication of children with oral Midazolam. *Can J Anaesth* 1992; 39(6):545-50.
9. Alderson PJ, Lerman J. Oral premedication for paediatric ambulatory anaesthesia: a comparison of Midazolam and Ketamine. *Can J Anaesth* 1994; 41(3):221-6.