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# Comparison of efficacy of oral ketamine and oral midazolam as premedicant in paediatric patients

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**Abstract:** *Background:* The usual goals of premedication are to reduce anxiety and to ease separation from parents and premedication for each child must be individualized. The aim of study was to compare the efficacy and safety of oral ketamine and oral midazolam as premedicant in pediatric patients aged 1 to 10yrs. *Methods:* The study was carried out in Medical college hospital Bijapur from November 2013 to October 2014. After obtaining institutional ethical committee clearance informed consent was taken from parents. Patients who were scheduled for elective surgeries aged between1 and 10 years were divided in two groups of 30 each, receiving Ketamine 50mg/ml in a dose of 6mg/kg and Midazolam 1mg/ml vial in a dose of 0.5mg/kg. We observed the degree of sedation using sedation score, anxiolysis using anxiety score, the behavior of the child at induction, reaction of the child to intravenous cannulation and any adverse effects. *Results:* Both the treatment groups were similar in respect of age, sex, weight, behaviour. After the administration of the medications, pulse, systolic or diastolic blood pressures or arterial oxygen saturation were not statistically different in the two patient groups. However, both venepuncture scores and acceptance of facemask was seen to be statistically better ($p < 0.001$) with ketamine as compared to midazolam. *Conclusion:* Oral administration of sedatives has become the standard of care at many institutions and our results show that premedication with 6mg/kg of oral ketamine is better than 0.5mg/kg of oral midazolam in achieving better acceptability, sedation and anxiolysis.
**Keywords:** Anxiety Ketamine, Midazolam, Premedication, Sedation.

## Introduction

The choice of premedication is based on the age and specific needs of the patient. The usual goals of premedication are to reduce anxiety and to ease separation from parents. Because most children fear needles, the oral administration of sedatives has become the standard of care at many institutions. Children who are younger than 8 months of age generally do not need premedication and separate easily from their parents. Children between 8 months and 8 years of age often experience enough preoperative anxiety that preoperative medication may be helpful [1].

Older children may be willing to have an intravenous line started preoperatively, especially if a topical anesthetic cream such as EMLA (eutectic mixture of local anesthetics) or ELA-Max is used. Factors to consider when selecting a drug or a combination of drugs for premedication include the child's age, ideal body weight, drug history, allergic status, underlying medical or surgical conditions and how they might affect the response to premedication or how the premedication might alter anesthetic induction, parent and child expectations; and the child's emotional maturity, personality, anxiety level, cooperation, and physiologic and psychological status.

The major objectives of pre-anesthetic medication are to:

1) Allay anxiety.
2) Block autonomic (vagal) reflexes.
3) Reduce airway secretions.
4) Produce amnesia.
5) Provide prophylaxis against pulmonary aspiration of gastric contents.
6) Facilitate the induction of anesthesia.
7) If necessary, provide analgesia.

Premedication may also decrease the stress response to anesthesia and prevent cardiac

 

arrhythmias [2]. The goal of premedication for each child must be individualized. Light sedation, even though it may not eliminate anxiety, may adequately calm a child so that the induction of anesthesia will be smooth and a pleasant experience. In contrast, heavy sedation may be needed for the very anxious child who is unwilling to separate from his or her parents [3].

Oral midazolam is considered to be effective as a premedicant without affecting the post-operative recovery. Recent reports have indicated that oral pre- medication with ketamine/midazolam is an acceptable, atraumatic route of administration of pre-medication in children with rapid and reliable onset, minimal side effects and rapid post-operative recovery. Hence we decided to compare the efficacy and safety of oral ketamine and oral midazolam as premedicant in pediatric patients aged 1 to 10yrs.

## Material and Methods

*Study design:* The study was carried out in the Medical College Hospital Bijapur from Oct 2013-Oct 2014. All patients in the age group of 1-10 years that satisfied the inclusion criteria posted for elective surgeries were included in the study. After taking informed consent from parents we enrolled 60 patients in the study, with 30 patients in Group I receiving ketamine and 30 patients in Group II who received midazolam. We allocated the patients to each group by simple random sampling (lottery method) [4]. Included patients were those who belonged to The American Society of Anesthesiologists (ASA) Grade I in the age group of 1-10 years and undergoing elective surgeries. We excluded patients of ASA grade II, III, IV and V. We excluded any patient with upper respiratory tract infection, lower respiratory tract infection, history of allergy to any of the study drugs, any child who did not receive partly or fully the calculated dose of the study drug and children who were already on other sedative drugs, antiepileptics and anticoagulants and emergency cases.

*Data collection and analysis:* During preoperative visit patients' detailed history was taken. General physical examinations and systemic examination were carried out and basic demographic information like ages, sex and weight were recorded. Investigation like haemoglobin level, total cell count, differential count, erythrocyte sedimentation rate, bleeding time, clotting time and complete urine examinations were carried out. Parents were allowed to stay with the child in the preoperative room, where the study drugs were administered. Group I patients received parenteral formulation of ketamine (50mg/ml) in a dose of 6mg/kg and Group II patients received parenteral formulation of midazolam (1mg/ml vial) in a dose of 0.5mg/kg, orally after mixing with equal volume of sugar crystal or dextrose. Thereafter the child was constantly observed to see changes in the mood, behavior and appearance. After giving oral ketamine or oral midazolam following variables were assessed.

The degree of sedation was assessed by five point sedation score. 1- Barely arousable, 2-eyes closed (light sleep), 3-eyes opened but looks drowsy, 4-awake, 5-agitated. Ease of parent child separation was assessed by separation score. 1-easy separation, 2-whimpers but is easily reassured, 3-cries and cannot be easily reassured, 5-crying and clinging to parents. Reaction to iv cannulation was assessed by 4 point scale. 0-none, 1-moving the hand, 2-wincing 3- crying or struggling. Adverse effects if any were assessed.

Data obtained from hospital was collected and entered into Microsoft excel sheets. Data were then entered in to Statistical Package for Social Sciences (SPSS) version 21and descriptive and analytical analysis was performed using appropriate statistical tests.

## Results

Table 1 shows the demographics data of the patients. The groups were similar in respect of age, sex, and weight. Table also shows the emotional status before peremedication, where 68% were calm and 32% patients were apprehensive in the group receiving Ketamine. Similarly 84% were calm and 16% were apprehensive in the group receiving Midazolam. The mean pulse rate in Group I was 91.57 (SD 18.71) and in Group II was 99.12 (SD 9.61). There was no statistical difference between two groups.

| Table-1: Demographic and clinical comparison of the two study groups | | |
|---|---|---|
| **Variable** | **Group I (Ketamine) *n*=30** | **Group II (Midazolam) *n*=30** |
| Age in years (mean ± SD) | 6.53 ± 1.94 | 6.08 ± 2.41 |
| Sex (Male/Female) | 15/15 | 14/16 |
| Weight in kg (mean ± SD) | 17.07 ± 4.29 | 16.04 ± 5.71 |
| *Emotional status before premedication* | | |
| Calm | 13 | 10 |
| Apprehensive | 4 | 6 |
| Crying | 13 | 14 |
| Pulse per minute before premedication (mean ± SD) | 91. 57 ± 18.71 | 99.12 ± 9.61 |
| Onset of sedation in minutes (mean ± SD) | 17.19 ± 3.52 | 16.24 ± 2.22 |

| Table-2: Clinical findings after premedication | | | | |
|---|---|---|---|---|
| **Variable** | **Group I** | **Group II** | **t-test** | **p value** |
| Pulse | 101.27 ± 19.39 | 96.43 ± 5.73 | 1.31 | 0.199 |
| Systolic BP | 98.47 ± 7.07 | 98.13 ± 6.02 | 0.20 | 0.85 |
| Diastolic BP | 61.87 ± 3.36 | 63.07 ± 4.38 | 1.19 | 0.23 |
| Arterial oxygen saturation | 97.37 ± 2.13 | 97.63 ± 0.72 | 0.65 | 0.51 |

Table 2 shows the clinical features of the patients after administration of premedication. Pulse, systolic or diastolic blood pressures or pulse oximeter oxygen saturation were not statistically different in the two patient groups. Both venepuncture scores and acceptance of facemask was seen to be statistically better ($p < 0.001$) with ketamine as compared to midazolam (Table 3). Table 4 shows the sedation score after administration of premedication. There was no statistical difference in sedation score between two groups.

| Table-3: Comparison of study groups with respect to venepuncture score and acceptance of face mask | | | | |
|---|---|---|---|---|
| **Variable** | **Group I** | **Group II** | **$X^2$ value** | **p value** |
| Venepuncture score | | | | |
| None | 7 | 8 | 19.518 | < 0.001 |
| Moving | 9 | 22 | | |
| Wincing | 14 | 0 | | |
| Acceptance of face mask | | | | |
| Unafraid | 13 | 1 | 22.28 | < 0.001 |
| Slight apprehension | 17 | 17 | | |
| Moderate fear | 0 | 12 | | |

| Table-4: Comparison of study group with respect sedation score | | | | |
|---|---|---|---|---|
| **Sedation score** | **Group A (n=30)** | | **Group B (n=30)** | |
| | **Before** | **After** | **Before** | **After** |
| 1 | - | - | - | - |
| 2 | - | - | - | 3 |
| 3 | 1 | 20 | - | 25 |
| 4 | 12 | 4 | 15 | 2 |
| 5 | 17 | - | 15 | - |

## Discussion

The aim of preanesthetic medication include decreased anxiety, analgesia if preoperative pain is evident, and if necessary, diminished airway secretions and diminished gastric acidity and volume. While varied premedications have been advocated to allay anxiety and facilitate smooth separation of children from parents, the ideal premedicant remains elusive. The ideal premedicant in

children should be readily acceptable, have rapid, reliable onset of action with minimal side effects. Recent reports suggest that both oral ketamine and oral midazolam, may fulfill many of these criteria. Midazolam, a short-acting, water-soluble benzodiazepine with an elimination half-life of approximately 2 hours, is the most widely used premedication for children [5]. The major advantage of midazolam over other drugs in its class is its rapid uptake and elimination. It can be administered intravenously, intramuscularly, nasally, orally, and rectally with minimal irritation, although it leaves a bitter taste in the mouth or nasopharynx after oral or nasal administration, respectively.

Orally administered midazolam is effective in calming most children and does not increase gastric pH or residual volume [6]. Two multicenter studies yielded slightly different responses to this preparation of oral midazolam in children. In one study, 0.25, 0.5, and 1.0 mg/kg all produced satisfactory sedation and anxiolysis within 10 to 20 minutes [7] whereas in the other study, 1.0 mg/kg provided greater anxiolysis and sedation than 0.25 mg/kg [8].

In a study conducted by Lt col Navdeep sethi et al there was no statistical difference in the onset of sedation in both groups.

The disadvantages of ketamine include sialorrhea, nystagmus, an increased incidence of postoperative emesis, and possible undesirable psychological reactions such as hallucinations, nightmares, and delirium, although to date no psychological reactions have been reported after oral ketamine. Larger doses of intramuscular ketamine are particularly useful for the induction of anesthesia in children in whom there is a desire to maintain a stable blood pressure and in whom there is no venous access, such as those with congenital heart disease.

In a short review it was noted that no head to head trials of intravenous ketamine versus intravenous midazolam for procedural sedation in children in the emergency setting could be found [9]. Secondary findings show that satisfaction of parents and physicians was greater with ketamine and that physicians felt it was safer. Based upon observational studies and randomized trials, ketamine alone or in combination with midazolam or propofol provides more effective sedation and anxiolysis for very painful procedures, such as fracture reduction or bone marrow aspiration. In a blinded trial of 260 children, 5 to 15 years of age, undergoing fracture reduction, patients who received ketamine combined with midazolam had clinically significantly lower distress during the procedure and higher orthopedist satisfaction than those who received midazolam and fentanyl [10].

In a trial of 113 children, 3 to 18 years of age, undergoing fracture reduction, patients who received ketamine and midazolam had clinically significantly less chance of oxygen desaturation [11]. So the current evidence favours ketamine.

In a RCT of 41 children under the age of 3 years undergoing dental treatment, combination of oral midazolam and ketamine was found to be effective for guiding the behaviour of children [12]. Dr Suranjit Debnath, Dr Yash Pande in their study of 60 children of ASA 1 aged 1-10years found that 77% of chidren in ketamine group attained sedation score of 3 or less and 36% of children in midazolam group attained sedation score of 3 or less within 30 minutes. Ketamine may be administered by intravenous, intramuscular, oral, nasal transmucosal, and rectal routes [13].

In a prospective randomized double blind study including patients aged 1-5 years with 10% burns. The combination of oral midazolan and ketamine provided better analgesia than combination of midazolam acetaminophen and codeine for painful procedures in burn patients [14]

## Conclusions

The present study concludes that both oral ketamine and oral midazolam are good premedicating agents in children with minimal side effects. However, premedication with 6mg/kg of oral ketamine is associated with better acceptance of face mask and venepuncture score than oral midazolam.

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