

# Intranasal midazolam Vs ketamine as premedication in paediatric surgical procedure for child separation and induction

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## ABSTRACT

In children pre-anaesthetic medications are frequently administered as pharmacological adjuncts to help alleviate the stress and fear of surgery as well as to ease child parental separation and promote a smooth induction. Oral, rectal, intravenous and intramuscular route has been used; however each route has its disadvantage. Pre-anaesthetic medication administered intranasal for avoidance of painful injection have made it a convenient way to pre-medication. To evaluate the efficacy of intranasal administered Midazolam 0.2mg/kg and Ketamine 5mg/kg respectively. Total 50 patients of ASA I and II of age group 1- 7 years, mean age  $3.88 \pm 1.26$  and  $4.56 \pm 1.21$  were included in group I and group II respectively, and Scheduled for elective surgery. Mean time of separation was  $17.12 \pm 1.21$  in-group I and  $15.68 \pm 1.62$  in group II with P value  $<0.001$  and  $0.322$ , shows significant difference during time of separation from parents and no significant difference for iv line insertion in both groups.

**Keywords:** Intra-nasal pre-medication, child separation, Midazolam and Ketamine.

## INTRODUCTION

Surgery and anesthesia induction cause considerable emotional stress upon children.<sup>1</sup> The consequence of this stress may remain in the child's psyche, long after the hospital experience has been passed away.<sup>2</sup> Emotional and behavioral changes that occur when the child is separated from their parents.<sup>3</sup> But it is difficult to determine which components of a child's hospitalization result in psychological problems. However, the child age, parental anxiety level, previous hospitalization and type of surgery are factors that can influence a child anxiety level and psychological well being.<sup>4</sup>

Preoperative anxiety stimulates sympathetic nervous system and endocrine system leading to cardiac excitability and causes increase in heart rate, blood pressure. This reaction reflect the child's fear of separation from parents and home environment, fear of physical harm, fear of unfamiliar routines, surgical instruments and hospital procedure.<sup>5</sup> This all will cause post operative psychological problem in pediatrics patients. Comprising of mal-adaptive behavioral responses such as general anxiety, nighttime crying, enuresis, separation anxiety, temper tantrums up to 44.0% of children two weeks after surgery, and about 20.0% of these children will continue to demonstrate negative behaviors 6 months after surgery.<sup>6</sup>

In children pre-anesthetic medications are frequently administered as pharmacological adjunct to alleviate the stress and fear of surgery as well as to ease child-parent separation and promote a smooth induction of anesthesia.<sup>7</sup> The introduction of new drugs and new routes of administered in the last decade. For example, intranasal (trans-mucosal) route, which avoid painful intramuscular injection, the most horrifying experience for a child, has facilitated for pediatric patient.<sup>8</sup> with keeping in view, the necessity of reducing pre-operative and post-operative psychological problems in pediatrics. We compare the sedative properties of Midazolam, water-soluble benzodiazepine and Ketamine, a phencyclidine derivative administered intranasal to 1-6 years old pediatrics surgical patients to alleviate the separation anxiety and time of intravenous line insertion for induction of anesthesia.

## MATERIALS AND METHODS

To compare the sedative effects of Midazolam and Ketamine administered intra-nasally as pre-anesthetic medication. 50 children aged 1-6 years with American Society of Anaesthesiologist physical status I and II scheduled for elective surgery were selected for this study. This study was performed in Nepal Medical College,

Kathmandu. Full explanation regarding the aim and route of administration of the drug were given to the parents and their written consent was obtained individually. Patients were randomly allocated to one of the two groups.

Group I (Midazolam), Group II (Ketamine). Midazolam 0.2mg/kg and Ketamine 5 mg /kg were installed either of nostril 20 minutes before the induction. Using a syringe of appropriate size (1/2/3 ml) without needle, and allowed to play the child with parents under constant observation to handle any adverse reaction.

The reaction of the child at the time of separation from parent and time of intravenous line insertion before induction of anesthesia was evaluated according to sedation score of Sury and Cole.

In our study, we assume no sedation G<sub>0</sub>, mild sedation G<sub>1</sub>, good sedation G<sub>2</sub>, over sedation G<sub>3</sub>. The results of two groups were evaluate and compared. The results with P- value < 0.005 were regarded significant.

## RESULTS

In this study patients randomly assigned to two groups and their mean age are shown in the Table-1.

The sedation score was assessed according to Sury and Cole sedation score at the time of separation from parent and insertion of intravenous line. No patients were too sedated in either group so we exclude G<sub>3</sub>. The results of sedation score were shown in Fig 1.

Comparing sedation score in Group I (Midazolam) score G<sub>0</sub> was achieved by 3 patients (12.0%), G<sub>1</sub> score by 6 patients (24.0%) and G<sub>2</sub> score by 16 patients (64.0%). The sedation score and time of separation from parent in Group I were (Midazolam) 17.12± 4.12 and Group II (Ketamine) 15.68±11.62 shows P value <0.001 and 0.332 respectively. It means there were significant differences between time of separation from parent in two Groups but no difference in Intravenous insertion between two groups in Table-2.

## DISCUSSION

The preoperative anxiety is two fold in un-pre-medicated children in comparison to the pre-medicated children. Children when pre-medicated properly and separated from their parents with-out anxiety of physical harm like needle insertion, this psychological effect leads to block autonomic reflex, prevent excessive secretion in airway, allays anxiety, facilitates smooth induction of anesthesia and reduce the dose of general anesthesia.<sup>3</sup> Hence, all the pediatrics patients to be premeditated in order to decrease preoperative anxiety, allow smooth induction and post operative psychological insult and behavior change.<sup>9,10</sup>

The route of pre-medication in pediatric age groups should be considered carefully. Intramuscular injections are painful, oral pre-medication is not effective in gastrointestinal disturbance and often rejected by small child.<sup>1,8</sup> Children and parents are very reluctant to allow rectal administration of drug. Since the use of nose drops is widely known in general practice, this route could well accepted by children and their parents for pre-medication. This route of pre-medication has been used successfully and safely by different researchers.<sup>11</sup> The study by Rosenberg *et al* and Daniel *et al* showed sedation usually occurs within 10-20 minutes with midazolam with anxiolysis and some ante-grade amnesia.

There are several reports about intranasal administration of Ketamine with good efficacy and no adverse effects for pre-medication and sedation in children. Another study performed by Kahreci *et al* showed intranasal Midazolam, Ketamine, Alfentanil and Fentanil pre-medication in 2-7 years children regarding reaction to separation from parents and response to intravenous cannulation. They concluded Midazolam and Alfentanil produce early sedation compared to Ketamine.

Abrams *et al* studies the safety and sedative effect of intra nasal Midazolam (0.4 mg/kg) and Ketamine 3mg/kg and found both were good sedative. In our study, intra-nasal Midazolam (0.2mg/kg) and Ketamine (5mg/kg) produce a good level of sedation regarding child separation from parents and response to intravenous line insertion.

Louon and Reddy used mixture of Ketamine 5mg/kg and Midazolam 0.56 mg /kg given intra-nasally to induce deep sedation for Computerized Tomography.

In addition the comparison of Midazolam and Ketamine groups, we found that intra nasal Ketamine is more effective than intra nasal Midazolam regarding separation of child from parents (G<sub>1</sub>=24.0% and 28.0%).In response of child to intravenous line insertion the sedative effect of intra nasal Midazolam and Ketamine was equal (G<sub>2</sub> =64.0% and 64.0%).

Midazolam 0.2mg/kg and Ketamine 5mg/kg administered intra-nasally in 1-6 years old children is equally effective for easier separation of children from their parents and obtunding their response to intravenous line insertion. A possible criticism of our study might be that we used volume of 0.2mg/kg and 5mg/kg Midazolam and Ketamine respectively for intranasal drug administered. Apart from drug absorption over the nasal mucosa, significant parts of the medication will go to pharynx where absorption via the pharyngeal mucosa occurs and remaining volume will be swallowed. Thus we must emphasize that the term nasal pre-medication describes the mode of drug administration and not necessarily the single route of drug absorption.

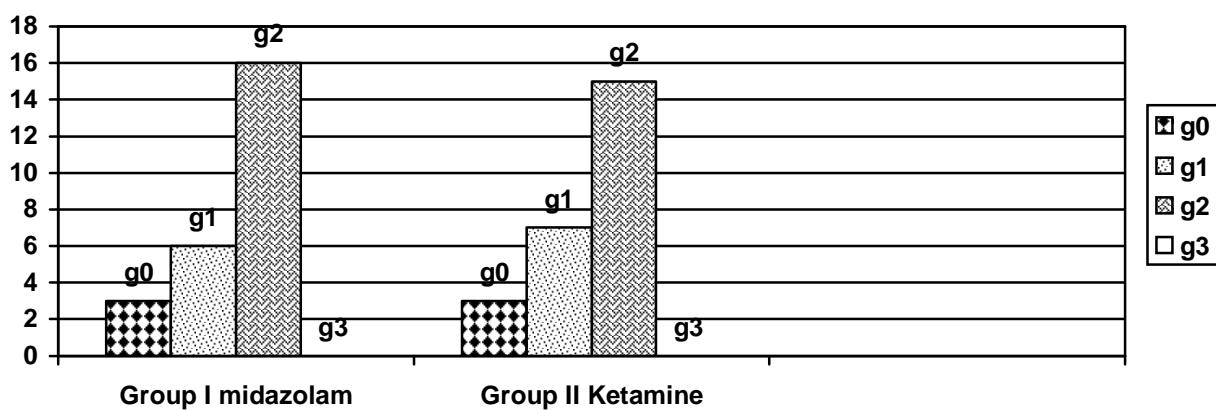
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**Table-1:** No. of patients and mean age

Groups/agents	no of patients (%)	Mean age $\pm$ SD
<b>I (Midazolam)</b>	<b>25 (50.0%)</b>	<b>3.88<math>\pm</math>1.26</b>
<b>II (Ketamine)</b>	<b>25 (50.0%)</b>	<b>4.56<math>\pm</math>1.21</b>

**Sedation score at the time of separation**



**Fig. 1.** Sedation score at the time of separation/ i.v insertion

G<sub>0</sub> Very restless, shows resistance to separate, G<sub>1</sub> Slight restless, shows mild resistance to separate

G<sub>2</sub> Relax, clam, co-operative doesnot resistance to separate, G<sub>3</sub> Too much sedated and not responsive to command

**Table-2:** Time of separation and iv insertion

Groups/Agents	Time of separation/ iv insertion (Mean $\pm$ SD)	Score achieve during separation/ iv insertion no (%)	Duration of surgery (Mean $\pm$ SD)
Gr I Midazolam	17.12 $\pm$ 4.12	G <sub>0</sub> 3 (12.0%) G <sub>1</sub> 6 (24.0%) G <sub>2</sub> 16 (64.0%)	37.4 $\pm$ 10.78 mins
Gr II Ketamine	15.68 $\pm$ 11.62	G <sub>0</sub> 3 (12.0%) G <sub>1</sub> 7 (28.0%) G <sub>2</sub> 15 (60.0%)	40 $\pm$ 10 mins