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editor.fpa1@gmail.com

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Comparison of oral midazolam as a premedication in children to oral midazolam combined with ketamine

MV Reddy, M Hanumanthappa
Department of **Pharmaceutical Analysis**

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Abstract

Ketamine and midazolam are frequently utilized as premedicants in pediatric patients. The effectiveness of oral midazolam vs the combination of midazolam and ketamine as premedicants in a pediatric age range of sixty children was examined in this prospective randomized research. The study comprised 30 patients in each group, ages 2–6, receiving major and intermediate surgery. Group A got oral midazolam (0.5 mg/kg) forty-five minutes before surgery, while group B received oral ketamine (3 mg/kg) and midazolam (0.25 mg/kg) in the recovery room. Sedation onset, emotional response, sedation score, intravenous cannulation response, and acceptance of the face mask were among the observations. The unpaired t-test and the chi-square test were used to analyze the data. Compared to the midazolam group alone, the outcomes shown in the midazolam and ketamine group were statistically significant. Both groups' intraoperative hemodynamic parameters were similar. The midazolam and ketamine (M+K) group experienced considerable post-operative analgesia. We therefore draw the conclusion that oral premedication greatly reduces anxiety and produces a patient who is composed and cooperative. Both midazolam and midazolam and ketamine (M+K) provide excellent sedation. In both groups, no notable adverse effects were noted.

Key-words: Ketamine, oral midazolam, and pediatric anesthesia.

Introduction

Inducing anesthesia in a pediatric population is a difficult task. A patient who is upset and crying due to separation anxiety, dread of an unfamiliar surroundings, or fear of needles and injections may worsen the challenging to induce anesthesia. Since young children's sensitive minds can be traumatized by the terror of operating rooms and injections, it becomes a skill-rich specialty (1). 70% of kids exhibit high levels of worry and anxiety prior to anesthesia (2). Children who have preoperative anxiety may experience detrimental physiological and psychological repercussions (3). Premedication has gained popularity since it is difficult to produce anxiety in children, and many strategies are tried to get around this problem. Benzodiazepines, ketamine, opioids, and other medicinal medications have all been utilized as premedication (4).

Easy administration, rapid start and recovery, and few adverse effects are essential components of the perfect premedication (5). For premedication, the oral method is better because it is simple to administer and children readily accept it. A good pre-medication should have easy acceptance, quick onset, short duration of action, and no serious adverse effects (6). Ketamine and midazolam are frequently administered orally, nasally, and rectalally. In this age group, ketamine and midazolam are frequently administered orally and rectally (7). Both medications produce a calm child for anesthesia and have a slow onset time of 15 to 30 minutes (8).

To assess the safety and effectiveness of two regimens, we used oral midazolam (0.5 mg/kg) versus oral midazolam (0.25 mg/kg) + ketamine (3 mg/kg) as premedication. This was done in a randomized double blind research. According to Warner, Cabert, and Velling, midazolam + ketamine works better as a premedication than midazolam by itself (9). The purpose of this randomized double-blind trial was to observe sedation, the reaction to intravenous cannulation, the acceptance of facemasks, **Sedation Scale** palatability, separation from parents, and any adverse effects

Subjects and Methods

Sixty children of either sex, aged between two and six years, undergoing 30- to 120-minute pediatric general, orthopaedic, ophthalmology, and plastic surgery with ASA grades I and II were included in the study following ethical committee approval. We excluded children with URTI, metabolic problems, and systemic disease, as well as those with ASA III. Children in a randomized controlled research were divided into two groups of thirty. Group (A) received 0.5 mg/kg of oral midazolam. Group (B) received oral ketamine (3 mg/kg) and midazolam (0.25 mg/kg). Written informed consent was obtained after each patient was examined. 45 minutes prior to operation, premedication drugs were administered. At 0, 10, 20, 30, and 40 minutes, all children underwent continuous assessments for PR, RR, B.P., and SP02; scoring was completed at the conclusion of the 40-minute period.

Score	Sedation	Anxiolysis	Parental Separation	Venepuncture
1	Alert	Thrashing	Need to restrain	Fight without success
2	Awake	Crying	Seperated with cry	Fight with success
3	Drowsy	Apprehensive	Seperated with cry	Minor resistance
4	Asleep	Friendly	Happily seperated	No reaction

The youngster underwent 30-minute preoperative, intraoperative, and postoperative observation. The sort of pre-medicant was unknown to the anesthesiologist who assessed the patient prior to surgery. The investigators (a resident physician and a staff nurse) only observed and evaluated patients; they had no idea what agent was administered. Prior to surgery and following premedication, baseline oxygen saturation and pulse rate were recorded. Every monitor in the operating room is connected. Injections of fortwin 0.03 mg/kg, ondensetron 0.1 mg/kg, and glycopyrrolate 0.04 mg/kg were administered. Sevoflurane 6% and air and oxygen (60:40) were used to induce general anesthesia. After intravenous (IV) atracurium (0.7 mg/kg), the trachea was intubated using an endotracheal tube of the proper size. Bupivacaine 0.25% 1ml/kg was injected for intraoperative anesthesia, and caudal block was used as an analgesic instead of intraoperative sedation. For every patient, reversal and extubation went smoothly. A single observer calculated the sedation score using the sedation scale.

Parameters observed were:

- The degree and grade of sedation.
- Emotional response: tears, fear, and serenity.
- Reaction to separation: good, fear, and tears.
- A response of acceptance to the face mask.
- Response to cannulation via intravenous means.
- Recovery time and side effects.

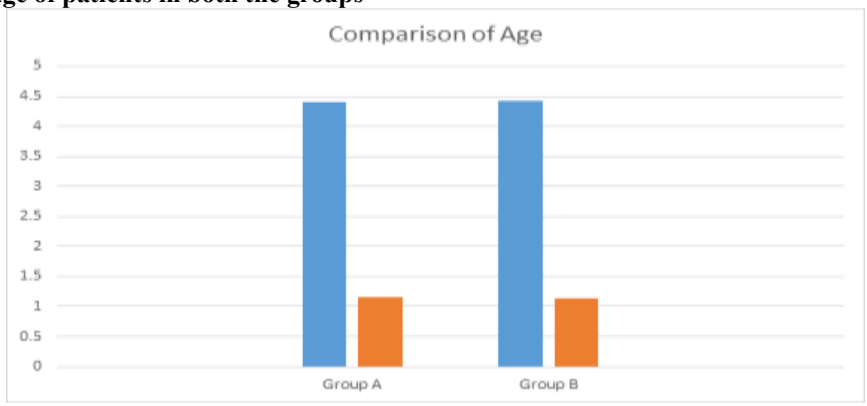
Following oral medication administration, sedation, anxiolysis, and cooperation were noted

at the following intervals: five, ten, twenty, thirty, and forty minutes. Throughout the process, oxygen saturation and heart rate were tracked. The chi square test and unpaired t-test were used for the statistical analysis.

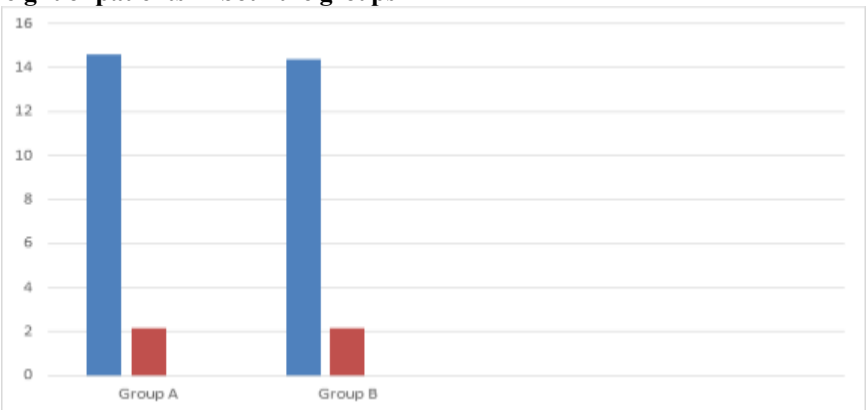
Results

Every child tolerated the oral medication well and did not throw up. Older children (over three years old) reported that the medicine tasted good because it was combined with rose syrup. Two groups of sixty kids were examined: Group A (Midazolam) and Group B (Midazolam + Ketamine). When age, gender, weight, and operating time were taken into account, the study's findings were similar. Age, sex, and weight did not show statistically significant differences.

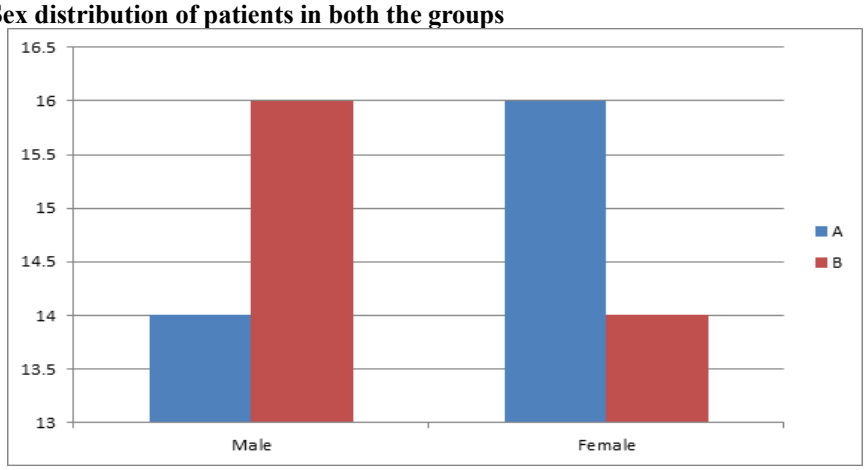
Comparison of age of patients in both the groups



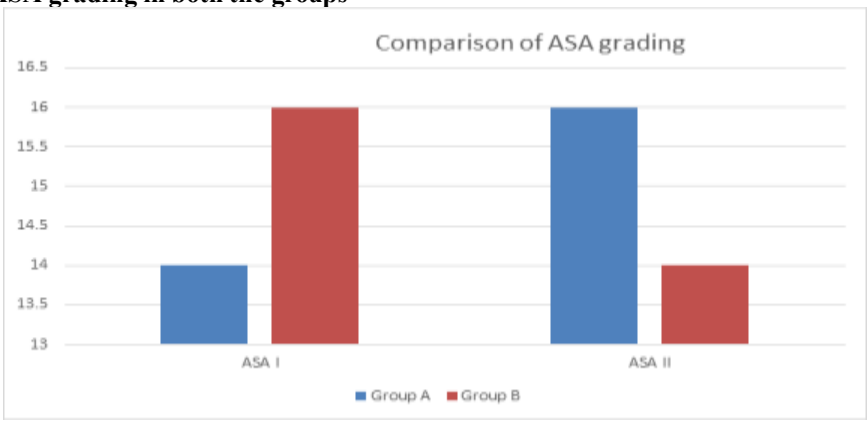
Comparison of weight of patients in both the groups



Comparison of Sex distribution of patients in both the groups



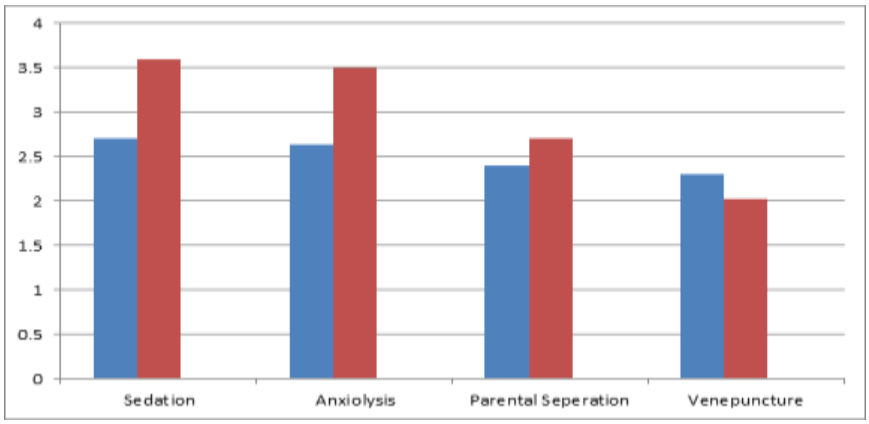
Comparison of ASA grading in both the groups



Sedation Score

Score	Group A		Group B		P Value
	Mean	SD	Mean	SD	
Sedation	2.7	0.47	3.6	0.56	<0.0001
Anxiolysis	2.63	0.49	3.1	0.4	<0.001
Parental Separation	2.43	0.5	2.77	0.43	<0.05
Vene Puncture	2.33	0.48	2.57	0.5	>0.05
Total	10.1	1.18	12.03	1.35	<0.0001

Comparison of sedation, anxiolysis, parental separation and vene puncture scores in patients of both the groups



Graph 2: Group wise distribution of Oxygen saturation & Pulse rate at various intervals

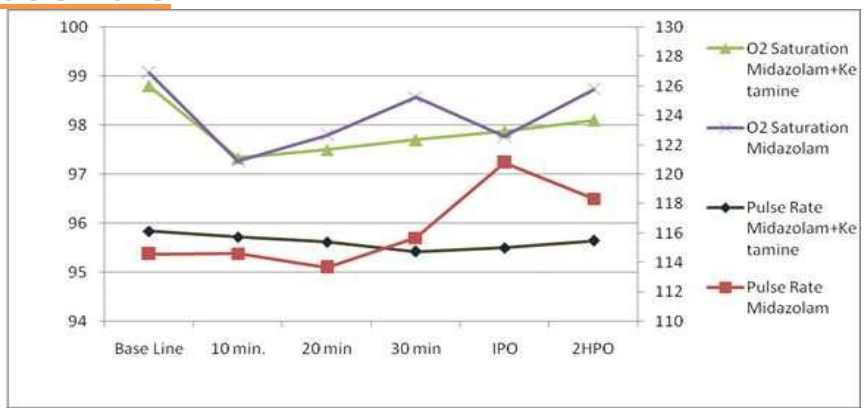


Table 5: Summary of results

Observation	Group (A) Midazolam	Group (B) Midazolam + Ketamine	p values	Statistical data
Onset time of sedation	22.35(+/- 3.35min)	22.05(+/-3.15 min)		difference is NOT significant
Post-operative recovery time	20(+/-8.17min)	25.3(+/- 6.15min)		difference is significant
Side effects secretions	3.70%	5%	0.381	difference is NOT significant
Nausea/vomiting	0%	6.70%	0.150	difference is NOT significant
Post op analgesic requirement	60%	33.30%	0.038	difference is significant

There was no evidence of leaking, and preoperative acceptability was good. The student's unpaired t-test was used to examine the post-operative findings that are described in Table 5.
The chi square test was used to examine the sedation score, anxiolysis score, and side effects that occurred before and after surgery.

The M group's mean sedation score was 2.7 +/- 0.47, but the B group's was 3.6 +/- 0.56. This difference was statistically significant. According to the table and graph, the A group's anxiety score was 2.63 +/- 0.49, while the B group's score was 3.1 +/- 0.4. As a result, it was found that taking two medications together significantly reduces anxiety more than taking them separately.
The statistically significant parental separation scores for the A and B groups were 2.77 +/- 0.43 and 2.77+/-, respectively.
The A group's reaction score to venepuncture was 2.33 +/- 0.48, whereas the B group's was 2.57 +/- 0.5, indicating a better outcome but one that is not statistically significant.
The sum of the four M-scores is 10.1 +/- 1.18, which is similar to the M+K combination of 12.03 +/- 1.35, which is quite important. When intraoperative vitals, such as PR and SPO2, were evaluated, no discernible differences were seen.
There were very few adverse symptoms, such as vomiting, nausea, and secretion. 3.41 patients were found to have nystagmus. The need for post-operative analgesia was 60% in group A and 33.30 in M+K, which was statistically significant (p – 0.038).

Talk about
For most people undergoing surgery, the preoperative phase is a difficult time. Therefore, the main goal of pediatric surgery is anxiolysis. Blood pressure, pulse rate, and behavioral anxiety rating have all been shown to correlate (3). Therefore, during the preoperative phase, a variety of premedications are used to reduce anxiety.
Children readily tolerate oral premedication, which is very simple to administer. Aspiration pneumonia risk is not increased by oral

premedication (10).
Although several medications have been explored for oral premedication, midazolam is the most widely used.
When Midazolam is taken orally, ketamine helps to lessen its effects.
45 minutes prior to surgery, premedicant was administered, and all vital signs, including PR, BP, SPO2, and RR, were monitored.
In the A group, the onset of sedation was 22 +/- 3.35 minutes, whereas in the B group, it was 21 +/- 2.50 minutes. After 40 minutes, there was a peak in activity, thus all scores were recorded at that point.
Sedation, anxiolysis, parental separation, and venepuncture were the four variables that were compared between the two groups.
Prior to premedication, every patient had a score of ¼. The mean sedation score was 2.7 +/- 0.47 in the A group and 3.6 +/- 0.56 in the B group after 40 minutes; the difference was statistically significant.
smooth induction and avoid behavioral and psychological abnormalities during surgery (11, 12).
Ketamine and midazolam also meet the best premedication requirements, including quick onset, strong anxiolysis, sedation, and quick recovery.
The simplest premedication method is oral administration; the onset is gradual, drowsiness takes 30 to 40 minutes, and the recommended dosage, as per McMillan, is between 0.5 and 0.75 mg (14).
When taken orally or intrarectally, midazolam and ketamine work better together than when taken separately (9).
Sedation began in the A group of our study at 22.35 (+/-3.35 minutes), but in the B group it began at 22.05 (+/- 3.15 minutes). The two groups' differences were not statistically significant. All observations at 40 minutes are tabulated because the peak action occurred after 30 minutes.
Group (A) had sedation scores of up to 80% for scores 3 and 4, but Group B had scores of 94%, indicating a significant statistical difference ($p<0.05$). These outcomes mirrored those
Our findings are supported by Darlong et al.'s 2004 comparison of oral midazolam with oral ketamine, which revealed an early onset of drowsiness after 20 minutes (11).
The anxiolysis score was similar.
The separation score is consistent with Ghai et al. 2005-M+K, which found that patients were more easily separable, calm, quiet, and aware (12).
Venepuncture score: According to Funk and Jacob et al. (2000), venepuncture is considerably less effective when combined with M+K (13).
Every vital sign was same in both groups. There were very few secretions and symptoms similar to nausea and vomiting. Three to four percent of patients had nystagmus.
A number of premedications are being researched since a calm separation of parents and children is a major concern. Easy administration, quick onset, and a seamless recovery are characteristics of the perfect premedicant.
All pediatric patients should receive premedication to reduce preoperative anxiety.
reported by Diaz et al. (15).
Group (B) outperformed Group (A) in terms of attitude, facemask acceptance, and intravenous cannulation. Diaz et al. also made these observations (15).
In group (A), the seperation reaction was good in 26.67% of cases, but in group (B), it was 56.70%.
These findings matched those reported by Ljungman et al. (16).
There was no discernible change in the group's intraoperative oxygen saturation, pulse rate, or respiration rate.
(A) and Group (B) according to research by Wilton et al. and Gulstien et al. (17).
Oral midazolam (0.5 mg/kg) and oral ketamine (5 mg/kg) were shown to be more successful than midazolam alone in a 2005 study on sedation, children's acceptance of mask breathing, and their response to being separated from their parents. The effectiveness of oral midazolam (0.25 mg/kg), oral ketamine (3 mg/kg), and their combination on the degree of drowsiness, the kind of conduct of children, and the peaceful separation of children from their parents was examined in the Darlong et al. study. After 10 and 20 minutes, the combination group's desired

sedation scores were noticeably more specific than those of the other groups. The behavior type score and children's separation did not differ significantly between the groups. Our analysis did not correlate with the findings of the Darlong et al. study. When examined at 20 and 30 minutes, oral midazolam, ketamine, and midazolam with ketamine delivered sedation and effect, demonstrating that the combination of midazolam and ketamine produced better quality than either drug alone. This was also seen in a research by Banerjee et al. (18). Group M in this trial was given 0.5 mg/kg of oral midazolam, while Group M+K was given 0.25 mg/kg of oral midazolam together with 3 mg/kg of oral ketamine. Both groups offered separating properties and anxiolytics that were equally effective. But the combination group offered more kids that were awake, quiet, and able to be quickly separated from their parents (7) before to premedication. Both groups did not experience nystagmus or other adverse effects like vomiting or increased salivation. According to Agrawal Nidhi et al.'s study, post-operative side effects were mild, and none of the patients experienced any emergent reactions (19). Because of the small sample size, fewer complications were seen. In addition to psychological preparation of children, oral acceptable premedication can prevent youngsters from being forcibly separated from their parents before anesthesia with stormy induction and painful injection.

Conclusions

Children can be sedated quickly and reliably using oral premedication. Both midazolam and midazolam plus ketamine provide a good degree of comfort and sedation. However, the midazolam plus ketamine group offers noticeably greater sedation, analgesia, and comfort quality. In both groups, there were no notable adverse effects.

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