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Original Research Article

Comparative Study of Oral Ketamine Versus Oral Midazolam as Premedicants in the Pediatric Population in Elective Surgical Procedures

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Abstract

Purpose: To compare oral ketamine and oral midazolam as premedicants in the pediatric population are undergoing elective surgical procedures.

Introduction: Oral ketamine produces predictable satisfactory sedation and anxiolysis without significant side effects. This comparative study was carried out to compare oral ketamine with oral midazolam to know the efficacy of both the drugs as premedicants in the pediatric population.

Material and Methods: This prospective, randomized study was conducted in 160 children who posted for elective surgery. These patients were divided in to two groups having 80 patients in each group. Group A which received 0.5mg/kg midazolam and group B: received 5mg/kg ketamine orally. Before and after premedication, sedation and anxiolysis score were assessed, after premedication it was assessed at 10, 20, and 30 minutes. Thirty-five minutes after oral premedication, children were separated from parents. During parental separation, parent child separation score was assessed and recorded.

Results: After premedication at 10 minutes, about 70% and 87.5% patients were unsuccessful while rest successful sedation scores in midazolam and ketamine group respectively. At 20 minutes 22.5% and 70% patients were unsuccessful and 77.5% and 12% were successful sedation scores in midazolam and ketamine group respectively. At 30 minutes, 10% and 42.5% patients were unsuccessful and 90% and 58.7% were successful sedation scores in midazolam and ketamine group respectively. This result was statistically significant.

Conclusion: We concluded that oral midazolam showing faster onset of sedation, higher sedation scores with lower anxiety scores as compared to ketamine. Oral midazolam is also provides better easy separation from parents and excellent mask acceptance in children.

Keywords: Ketamine, Midazolam, Sedation, Premeditates.

Introduction

Pediatric population is different from adults due to anatomical/physiological difference and difference in their pharmacodynamics and pharmacokinetics response. Usually, aggressive psychological response and reacts violently to parental separation are found among the pediatric age group especially preschool going children [1-4]. Hence, the anesthesiologists involved in pediatric anesthesia have to be very careful in selecting a premedicant among the long list with emphasis to preoperative sedation, transfer to operating room, and subsequent smooth induction of anesthesia. Premedication causes sedation and reduction of anxiety during separation from parents. It also provides a calm and cooperative child for smooth induction of anesthesia.

Although many sedative agents such as hyoscine, phenothiazine, clonidine, midazolam, phencyclidine derivatives, and tramadol all have been used for the purpose of premedication with a view to have calm and quiet child for smooth induction of anesthesia, few of them can be given orally and can help in avoiding the pricks Midazolam, a benzodiazepine, has been routinely used orally for premedication in children scheduled for surgery [5]. It has a rapid onset and short duration of action. It is reliable in achieving sedation and anxiolysis [6,7]. However, search for a better alternative continues due to concerns such as bitter taste, cognitive impairment, long-term behavioral disturbances, paradoxical reactions, hiccups, and respiratory depression [8,9].

Oral ketamine has similar pharmacodynamic after oral administration and has been investigated as an alternate premedication [10-12]. It acts at the thalamo-cortical projection to produce dose-dependent sedation and dissociative anesthesia. Oral ketamine produces predictable satisfactory sedation and anxiolysis without significant side effects like respiratory depression or emergence delirium in children [10,13,14].

We conducted this study to compare Oral ketamine with oral midazolam to know the efficacy of both the drugs as premedicants in the paediatric population undergoing elective surgical procedures and ascertain the minimum interval required between premedication and parental separation.

Material and Methods

This Prospective randomized study was conducted in the department of Anesthesiology on total 160 children. Ethical clearance was taken from Institutional Ethical review committee. An informed written consent was obtained from all the parents or Guardian.

Inclusion Criteria:

- Patients with ASA class I and II.
- Patients aged between 4 to 12 years who were, undergoing elective surgery.

Exclusion criteria:

- Allergies to benzodiazepines and ketamine.
- Central nervous system dysfunction – epilepsy or raised intracranial tension,
- Cardiovascular malformation.
- Respiratory dysfunctions such as asthma, chronic bronchitis.
- Prolonged therapy with hepatic enzyme – inducing drugs.
- Children refusing to take the whole dose of premedication.

Procedure:

Patients were allocated into two groups using simple computerized based randomization techniques into two groups of 80 each: Group A: received 0.5mg/kg midazolam and group B: received 5mg/kg ketamine orally.

Before the premedication, the children were brought to the preoperative room along with

their parents. Patient received the premedication around 45 minutes before surgery. The drugs were mixed with freshly prepared sugar solution to make the volume 5ml and to ensure palatability of the preparation.

Sedation and anxiolysis score were assessed before and after premedication at 10, 20, and 30 minutes. 35 minutes after oral premedication, children were separated from parents. During parental separation, parent child separation score was assessed. Children were then transferred to the operating room. In the operating room, routine monitoring with ECG, non-invasive arterial pressure and pulse oximetry was commenced. Venepuncture was done approximately 5 minutes later in the induction room. After venepuncture, patients were induced with inhalational agent through face mask and the remaining part of the anaesthesia was conducted with standard anaesthesia protocol.

Statistical analysis

The data were analyzed using SPSS version 27 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

The two groups were comparable with respect to age, gender, and weight [Table 1].

Table 1: Demographic data of patients

Variable	Group A	Group B	P value
Age (months)	44.12±10.42	38.52±09.48	0.12
Gender (Male) **(Female)**	29 (72.5%) 11 (27.5%)	27 (67.5%) 13 (32.5%)	0.2
Weight (kg)	16.01±1.74	13.99±2.10	0.31

Statistically significance at p≤0.05

All Before premedication, all the patients belonged to unsuccessful sedation score category and baseline sedation and anxiolysis score was comparable between two groups. At 10 minutes of premedication, 56(70%) and 70(87.5%) patients had unsuccessful and 24(30%) and 10(12.5%) had successful sedation scores in midazolam and ketamine group respectively. At 20 minutes of premedication, 18(22.5%) and 56(70%) patients had unsuccessful and 62(77.5%) and 24(12%) had successful sedation scores in midazolam and ketamine group respectively. While at 30 minutes of premedication, 8(10%) and 34(42.5%) patients had unsuccessful and 72(90%) and 46(58.7%) had successful sedation scores in midazolam and ketamine group respectively. These results were statistically significant ($P \leq 0.05$) (Table 2).

Table 2: Sedation between two groups at 10, 20 and 30 minutes

Groups	10 Minute		20 minutes		30 minutes	
	Unsuccessful	Successful	Unsuccessful	Successful	Unsuccessful	Successful
Group A	56 (70%)	24(30%)	18(22.5%)	62(77.5%)	8(10%)	72(90%)
Group B	70(87.5%)	10(12.5%)	56(70%)	24(12%)	34(42.5%)	46(58.7%)
P value	0.02*		0.001*		0.05*	

*indicates statistically significance at p≤0.05

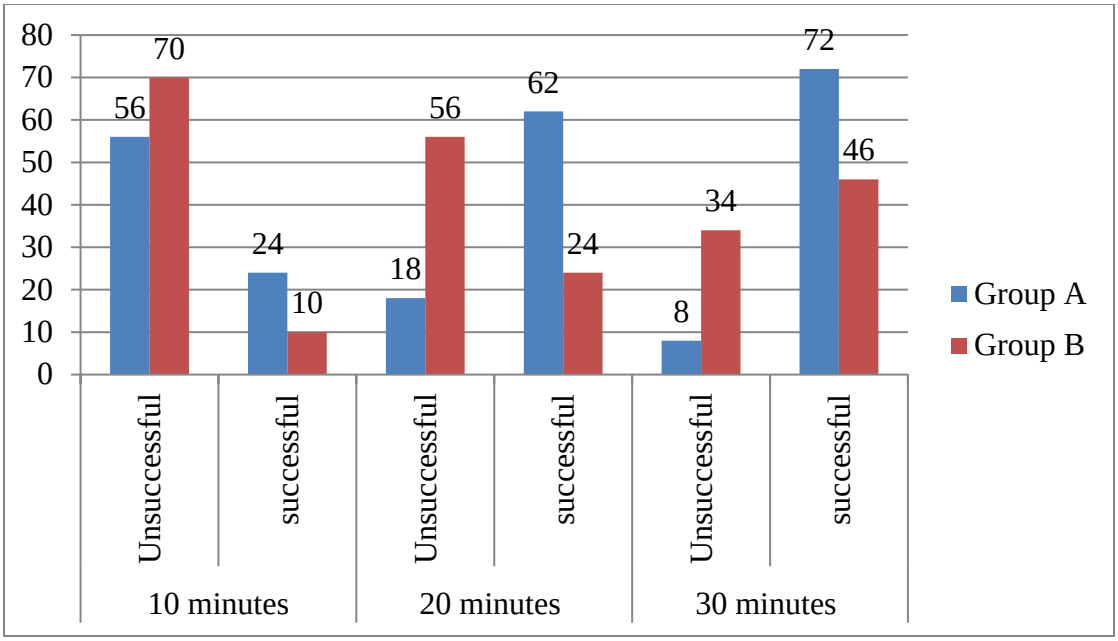

Figure 1: Sedation between two groups at 10, 20 and 30 minutes

Similarly, at 10 minutes of premedication 32(40%) and 66(82.5%) patients had unsuccessful and 48(60%) and 14(17.5%) had successful anxiolysis scores in midazolam and ketamine group respectively whereas at 20 minutes of premedication, 16(20%) and 32(40%) patients had unsuccessful and 64(80%) and 48(60%) had successful anxiolysis scores in midazolam and ketamine group respectively while at 30 minutes of premedication, 10(12.5%) and 40(50%) patients had unsuccessful and 70(87.5%) and 40(50%) had successful anxiolysis scores in midazolam and ketamine group respectively. Also, these results were statistically significant ($P \leq 0.05$) (Table 3). At 35 minutes of premedication, results were also statistically significant (p=0.001).

Table 3: Comparison of anxiolysis between two groups at 10, 20 and 30 minutes

Groups	10 Minute		20 minutes		30 minutes	
	Unsuccessful	Successful	Unsuccessful	Successful	Unsuccessful	Successful
Group A	32(40%)	48(60%)	16(20%)	64(80%)	10(12.5%)	70(87.5%)
Group B	66(82.5%)	14(17.5%)	32(40%)	48(60%)	40(50%)	40(50%)
P value	0.001*		0.03*		0.004*	

* indicates statistically significance at p≤0.05

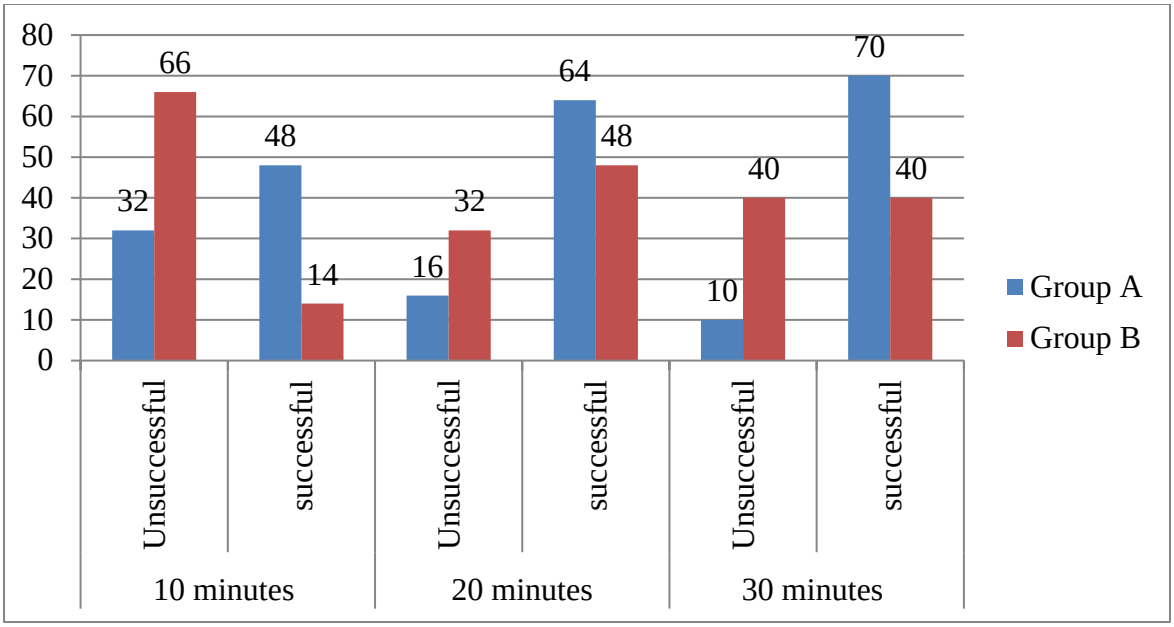

Figure 2: Comparison of anxiolysis between two groups at 10, 20 and 30 minutes

Discussion

Psychological preparation of children before induction of anesthesia results in better perioperative outcome. Reduction of anxiety, calm, and sedated child in preanesthesia room has better postoperative emergence. Kain *et al*. [15] primary goal of premedicating the child is to produce amnesia, anxiolysis, and prevention of stress response during preinduction period. Although a drug given parenterally is more effective, in pediatric practice, needle pricks is feared most. Some studies [1,6] suggest that oral midazolam is an ideal premedicant when compared with triclofos which is used as a second-line drug for insomnia in children while other drugs have failed.

Previous studies[16-20] has shown that both midazolam and ketamine are effective oral premedicants in children. Though several routes of administration of the pre-medicant have been studied, the oral route is the least traumatic for children [21-24]. Both the drugs (midazolam and ketamine) produced sedation and anxiolysis with variable percentage of success over different time course. Overall success rate for midazolam was higher in all the time frame. At 10-minute, midazolam produced sedation in 30% of patients and it was improved over time to 77.5% of patients at 20 minutes and 90% at 30 minutes. Similarly, at 10-minute ketamine produced sedation to 12.5% of patients and successful sedation was improved over time to 12% at 20 minutes and 58.7% at 30 minutes.

We have documented that at 30 minutes, the number of successfully sedated patient was increased in both the groups over progression of time, the increment was significantly higher in group A compared to group B. Among the different time frames at 10-minute, effect of ketamine was negligible, but this effect was improved over time. This may be due to longer onset of action of ketamine compared to midazolam. Similarly, the success rate of midazolam for anxiolysis was improved over time. Initially, at 10 minutes, the success rate for anxiolysis was higher than the sedation and rate of improvement of sedation was higher than anxiolysis. At 10 minutes, there was an increase in the number of patients with successful sedation and anxiolysis that was supported by the study of Funk *et al*.24 Comparison of sedation and anxiolysis produced by midazolam and

ketamine at 10 minutes revealed that midazolam produced a higher percentage of successful sedation and anxiolysis and that was statistically significant but the difference of success rate at 20 minutes was statistically highly significant (0.000). Also, on the same time frame (20 minutes), the success rate of anxiolysis was significantly higher in midazolam group (80%) than ketamine group (60%). Our finding was corroborated with the finding of Funk *et al*, [24] At 30-minute, difference was statistically significant (P=0.001) for anxiolysis between group A and group B respectively. Our finding of anxiolysis score at 30 minutes was corroborated with the findings of Funk *et al*. [24] and Damle*et al*. [25] Successful venepuncture was obtained in 92.5% and 89.5% of patients in group A and group B respectively. This higher rate of success during venepuncture was probably due to the use of EMLA cream prior to venepuncture. Our findings were correlated with previous studies [24,25].

Conclusion

We concluded that oral midazolam showing faster onset of sedation, higher sedation scores with lower anxiety scores as compared to ketamine. Oral midazolam is also providing better easy separation from parents and excellent mask acceptance in children.

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