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Original Research Article

Evaluate Potential Adverse Effects of Varying Doses of Midazolam Administered as Premedicattion in Pediatric Patients

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Abstract:

Background: Study was conducted on 60 patients of both sexes taken for various surgical procedures taking from 30 to 90 minutes at BMIMS Pawapuri Nalanda. Midazolam maleate is a colourless crystal, which manifests a pH dependant ring phenomenon. In the prepared form it is buffered to a pH of 3.5 which keeps the benzodiazepine ring open while administration physiologic pH maintains the closed ring structure and the drug efficacy.

Result: More of the children in the control group (25%) were anxious on reversal of residual paralysis than in the 0.5 mg/kg dose group and the 0.75 mg/kg dose group (5%, 0%, resp.) The number of children who were drowsy but arousable was the highest in the 0.75mg/kg dose group (50%) followed by the 0.5 mg/kg dose group (20%) and the control group (10%). The differences observed between the 0.75mg/kg dose group and the control group were statistically significant. Also, the percentage of children who were calm were significantly higher in the 0.5 mg/kg dose group (75%) compared to the control group (25%).Most of the children in the three groups recovered spontaneous ventilation and could be extubated within 5 minutes. However, 2 children in each of the 3 groups were extubated within 5–10 minutes of reversal. Recovery of spontaneous ventilation and extubation was delayed by over 15 minutes in 2 children in the 0.75 mg/kg dose group. Midazolam dose did not impact the overall recovery times for children in any of the 3 groups, as the average time interval from premedication to full recovery was similar for all 3 groups.

Conclusion: Observation were made in terms of pulse rate, respiratory rate,SpO_2, patient's acceptance of the medication, reaction to separation from parents, sedation scores, and recovery conditions. No side effects reported with Midazolam syrup like nausea, vomiting, hiccoughing, apnoea and laryngospasm.

Keywords: Adverse, Midazolam, Premedication & Paediatrics.

Introduction

Midazolam has been found to be a good preanesthetic agent in preschool children and produces rapid sedation and anxiolysis. Midazolam syrup, as a sedative agent in children, has withstood the test of time. It is a safe and effective drug with low complication and failure rates.

Midazolam maleate is a colourless crystal, which manifests a pH dependant ring phenomenon. In the prepared form it is buffered to a pH of 3.5 which keeps the benzodiazepine ring open while administration physiologic pH maintains the closed ring structure and the drug efficacy. Because of the pH of solution midazolam maleate should not be administered concomitantly with alkaling solutions. [1]

Testing has shown midazolam maleate to be a typical benzodiazepine i.e. it is a hypnotic, has anti-anxiety and muscle muscle relaxant properties and has a less margin of safety (greater than that of diazepam). [2]

Midazolam produces sleep quickly and smoothly. On injection it is a painless and have a short half-life. The elimination half-life of midazolam maleate was about

2 hours, with the urinary excretion data showing recovery of approximately 30-40% of administered dose as the conjugated form of first metabolite in first 12 hours. [3]

It is generally agreed that most children who are undergoing medical procedures and who are fearful and uncooperative can and should be managed with behavioral (nonpharmacologic) management techniques. Unfortunately, a small percentage of pediatric patients cannot be successfully managed solely with these techniques. When behavioral management strategies fail, some form of pharmacologic sedation or anesthesia becomes a valuable and necessary alternative. [4]

Material and Method

Study was conducted on 60 patients of both sexes taken for various surgical procedures taking from 30 to 90 minutes at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri nawada. Study Duration May 2022 to April 2024.

Age group considered was between 1-5 years.

All patients were of ASA grade - I or Grade II in every patients consent, physical examination entire investigation and special investigation (if required) were checked.

Drugs and anaesthetic gain and inj atrapine 0.01mg/kg iv or im

- Inj Ketamin 2 mg/kg
- Inj. Succinylcoline 2 mg/kg
- Oxygen
- Nitrous oxide

The exclusion criteria were as follows:

- Children having upper respiratory infections, rhinopharyngitis.
- History of drug allergies to the study drugs.
- Those requiring an intravenous anesthetic induction.

Patients were premedicated after being sure of nil oral by mouth, written consent and anesthetically fit. Study group A: patients in this group were administered oral midazolam syrup 0.5mg/kg dose 30 min. prior to surgery

Study group B: patients in this group were administered oral midazolam syrup 0.75mg/kg dose 30 min. prior to surgery.

Control group C: patients in this group were administered apple juice 30 min. prior to surgery.

Premedication was done with inj. atropin 0.01mg/kg and all procedure was The observation were discussed in terms of pulse rate, respiratory rate, SpO_2, patient's acceptance of the medication, reaction to separation from parents, sedation scores, and recovery conditions performed under general anaesthesia.

Anaesthesia was induced with inj. Ketamin 2mg/kg and orotracheal intubation was facilitated with inj. succinylcoline 2mg/kg. Anaesthesia was maintained with nitrous oxide +oxygen +Atracurium with intermittent positive pressure ventilation.

The observation were discussed in terms of pulse rate, respiratory rate, Spo_2, patient's acceptance of the medication, reaction to separation from parents, sedation scores, and recovery conditions.

Results

Table 1: Sedation score on reversal of residual paralysis. RVC, responding to verbal commands.

Groups Midazolam Dose	**A**	**B**	**C**
	0. 5 mg/kg (%)	**0.75 mg/kg (%)**	**Placebo (%)**
Anxious	5	0	25
Oriented, calm	75	25	65
Drowsy-RVC	20	50	10
Not RVC but to painful stimuli	0	25	0
Not responding to painful stimuli	0	0	0

More of the children in the control group (25%) were anxious on reversal of residual paralysis than in the 0.5 mg/kg dose group and the 0.75 mg/kg dose group (5%, 0%, resp.)

The number of children who were drowsy but arousable was the highest in the 0.75mg/kg dose group (50%) followed by the 0.5 mg/kg dose group (20%) and the control group (10%). The differences observed between the 0.75mg/kg dose group and the control group were statistically significant. Also, the percentage of children who were calm were significantly higher in the 0.5 mg/kg dose group (75%) compared to the control group (25%).

Table 2: Recovery Profile

After reversal of residual paralysis		**A**	**B**	**C**
		0. 5 mg/kg (%)	**0.75 mg/kg (%)**	**Placebo (%)**
Time to spontaneous ventilation and extubation (minutes)	<5	90	80	90
	5–10	10	10	10
	15–60	0	10	0
Time from premedication to full recovery	(hours)	3.17±0.38	3.39±0.38	3.20±0.41

Most of the children in the three groups recovered spontaneous ventilation and could be extubated within 5 minutes.

However, 2 children in each of the 3 groups were

extubated within 5–10 minutes of reversal. Recovery of spontaneous ventilation and extubation was delayed by over 15 minutes in 2 children in the 0.75 mg/kg dose group. Midazolam dose did not impact the overall recovery times for children in any of the 3 groups, as the average time interval from premedication to full recovery was similar for all 3 groups.

Discussion

Midazolam is the most commonly used drug for premedication and is used in greater than 90% of surgical cases involving premedication in the United States. The combination of the sedative and anxiolytic characteristics is believed to create a calming effect which makes children less anxious when they are separated from their parents and during mask placement. [5,6] Finley et al.(2006) showed that a midazolam induced decrease in anxiety was more pronounced for children with higher baseline levels of anxiety. Oral midazolam was found to be superior when compared with other commonly used premedications. oral midazolam was reported to give a more predictable and effective sedation than oral diazepam. It was also associated with a faster and smoother recovery, when compared with oral ketamine. Our study match with this study. [7] Patel and Meakin et al.(1997) also reported greater anxiolysis after oral midazolam (0.5 mg/kg) than after a combination of diazepam (0.25 mg/kg) with droperidol (0.25 mg/kg) or trimeprazine (2 mg/kg). [8]

Conclusion

Observation were made in terms of pulse rate, respiratory rate, SpO_2, patient's acceptance of the medication, reaction to separation from parents, sedation scores, and recovery conditions. No side effects reported with Midazolam syrup like nausea, vomiting, hiccoughing, apnoea and laryngospasm.

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