Comparative Study of Oral Premedication in Children with Ketamine and Midazolam

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ABSTRACT

Introduction: Pre-operative anxiety (anxiety regarding impending surgical experience) in children is a common phenomenon that has been associated with a number of negative behaviors during the surgical experience (e.g. agitation, crying, spontaneous urination and the need for physical restraint during anaesthetic induction). If children are less anxious during the peri-operative period, not only will they often exhibit less behavioral disturbances post-operatively, but they may face subsequent medical care more easily. The aim of the study was to compare the efficacy and safety of orally administered midazolam and ketamine for pre-medication.

Material and Methods: Sixty children of either gender participated in the study. All of them belonged to ASA physical status I as outlined by the American Society of Anaesthesiologists (ASA). They are randomly divided into two groups, 30 children in group A and 30 children in group B. Group A patients received 0.5mg/kg of oral midazolam as a premedicant 45 minutes before induction. Group B Patients received 6mgs/kg of oral ketamine as a premedicant 45 minutes before induction. Time of onset of sedation and sedation score at 30 minutes were noted. Anxiety score at separation from parents, room air saturation, response to pre-oxygenation, side effects, if any, preoperatively and postoperatively were also noted.

Results: The study groups were similar with respect to age, weight, parent-child separation times and duration of surgery. In our study, the mean time of onset of sedation was lower with ketamine group (19.48 minutes) as compared to the midazolam group (25.63). The sedation score at 30 minutes and anxiety score at separation from parents were also satisfactory. The study found that ketamine was well accepted by all children. In our study, the mean sedation score at 30 minutes was 1.9 with ketamine group and 3.03 in midazolam group. Similarly the mean anxiety score at separation was 1.8 with ketamine group and 2.53 in midazolam group. All patients allowed calm separation from parents.

Conclusion: It is concluded that pre-medication with ketamine at a dose of 6 mgs/kg orally provides better sedation and anxiolysis in children with minimal side effects than oral pre-medication with midazolam at the dose of 0.5 mg/kg.

Keywords: Oral Premedication, Preoperative Anxiety, Sedation, Ketamine, Midazolam, Paediatric Population.

INTRODUCTION

The induction of anaesthesia for surgery is a stressful time for both the child and its parents.[1] Children suffer from varying degrees of terror while facing the prospects of surgery depending upon the age, developmental maturity and past surgical experiences. Pre-operative anxiety (anxiety regarding impending surgical experience) in children is a common phenomenon that has been associated with a number of negative behaviors during the surgical experience (e.g. agitation, crying, spontaneous urination and the need for physical restraint during anaesthetic induction). Pre-operative anxiety has also been associated with the display of a number of maladaptive behaviors post-surgery, including post-operative pain, sleep disturbances, parent-child conflict and separation anxiety.[2]

Younger children, previously anaesthetized children and children who experience turbulent anaesthetic inductions are at risk of developing behavioral disturbances.[3] The risk factors associated with high incidence of perioperative anxiety in children include shy and inhibited nature, previous poor quality medical encounters, poor social adaptability and increased parental anxiety.

Interventions such as sedative pre-medication, parental presence during anaesthetic induction, behavioral preparation programs, music therapy and acupuncture have been sought to treat or prevent childhood pre-operative anxiety and possibly decrease the development of negative behaviors post-surgery.[2] If children are less anxious during the peri-operative period, not only will they often exhibit less behavioral disturbances post-operatively, but they may face subsequent medical care more easily.[3] Thus, there are several compelling reasons to treat children's anxiety. The aims of premedication in paediatric population is to alleviate the stress and fear of surgery as well as to ease parent – child separation and promote a smooth induction of anaesthesia thereby reducing the occurrence of post-operative behavioral disturbances associated with bad pre-operative experience preoperatively. The most commonly used sedative pre-medicant is midazolam followed by ketamine, transmucosal fentanyl and meperidine. All possible routes have been described – oral, intranasal, intramuscular, rectal etc. The oral route has several advantages as it is painless, quick and reliable.

An ideal sedative pre-medicant should be easily available, cheap, reliable with rapid onset, able to reduce anaesthetic and analgesic requirements and with no side effects during induction, emergence or discharge from the post-anaesthetic care unit. So the aim of the study was to compare the efficacy and safety of orally administered midazolam and ketamine for pre-medication.

MATERIAL AND METHODS

This was a prospective observational comparative study conducted between July 2005 and November 2007 in which 30 paediatric patients received oral pre-medication. This study

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was conducted after obtaining approval from the departmental dissertation committee. Informed consent was obtained from the parents.

Sixty children of either gender participated in the study. All of them belonged to ASA physical status I as outlined by the American Society of Anaesthesiologists (ASA). They were randomly divided into two groups, 30 children in group A and 30 children in group B.

The study was conducted mostly among children who underwent corrective surgeries for cleft lip and cleft palate. The operative time was between 60 and 90 minutes. Inclusion Criteria were age between 10 months and 10 years and weight between 8 and 20 kgs. Exclusion Criteria were age below 10 months and above 10 years, ASA physical status III (or) higher, Allergies to Benzodiazepines and ketamine, epilepsy (or) raised intracranial pressure, cardio vascular anomalies, respiratory Tract infections and children with anticipated difficult airway.

All the children were evaluated the day before surgery and instructed for nil per oral for the anticipated six hours before surgery. An intravenous line was started on the previous day to receive prophylactic antibiotics. On the day of Surgery, 45 minutes before induction, Group A received 0.5 mg/kg oral midazolam and Group B received 6 mgs/kg oral ketamine.

Parenteral formulations (ketamine vial 50 mgs/ml and midazolam ampoule 5mgs/ml) of both the drugs were mixed with sugar solution and were administered to children orally in the pre-operative holding area.

Thereafter the child was constantly observed to see changes in mood, behaviour and appearance. Onset of sleepiness, closure of eyes and any side effects like nausea, vomiting, increased salivation, hallucination, nystagmus, hiccough and the like were noted.

Subsequently, the following observations were made and recorded:

1. Time of onset of sedation when the sedation score was 3 or less
2. Level of sedation at 30 minutes after pre-medication
3. Level of anxiety at the time of separation from the parents
4. Room air SPO_2
5. Response to pre-oxygenation/mask application
6. Post-operative recovery time
7. Side effects - Pre-operative
   - Post-operative

Level of sedation was noted on a five-point scale as per table 1 and level of anxiety was noted on a four-point scale as per table 2.

After separation from the parents, the children were transferred to the operation theatre. Pulse oximeter was applied and room air SPO_2 was noted. Other appropriate monitors were also applied.

Now, the response to pre-oxygenation with the mask was noted, that is whether the child showed signs of refusal or remained calm.

Then all the children were induced with intravenous Thiopentone sodium at a dose of 6mgs/kg and Atracurium at a dose of 0.5 mgs/kg was used to facilitate endo tracheal intubation. Ventilation was controlled and anaesthesia was maintained with oxygen, nitrous oxide and sevoflurane. For intra operative analgesia, fentanyl was used at a dose of 1 microgram/kg. Towards the end of the surgery, all children received paracetamol suppositories for post-operative pain relief. The recovery time was noted between the end of surgery and the spontaneous eye opening. After ensuring adequate recovery of muscle power, children were extubated and transported to the recovery room. Children were closely monitored until transferred to the post-operative ward and any unwanted effects during the period were noted.

Score	Sedation Level
1.	Barely arousable (Fully asleep)
2.	Eyes closed (Light sleep)
3.	Eyes opened but looks drowsy
4.	Awake
5.	Agitated

Table-1: Level of sedation on five point scale

Score	Anxiety Level
1.	Calm and Sleepy
2.	Apprehensive but withdrawn from surroundings
3.	Crying
4.	Agitated and difficult to control

Table-2: Level of anxiety on four point scale

For the purpose of data analysis, sedation scores of 1 and 2 were taken as satisfactory and scores 3 and 4 were taken as unsatisfactory. Similarly anxiety scores of 1 and 2 were taken as satisfactory and scores of 3 and 4 were taken as unsatisfactory induction.

STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002). Using this software, frequencies, percentage, mean, standard deviation, x2 and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS

This study was conducted on 60 patients divided into two groups. Group A – 30 patients and Group B – 30 patients. Group A patients received 0.5mg/kg of oral midazolam as a premedicant 45 minutes before induction. Group B patients received 6mgs/kg of oral ketamine as a premedicant 45 minutes before induction.

The mean and standard deviation for the time of onset of sedation were 25.63 ± 6.96 and 19.48 ± 8.7 minutes in the groups A and B respectively. The mean time of onset of sedation was lower in group B which was statistically significant.

The mean sedation score at 30minutes is lower (1.9) in ketamine group which was statistically significant (Table 3).

The mean anxiety score at separation from parents was lower (1.8) in the ketamine group which was statistically significant (Table 4).

Only 1/3 of children in group A (Midazolam) refused pre-oxygenation with mask whereas 2/3 of children in group B (Ketamine) refused, which was statistically significant.

The mean and the standard deviation for the recovery time were 14.83 ± 4.04 and 15.17 ± 3.34 minutes in the groups A (Midazolam) and B (Ketamine) respectively. There was no significant difference in the recovery times between the groups.

Sedation Score in 30 minutes	Group A (Midazolam)		Group B (Ketamine)	
	No	%	No	%
1	1	3.3	11	36.7
2	6	20	13	43.3
3	15	50	5	16.7
4	7	23.3	-	-
5	1	3.3	1	3.3
Total	30	100	30	100
Mean S.D	3.03 2.5		1.9 0.9	
'p'	0.0001			

Table-3: Sedation score in 30 minutes

Anxiety Score at separation	Group A (Midazolam)		Group B (Ketamine)	
	No	%	No	%
1	5	16.7	12	40
2	8	26.7	12	40
3	13	43.3	6	20
4	4	13.3	-	-
Total	30	100	30	100
Mean	2.53		1.8	
S.D	0.94		0.76	
'p'	0.0025			

Table-4: Anxiety Score at separation

DISCUSSION

Paediatric anaesthesia always presents with major challenges as it deals with the most psychologically vulnerable age group. Although anaesthesia during surgery prevents children from recalling actual surgical events, they are subjected to stress while preparing for surgery. Use of an effective sedative pre-medicant significantly minimizes the emotional trauma associated with perioperative anxiety and its sequelae. Currently oral midazolam and oral ketamine are the most commonly used pre-medicants. Use of opiods for pre-medication has been declining owing to concerns for respiratory depression.

In our study, the mean time of onset of sedation was lower with ketamine group (19.48 minutes) as compared to the midazolam group (25.63). The sedation score at 30 minutes and anxiety score at separation from parents were also satisfactory.

These results coincide with the studies conducted earlier by several others. JA Kulkarni[4] point out that ketamine orally is an effective pre-medicant in paediatric patients. The study found that ketamine was well accepted by all children. All patients allowed calm separation from parents.

Granry et al[5] conclude that ketamine is an unique anaesthetic, analgesic and sedative drug. Guidelines for ketamine sedation in Emergency Departments from British Association quote that ketamine is a powerful anaesthetic agent with anxiolytic and analgesic and amnesic properties with a wide safety margin.

Dr. Suranjit Debnath and Dr. Yash Pande[6] in their comparative study of premedication in children with oral ketamine and midazolam, conclude that sedation and anxiolysis were better in ketamine than in the midazolam group, during separation from parents and at intravenous cannulation. Recovery was also smooth in ketamine group.

In our study, the mean sedation score at 30 minutes was 1.9 with ketamine group and 3.03 in midazolam group. Similarly the mean anxiety score at separation was 1.8 with ketamine group and 2.53 in midazolam group. However, 66.7 per cent of children in ketamine group refused pre-oxygenation with mask while only 33.3 per cent of children in midazolam group refused pre-oxygenation. There was no significant difference in the recovery time between the groups.

Preoperatively excessive salivation (6 children) and sweating (2 children) were noted in ketamine group. Few children in midazolam group had hiccoughs (3 children) and sighing (1 child).

Postoperatively 16.7 per cent of children in ketamine group had nausea and few children (12) in midazolam group were irritable and crying. Postoperatively recovery was smooth in ketamine group.[8,9]

CONCLUSION

It is concluded that pre-medication with ketamine at a dose of 6 mgs/kg orally provides better sedation and anxiolysis in children with minimal side effects than oral pre-medication with midazolam at the dose of 0.5 mg/kg.

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