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Oral Premedication in Paediatric Surgeries under General Anaesthesia with Ketamine versus Midazolam: A Comparative Study

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Abstract

Background: 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 behaviourspost surgery, including post-operative pain, sleep disturbances, parent-child conflict and separation anxiety [1]. 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 [1]. 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 [2]. Thus, there are several compelling reasons to treat children's anxiety preoperatively. The aim of our study was to compare the efficacy and safety of oral midazolam versus oral ketamine for pre-medication in paediatric surgeries under general anaesthesia.

Materials and Methods: Sixty children belonging to ASA physical status I as outlined by the American Society of Anaesthesiologists (ASA) of either gender were included in the study. They were randomly divided into two groups of 30 children in each group, group A and group B. Group A patients received 0.5mg/kg of oral midazolam as a premedicant 45 minutes before induction and 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: 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. In our study we found that the mean sedation score at 30 minutes was 1.9 with ketamine group and 3.03 in midazolam group.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 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: Preoperative Anxiety; Ketamine; Midazolam; Paediatric Population; Oral Premedication.

Introduction

Children suffer from varying degrees of stress while facing the prospects of surgery depending upon the age, developmental maturity and past surgical experiences. They are principally worried about pain and separation from their parents. Pre-operative anxiety in children is a common phenomenon. It has been associated with a number of negative behaviors

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such as agitation, crying, spontaneous urination and the need for physical restraint during anaesthetic induction. Pre-operative anxiety is also associated with the display of a number of maladaptive behaviors post surgery, including post-operative pain, sleep disturbances, parent-child conflict and separation anxiety [1].

Younger children, previously anaesthetized children and children who experience turbulent anaesthetic inductions are at risk of developing behavioral disturbances [2].

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. Children younger than 5 years of age or living in a one parent family appear to have a higher incidence of problematic behavior in a two week follow-up after anaesthesia [3].

Interventions like sedative pre-medication, parental presence during anaesthetic induction, behavior preparation programs, music therapy and acupuncture have been sought to treat or prevent childhood pre-operative anxiety and possibly decrease the development of negative behaviours post-operatively [1].

If children face less stress during the peri-operative period, then they will often exhibit less behavioural disturbances post-operatively, but they may face subsequent medical care more easily.[2] Hence it is very important to treat children's anxiety preoperatively.

The aims of premedication in children 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 post-operative behavioral disturbances associated with bad pre-operative experience. Almost all sedative pre-medicants are effective in this regard. Children six months to four years of age have been reported to experience the greatest negative post-operative behaviour changes and pre-medication is very useful in them.

Midazolam is the most commonly used sedative pre-medicant 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 cheap, easily available,have rapid onset of action, able to reduce anaesthetic and analgesic requirements and with no side effects during induction, emergence or discharge from the post-anaesthetic care unit.

Materials and Methods

This is a prospective comparative study conducted between July 2007 and November 2008 in which 30 paediatric patients in each group received oral pre-medication.

This study 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 belonging to ASA physical status 1. They were randomly divided into two groups, 30 children in group A and 30 children in group B.

The study was conducted in children undergoing surgeries from various specialities under general anaesthesia. The duration of surgeries were between 60 and 90 minutes. Inclusion Criteriawere 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, children allergic to Benzodiazepines and ketamine, epilepsy (or) raised intracranial pressure, cardio vascular anomalies, respiratory tract infections and children with anticipated difficult intubation.

Preoperative evaluation for all the children was doneon the day before surgery and instructed for nil per oral for the anticipated six hours before surgery.

On the day of Surgery, 45 minutes before induction, Group A children received 0.5 mg/kg oral midazolam and Group Bchildren received 6 mgs/kg oral ketamine.

Parenteral formulations (ketamine vial 50 mgs/ml and midazolam ampoule 5mgs/ml) of both the drugs were made palatable by mixing with sugar solution and were administered to children orally in the pre-operative holding area. The child was then monitored constantly 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 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 30minutes after pre-medication
3. Level of anxiety at the time of separation from the parents
4. Room air SP02
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 premedication, the children were transferred to the operation theatre. Appropriate monitors were applied. Pulse oximeter was applied and room air SpO_2 was noted.

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

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.

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

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 considered as significant.

Results

Our 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.

Table 1: Level of sedation on five point scale

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

Table 2: Level of anxiety on four point scale

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

Table 3: Time of onset of sedation

Time of sedation in minutes	Group A (Midazolam) No	%	Group B (Ketamine) No	%
< 15 minutes	4	13.3	13	43.3
16 – 30	16	53.3	13	43.3
31 – 45	4	13.3	3	10
Not sedated	6	20	1	3.3
Total	30	100	30	100
Mean	25.63 minutes		19.48 minutes	
S.D	6.96		8.7	
'p'	0.0018 (Significant)			

Table 4: Sedation score in 30 minutes

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	3.03		1.9	
S.D	2.5		0.9	
'p'	0.0001			

Table 5: Anxiety Score at separation

Response to Pre-oxygenation	Group A		Group B	
	No	%	No	%
Refused	10	33.3	20	66.7
No refusal	20	66.7	10	33.3
'p'	0.0201 (Significant)			

Table 6: Response to Pre-oxygenation (Face mask application)

Response to Pre-oxygenation	Group A		Group B	
	No	%	No	%
Refused	10	33.3	20	66.7
No refusal	20	66.7	10	33.3
'p'	0.0201 (Significant)			

Table 7: Side Effects

Side Effects	Group A (Midazolam)		Group B (Ketamine)	
	No	%	No	%
Pre operative				
Hiccoughs	3	10	-	-
Laughing	2	6.7	-	-
Salivation	-	-	6	20
Sighing	1	3.3	-	-
Sweating	-	-	2	6.7
Total side effects	6	20	8	26.7
No side effects	24	80	22	73.3
Total	30	100	30	100
Post Operative				
Crying	11	36.7	4	13.3
Irritable	1	3.3	-	-
Nausea	-	-	5	16.7
Total side effects	12	40	9	30
No side effects	18	60	21	70
Total	30	100	30	100

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 is lower in group B which is statistically significant (Table 3).

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

The mean sedation score at 30minutes is lower (1.9) in ketamine group. This is statistically significant.

The mean anxiety score at separation from parents is lower (1.8) in the ketamine group. This is statistically significant (Table 5). Only 1/3 of children in group A refused pre- oxygenation with mask whereas 2/3 of children in group B refused. This is statistically significant (Table 6).

Increased salivation and sweating were noted in 20% and 6.7% of patients in group B respectively. Hiccoughs (10%), laughing (6.7%) and sighing (3.3%) were noted in group A. Post-operatively, 36.7%of

children in group A remained crying and 3.3% irritable. 16.7% of children in group B had nausea and 13.3% remained crying.

Discussion

Anaesthesia for children presents major challenges as it deals with the most psychologically vulnerable age group. Anaesthesia during surgery prevents children from recalling actual surgical events. They are subjected to stress while preparing for surgery. Most of the children experience significant anxiety before anaesthetic induction. Pre-operative anxiety is a global concern for health care providers [4]. Main aim ofanaesthesiologist is ensuring adequate reduction of preoperative anxiety and there by reducing occurrence of postoperative negative psychological and behavioral changes.

There are many pharmacological (pre-medication) and behavioral methods (parental presence during induction of anaesthesia) to treat pre-operative anxiety in children [5], but none of these methods have been satisfactorily effective and practicable. 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.

An ideal pre-medicant for children should be easily available, palatable, have both rapid onset and short duration of action, be able to reduce anaesthetic and analgesic requirements and possess minimal side effects without significant delay in recovery period.

In our study children aged between 10 months and 10 years were chosen for the study. Sixty healthy children awaiting elective surgery who didn't meet the exclusion criteria were randomly assigned into two groups of 30 each. Group A received 0.5 mgs/kg of midazolam and Group B received 6mgs/kg of ketamine orally in the preoperative room. Palatability was ensured by mixing with sugar solution. 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.

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 [6] points out that ketamineorally 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. [7] 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, analgesic and amnesic properties with a wide safety margin.

Dr. Suranjit Debnath and Dr. Yash Pande [8] 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 midazolamgroup 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.

Main goal of anaesthesiologists in treating paediatric patients has always been to provide access to care for all children especially those with behavioral issues. The introduction of oral ketamine and midazolam provides safe, effective method of sedating the uncooperative paediatric patients.

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

when compared with oral pre-medication with midazolam at the dose of 0.5 mg/kg.

References

1. Wright KD, Stewart SH, et. al., Prevention and intervention strategies to alleviate preoperative anxiety in children: a critical review. Behav Modif 2007 Jan;31(1) 52-79.
2. Goresky GV, Whitsett SF., Psychological preparation of children for surgery. Can J Anaesth. 1994 Nov;41 (11):1033-5.
3. Karling, M. and Hägglöf, B. Child behaviour after anaesthesia: association of socioeconomic factors and child behaviour checklist to the post-hospital behaviour questionnaire. Acta Paediatrica, 2007;96: 418–423.
4. Dreger, Victoria A. et. al. Management of preoperative anxiety in children AORN Journal, 2008;84(5):796-799.
5. Hatice K et. al. The effects of maternal presence during anesthesia. Paediatric Med Chir 2004 May-June;26(3) 169-174.
6. Kulkarni J.A., Oral Ketamine for Pre-medication in Children, Bombay Hospital Journal (BHJ).
7. Granry J.C., Dube L., et. al., Ketamine: New Uses for an Old Drug. Current Opinion in Anaesthesiology 2000 July;13(3):299-302.
8. Suranjit Debnath and Yash Pande., A Comparative Study of Oral Pre-medication in Children with Ketamine and Midazolam, Indian Journal Anaesthesia, 2003;47(1):45-47.
9. Andrea Messeri, Simona Caprilli and Paolo Busoni., Anaesthesia induction in children: a psychological evaluation of the efficiency of parents' presence Paediatric Anaesthesia 2004 July;14(7):551-556.
10. Damle SG, Gandhi M, Laheri V. Comparison of oral ketamine and oral midazolam as sedative agents in pediatric dentistry. J Indian SocPedodPrev Dent 2008;26:97-101.