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Supplementary Low - Dose Oral Ketamine Provides Better Parental Separation and Face Mask Acceptance

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Abstract

Background: Anesthesia is stressful for children and parents. Although anxiolytics can keep children calm, side effects may exist. No single method shows a clear advantage in keeping the child calm and cooperative. This study aimed to test the efficacy and safety of adding a small dose ketamine to midazolam-based oral premedication on child-parents separation and acceptance of face mask.

Methods: Eighty preschool children scheduled for elective surgeries were included. Patients were allocated into 2 groups: A control group (group C), patients received oral midazolam 0.5mg/kg, and a study group (group S), patients the same dose of midazolam in addition to ketamine 2mg/kg. Child reaction to parent separation and parent satisfaction was rated according to separation and satisfaction scores. Induction of anesthesia was carried out using Sevoflurane 6 Vol% in 100% oxygen via face mask; child's acceptance of the mask was reported.

Results: Group (S) children were more cooperative regarding parents separation and acceptance of the face mask than group (C) children (P=0.000&0.02) respectively. No child developed deep sedation in both groups and Sedation score was more satisfactory in group (S), with better parent satisfaction in the same group (p=0.008, P=0.03respectively).

Conclusion: Adding a small dose oral ketamine to midazolam-based premedication in preschool children proved to be a safe and effective technique in improving child -parent separation and pleasant face mask acceptance.

Keywords

Pediatric anesthesia, Premedication, Ketamine, Midazolam

One of the challenges for pediatric anesthetists is to minimize the child and parents stress at induction of anesthesia. A wide range of techniques has been used, including education of the child and family, as almost 50% of these children become anxious in the peri-operative period. Children are principally worried about pain and separation from their parents. Up to 60% of children undergoing routine outpatient surgery present at two weeks, postoperatively, with new onset behavioral disturbances such as anxiety, nighttime crying, enuresis, and sleep or eating disturbances. It is generally agreed that behavioral, non-pharmacological techniques help in reducing the incidence of these delayed sequaelae. These techniques include the use of music, stories, and flavored face masks. Psychological preparation of the child and the family in the preoperative visit is more important than the choice of premedication [1]. Unfortunately, a small percent of fearful and uncooperative children cannot be managed solely with these techniques [2]. Parents' anxiety may be transferred to the child, so any practice that reduces anxiety in parents may also reduce anxiety in children [3].

When behavioral management strategies fail, some form of pharmacologic sedation or anesthesia becomes a valuable and necessary alternative. The role of an anesthesiologist in preparing children for surgery is to minimize potentially adverse psychological and physiological effects of anesthetic techniques. Premedication is best given by an oral rout in children as they often exhibit an exaggerated psychological response to a needle, and it is easier to distribute a medication orally than to use nasal or rectal routes [4,5]. Midazolam, with its rapid onset and relatively short duration of action, has proven to be a useful premedication to decrease preoperative anxiety and facilitate separation from parents with fewer unwanted side effects [5]. Several studies suggested that different doses of oral ketamine is a better than oral Midazolam 0.5mg/kg in providing sedation and anxiolysis in children with minimal side effects [6,7] children receiving high dose of Ketamine may experience nystagmus or vomiting [8]. Therefore, a relatively low dose ketamine was selected in the current study to overcome its side effects if given in high doses.

The primary aim of this study was to investigate the efficacy of adding a low oral dose of ketamine to midazolam premedication in preschool children undergoing elective surgeries on pleasant child-parent separation. Secondary aims include its effectiveness on face mask acceptance and parent satisfaction.

Patients and Method

After obtaining approval from the Hospital Ethics Committee and written informed consent from parents, eighty healthy preschool children (ASA 1 & 11), aged between 2–5 years and scheduled for elective pediatric surgeries under general anesthesia were enrolled into the study (Table 1). Different types of surgeries include; ENT surgeries, Circumcision, hernia repair, and dental rehabilitation (Table 1). Sample size calculation based on a previous study of Kain ZN et al. who calculated that the sample size of 30 participants per group provided 80% power to detect a clinically meaningful, medium

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Table 1: Patients demographic and operative dat (mean ± SD).

Variables	Group C N=40	Group S N=40	t	P	95% CI
Age(yrs)	3.78 ± 0.8	3.64 ± 0.9	0.67	0.5	(-0.79-0.83)
Weight (Kg)	15.72 ± 2.5	15.4 ± 2.9	0.32	0.59	(-1.7-1.3)
Gender Male Female	24(56.5%) 16(43.5%)	28(60.9%) 12(39.1%)	0.2	0.45	(0.33-2.08)
Type of surgery Hernia Repair Circumcision ENT Dental	 3(7.5%) 8(20%) 22(55%) 7(17.5%)	 3(7.5%) 9(22.5) 18(45%) 10(25%)			
Premedication Onset(min.)	19.72 ± 3.25	16.12 ± 2.5	0.000	-5.55	-4.89- -2.3

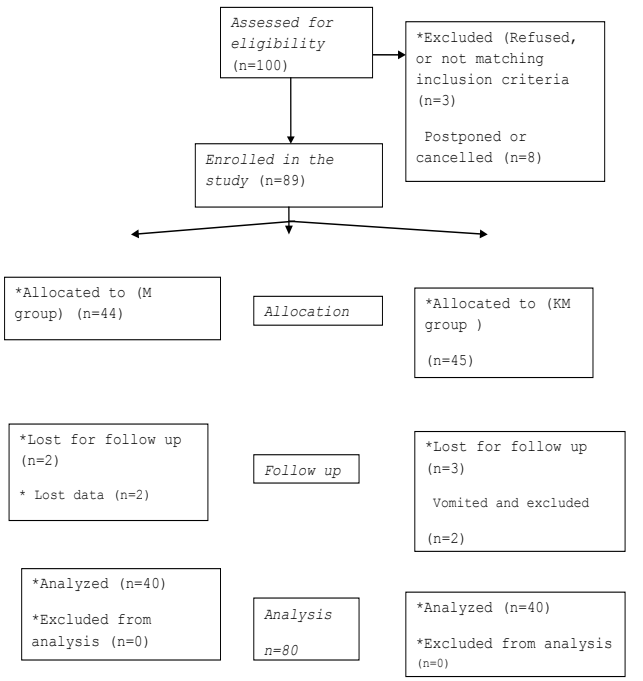

Figure 1: Flow chart of patients through the trial.

effect size in child anxiety [9]. This sample size calculation was based on anxiety levels of the child as the primary outcome and anxiety levels of the one-parent group from his previous investigations [10]. We calculated that 40 patients per group will provide approximately 90% power of analysis. Because of the frequent cancelation and postponing in pediatric patients, we increased the number of enrolled children to hundred patients.

Flow chart of patients through the trial is shown in Figure 1.

Children were randomly allowed to participate in this double blind randomized study. Exclusion criteria included children with neurological problems, inborn errors of metabolism, morbid obese children, and patients with known allergy to any of the medications used. Patients were randomly assigned via computer-generated random numbers to receive either midazolam (Control group «group C ») or ketamine–midazolam (study group «group S ») as an oral premedication.

During the preoperative visit, the anesthetist explained to the child and family what is going to occur in the morning of surgery. The child was blind to the used drug and was asked to choose a sealed envelope with his/her code number inside. The name, file number and body weight were recorded on the sealed envelope after been chosen. The anesthetist who saw the patient preoperatively and anaesthetized him was blind to the premedication.

Parents were not aware of the premedication components, but oriented and agreed with our protocol. In the morning of operation,

Table 2: Preoperative Behavior Scales.

1-Readily accept
2-Dislike, but accept
3-Held down/forced to accept
4-Refuses to open mouth after tasting

A) Drug acceptance score.

Success	1-Excellent: happily separated
	2-Good: separated without crying
Un successful	3-Fair: separated with crying
	4-Poor: need for restraint

B) Parent Separation Score.

Score 1-	Cooperative
Score 2-	Mildly resistant
Score 3-	Resistant to face mask placement

C) Cooperation Score at induction.

Score 1	Barely arousable (full sleep)
Score 2	Eyes closed (Light sleep)
Score 3	Eyes opened but looks drowsy
Score 4	Awake
Score5	Agitated

D) Level of sedation on five point scale.

Table 3: Comparison between both groups as regard child behavior and sedation after premedication.

Variables	Group CI N=40	Group S N=40	P	t	(95% CI)
Drug acceptance Accept Dislike Forced to accept **Refuse**	30(75%) 8(20%) 2(5%) 0	26(65%) 13(32.5%) 1(2.5%) 0	**0.54**	**-0.60**	**-0.32-0.17**
Sedation score 1- (full sleep) 2- Eyes closed (Light sleep) 3 -Eyes opened but looks drowsy 4- Awake 5- Crying	 0 0 24 (60%) 16(40%) 0	 0 1(2.5%) 33 (82.5%) 6(15%) 0	**0.008**	**2.71**	**0.073-0.47**
Reaction to separation Excellent Good Faire Poor	 8(20%) 18(45%) 14(35%) 0	 28(70%) 10(25%) 2(5%) 0	**0.000**	**5.403**	0.5-1.09
Acceptance of mask Cooperative Mildly resistant Resistant to face mask placement	 17(42.5%) 8(20%) 15(37.5%)	 22(55%) 14(35%) 4(10%)	0.02	2.2	0.044-0.755

the study medications were prepared by a trained nurse (who was not involved in any other part of the study) into identical 10ml syringes that were sequentially numbered. Each labeled syringe was mixed with apple juice to be given to the children. Premedication was given by one of the parents under supervision of another nurse.

(Group C) patients received oral midazolam (Dormicum 5mg/ml; F. Hoffmann, La Roche Ltd, Switzerland) in a dose of 0.5mg/kg mixed with apple juice to fill the syringe up to 10ml, and (group S) patients received the same dose of Dormicumin addition to Ketamine (50mg/ml, Ketalar; Pfizer, La Jolla, California, USA) in a dose of 2mg/kg. All children were monitored by pulse oximetry to detect hypoxia (due to respiratory depression) if any. Child behavior scores [10] (Acceptance of the drug, Parent separation score and mask acceptance score) and sedation score are shown in (Table 2).

The attending ward nurse reported the onset of premedication action (Table 1) and level of sedation (Table 3) and the occurrence of vomiting was also monitored; children who vomited were excluded from the study. 30 min after premedication, Parents accompanied their children till the operating room, but their presence in the induction room was not permitted according to the policy of the hospital.

Child reaction to parents separation was rated according to separation score (Table 3). Induction of anesthesia was carried out

Table 4: Parents satisfaction score.

Parents satisfaction score	
Score 1	Excellent (Accept to give the same premedication to his child if he requires anesthesia next time)
Score 2	Acceptable
Score 3	Un acceptable/Unpleasant

Table 5: Comparison between both groups as regard parents satisfaction.

Variable	Group C N=40	Group S N=40	P	t	95% C I
Parents satisfaction Score 1- Excellent Score 2- Acceptable Score 3- Un acceptable	 30(75%) 10(25%) 0	 37(92.5%) 3(7.5%) 0	0.03	2.15	0.013-0.33

using Sevoflurane (Abbott, Abbott Park, Illinois, USA) 6vol% in 100% oxygen (6L/min) through a face mask. The anesthetist asked the child to blow the balloon. Acceptance and tolerance of face mask (Cooperation Score at induction) was recorded according to Cooperation Score at induction (Table 3). Peripherali.v.cannulation was allowed 60 seconds from initiation of mask induction. Atropine 0.02mg/kg, Fentanyl 1-2μg/kg and cisatracurium 0.15mg/kg were given.

Three minutes after starting manual ventilation, intubation was carried out with a suitable sized, lubricated airway device according to the type of surgery. Anesthesia was maintained using Sevoflurane 1.5–2 vol% in (35: 65%) oxygen and air ratio. All patients were monitored using routine non invasive monitoring. At the end of surgery, anesthetic agents were discontinued and replaced with O2 100% (6L/min). Residual neuromuscular blockade was reversed by neostigmine and atropine. Children were extubated.

All scores and observations were recorded by the anesthesia technician or nurse who was unaware of the type of premedication.

Before discharge from the hospital the parents were asked to fill a short questionnaire regarding their satisfaction of the premedication of their child on a 3 point scale, and parent satisfaction score was rated (Table 4,5).

Statistical Methodology

Analysis of data was done by IBM computer using SPSS (Statistical Program for Social Science, version 12; SPSS, Chicago, Illinois, USA) as follows:

(1) Quantitative variables were described as mean, SD and range.

(2) Qualitative variables were described as number and percentage.

(3) Chi-square test was used to compare qualitative variables between groups.

(4) Fisher exact test was used instead of chi-square when one expected cell or more less than or equal to 5.

(5) Unpaired t-test was used to compare two groups as regards to quantitative variable in parametric data (SD <50% mean).

Results

Eighty patients {40 of them were premedicated using midazolam only «group C» and 40 with midazolam and ketamine «group S», were included in this study. Demographic and operative data are presented in table 1, and showed no evidence of differences between groups. Children of both groups nicely accepted the premedication mixture according to the *Acceptance Score*, as shown in table 3 (P=0.54). No recorded evidence of respiratory depression (no hypoxia) but vomiting was recorded in one patient within group S, and this patient was excluded from the study. The onset of action of premedication was shorter in group S (16.12 ± 2.5 min) than in group C (19.72 ± 3.25 min) (P=0.000) Table 1. Meanwhile, a reliable degree of sedation was noticed in both groups with no reported cases of deep sedation or crying but the results was more satisfactory with group S as 82.5% of children were drowsy with eye opening versus 60% of group C and 15% versus 40% were awake and calm in both groups respectively (P=0.008). Reaction to parent separation was better in group S compared to group C, (P=0.000). Group S children were more cooperative regarding acceptance and tolerance of the face mask than those of group C, showing significant statistical difference (p=0.02), as shown in Table 3. Parent of groups show greater satisfaction with good evidence for difference between both groups (P=0.03), Table 4.

Discussion

In the present study, adding oral ketamine 2mg/kg to Midazolam-based premedication 0.5mg/kg facilitates child-parent separation and induction of anesthesia in comparison to Midazolam alone, without affecting drug palatability and provides shorter onset of action [11,12]. Degree of Sedation was similar to the results of Ghai B et al. [13] who proved that the combination of 0.25mg/Kg midazolam with 2.5mg/Kg ketamine provided more children in an awake, calm and quiet state who could be separated easily from parents than 0.5mg/Kg oral midazolam alone, they found that both Midazolam and a combination provided equally effective anxiolysis and separation characteristics but the combination doses in the current study gave better results. Warner DL et al. and Funk et al. found that the mixture of ketamine 4mg/Kg and midazolam 0.4mg/kg & Ketamine 3mg/Kg and Midazolam 0.5mg/kg respectively proved to be more effective premedication than either drug alone [14,15]. These findings suggested the same results of the current study with different doses as we used a smaller dose of ketamine to overcome any of its adverse effects. However they did not investigate the effect of premedication on parents' satisfaction as proved by the current study. Ketamine Dormicum combination offers the advantage of decreasing the psychological side effects of ketamine by Midazolam sedation. Also, any respiratory and cardiovascular depression of midazolam [16] is counteracted by the ketamine.

In contrast to Lin et al. who reported no difference in behavior at separation or induction after administration of midazolam (0.75mg/kg) or ketamine (6mg/kg) or a combination of ketamine (3mg/kg) with midazolam (0.5mg/kg) [17]. Their success rate using the combination was 80% at separation and 70% at induction. However, they found few advantages in the combination group, i.e. faster onset time (versus both group), fewer secretions and nystagmus (versus ketamine) and faster recovery (versus midazolam). Non-drug methods offer alternatives, but a new review of studies finds that no single method shows a clear advantage in keeping the child calm and cooperative [18].

The ideal premedication in children should be readily accepted by children, with rapid and reliable onset, provide anxiolysis with sedative effect, and have minimal side effects with, rapid elimination to facilitate rapid recovery for early discharge. Earlier studies have indicated that both oral Midazolam and oral Ketamine fulfill many of these characteristics, and both may be useful premedicants in pediatric anesthesia [6].

An effective premedication may facilitate a smoother induction of GA (general anesthesia) with minimal hemodynamic alterations and minimize the emotional trauma in children undergoing surgery. Premedication is best given by an oral route in children as children often exhibit an exaggerated psychological response to a needle, and it is easier to distribute a medication orally than to use nasal or rectal routes [19,20].

We conclude that adding low dose oral ketamine to midazolam-based premedication provided better pre-induction situation and pleasant child-parent separation with higher parent satisfaction.

References

1. Coté CJ (1999) Preoperative preparation and premedication. Br J Anaesth 83: 16-28.

2. Creedon RL and Dock M (2004) Pharmacological management of patient behavior. In: McDonald RE and Avery DR (8th edn). Dentistry for the Children and Adolescent: 285-311.

3. Raybould D, Bradshaw EG (1987) Premedication for day case surgery. A study of oral midazolam. Anaesthesia 42: 591-595.

4. Connors K, Terndrup TE (1994) Nasal versus oral midazolam for sedation of anxious children undergoing laceration repair. Ann Emerg Med 24: 1074-1079.

5. Haas DA (1999) Oral and inhalation conscious sedation. Dent Clin North Am 43: 341-359.

6. Remadevi R, Ezhilarasu P, Chandrasekar L, Vasudevan A (2009) Comparison of Midazolam and Ketamine as Oral premedicants in pediatric patients. The Internet Journal of Anesthesiology 21: 2.

7. Debnath S Pande YA (2003) Comparative Study of Oral Premedication in Children with Ketamine and Midazolam. Indian J Anaesth 47: 45-47.

8. Sekerci C, Dönmez A, Ateş Y, Okten F (1996) Oral ketamine premedication in children (placebo controlled double-blind study). Eur J Anaesthesiol 13: 606-611.

9. Kain ZN, Maclaren J, Weinberg M, Huszti H, Anderson C, et al. (2009) How many parents should we let into the operating room? Paediatr Anaesth 19: 244-249.

10. Kain ZN, Caldwell-Andrews AA, Mayes LC, Wang SM, Krivutza DM, et al. (2003) Parental presence during induction of anesthesia: physiological effects on parents. Anesthesiology 98: 58-64.

11. Pandit UA, Collier PJ, Malviya S, Voepel-Lewis T, Wagner D, et al. (2001) Oral transmucosal midazolam premedication for preschool children. Can J Anaesth 48: 191-195.

12. Feld LH, Negus JB, White PF (1990) Oral midazolam preanesthetic medication in pediatric outpatients. Anesthesiology 73: 831-834.

13. Ghai B, Grandhe RP, Kumar A, Chari P (2005) Comparative evaluation of midazolam and ketamine with midazolam alone as oral premedication. Paediatr Anaesth 15: 554-559.

14. Warner DL, Cabaret J, Velling D (1995) Ketamine plus midazolam, a most effective paediatric oral premedicant. Paediatr Anaesth 5: 293-295.

15. Funk W, Jakob W, Riedl T, Taeger K (2000) Oral preanaesthetic medication for children: double-blind randomized study of a combination of midazolam and ketamine vs midazolam or ketamine alone. Br J Anaesth 84: 335-340.

16. Quario Rondo L, Thompson C (2008) Efficacy of propofol compared to midazolam as an intravenous premedication agent. Minerva Anestesiol 74: 173-179.

17. Lin YC, Moynihan RJ, Hackel A (1993) A comparison of oral midazolam, oral ketamine and oral midazolam combined with ketamine as preanesthetic medication for pediatric outpatients. Anesthesiology 70: A1177.

18. DeBenedette V (2009) Contributing Writer Calming Parents Might Help Kids Cope With Anesthesia Health Behavior News Service.

19. Connors K and Terndrup TE (1994) Nasal vs oral midazolam for sedation. Annals of Emergency Medicine 24: 1074-1079.

20. Haas DA (1999) Oral and inhalation conscious sedation. Dent Clin North Am 43: 341-359.