



A Comparative Evaluation of Intranasal Ketamine and Intranasal Midazolam for Premedication in Children

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Abstract

Introduction: Surgery and anaesthesia induce considerable emotional stress upon children. Premedicant should relieve this anxiety and facilitate smooth induction. Intranasal route is preferred, as it is noninvasive and more convenient with high bioavailability.

Aim: To compare the efficacy of intranasal ketamine and Intranasal midazolam for paediatric premedication.

Method: In this prospective, randomised controlled trial 100 patients of 1 to 10 years of age of either sex belonging to ASA class 1 and 2 undergoing various elective surgery were divided into two groups. Group-M received 0.2 mg / kg intranasal midazolam, group-K received 5 mg/kg intranasal ketamine 45 minutes prior to induction. Onset of sedation, degree of sedation, parent separation anxiety scale, acceptance of mask and venipuncture score were assessed.

Results: The mean time of onset of sedation was faster in Group M (10.4 ± 1.5 Vs 15.58 ± 2.18) which was statistically significant ($P < .0001$). Mean sedation score was lower in group M (2.86 ± 0.99 Vs 3.14 ± 1.1) which was statistically insignificant ($P = 0.17$). The mask acceptance was better in group M (1.32 ± 0.5 Vs 1.66 ± 0.6) which was statistically significant ($P = 0.003$). The mean venipuncture score was lower in group M (2.22 ± 0.68 Vs 2.34 ± 0.7) which was statistically insignificant ($P = 0.4$). The mean parental separation anxiety score was lower in group M (2.48 ± 0.97 Vs 2.9 ± 1.1) which was statistically insignificant ($P = 0.05$).

Conclusion: Intranasal midazolam group had faster onset of sedation and better mask acceptance than intranasal ketamine. Both groups were comparable in terms of degree of sedation, parent separation anxiety and venipuncture score.

Introduction

Anxiety and psychological trauma due to parental deprivation are major challenges in paediatric anaesthesia. Fear of operation theatre, injections and separation from parents prior to anaesthesia produces traumatic experiences in tender mind of young children which can lead to postoperative maladaptive behaviours. Pre-anaesthetic medication in children should aim at relieving this anxiety and psychological trauma and also to facilitate induction of anaesthesia without

prolonging the recovery. So, a premedicant drug must have an acceptable, non-traumatic route of administration in order not to add extra stress to the child and should act rapidly with adequate sedation and analgesia, cause less respiratory depression, no postoperative sickness and no hypersensitive reaction.

Earlier, drugs such as meperidine and promethazine were commonly used, but now-a-days most commonly used drugs are midazolam, ketamine, dexmedetomidine and fentanyl.

Intranasal route is relatively easy, non-invasive route with high bioavailability and rapid onset of action comparable to that of IV administration because of rich blood supply of nasal mucosa and bypassing first pass hepatic metabolism. Also, this route is not painful and does not require trained personnel.

Midazolam is a water-soluble benzodiazepine known to have a rapid onset and short duration of action, as well as properties of amnesia and anxiolysis.

Ketamine is a dissociative anaesthetic agent that creates a trance-like state with properties of sedation, amnesia, analgesia.

Hence, in this study, we compared the efficacy of intranasal ketamine (5 mg/kg) and intranasal midazolam (0.2 mg/kg) as premedicants in pediatric age group.

Material & Methods

After approval by the Institute Ethics Committee & written informed consent from patient's parents or caretaker, the study was conducted as hospital based prospective randomized double blind observational study in 100 ASA Grade I & II patients, Age 01 to 10 yrs, undergoing various elective surgeries under general anaesthesia, performed in the year 2017-2018.

Exclusion

Patients aged < 01 years and > 10 years, history of clinically significant cardiovascular, pulmonary, renal, neurologic disease, history of coexisting disease, allergic to anaesthetic drugs, mental retardation, any nasal disorder that may interfere with nasal administration of drugs, patient's parents or caretaker's refusal were excluded from study.

On the day prior to surgery a thorough clinical examination of the patient was performed including general physical examination and systemic examination. All patients were explained about the anaesthesia technique and written informed consent was taken from parents. Patient was kept NBM for 8 hours (for solid foods), 6 hours (for formula & fortified breast milk), 4

hours (for breast milk), 2 hours (for clear liquids) prior to surgery. Routine investigations (HB%, BT, CT, urine analysis, chest x-ray, blood urea, serum creatinine and fasting blood sugar) were done.

100 children aged 01 –10 years were selected for this study in accordance with American Society of Anesthesiologists (ASA) physical status I & II scheduled for various elective surgeries divided into two groups: intranasal midazolam group (group M) (n = 50) 0.2 mg/kg and intranasal ketamine group (group K) (n = 50) (5mg/kg). Medications were administered 45 min. prior to induction, in the pre-anesthesia area, with the parent(s) attendance. Calculated dose of drug was diluted to a total volume of 1 ml was administered 0.5 ml in each nostril using a 2-mL syringe with the child in the recumbent position. Before induction in operation theatre, each patient was observed for onset of sedation, degree of sedation, parental separation anxiety, response to venipuncture & acceptance of mask. Inhalation induction was initiated by face mask with a mixture of sevoflurane 8% with O₂ 100%. When adequate depth of anesthesia reached, appropriate LMA was placed and the patient was left to breath spontaneously. The anesthetic level was delivered in a concentration that maintained a stable heart rate, blood pressure and respiratory rate (baseline \pm 20%). Standard monitoring was done by using ECG, noninvasive blood pressure, respiratory rate, pulse oximetry and capnography. After the end of surgery anesthetic gases were discontinued to 0% and replaced with O₂ 100% \geq 4 L/min. LMA was removed when the patient awakened. In postoperative monitoring, each patient was monitored for vital signs (NIBP, PR, SPO₂ & RR), restlessness, PONV, emergence reactions. Each patient was followed and observed in post anaesthesia care unit for monitoring of vital signs and any adverse effects.

Five point sedation scale

- 1) Asleep
- 2) Drowsy
- 3) Calm

- 4) Alert
- 5) Agitated

Acceptance of mask

- 1) Accepts readily
- 2) Accepts with persuasion
- 3) Refuses

Venipuncture score

- 1) Asleep
- 2) Calm-no withdrawal for IV cannulation
- 3) Withdrawal for painful stimuli
- 4) Crying, uncooperative, not able to start IV line

Parent separation anxiety scale

- 1) Asleep, cooperative, unafraid
- 2) Slight fear or crying, quiet with reassurance
- 3) Moderate fear, crying not quiet with reassurance
- 4) Crying need for restraint

Statistical Analysis

- Collected data were entered into excel sheet & analysed with help of SPSS software version 21.
- Results were interpreted in terms of mean, standard deviation and p value.
- Student’s unpaired t-test for Quantitative data.
- P<0.05 was considered statistically significant.

Results

Statistical analysis shows no significant difference in average taken for age, weight and gender among two groups.

Out of 50 patients, all 50 patients were in ASA grade I in both groups.

Maximum number of patients in both groups had undergone uro-genital surgeries (88% in group M and 94% in group K). Both groups were comparable in terms of type of surgery.

Table no. 1. Mean age (years) in both groups

Group	Mean age (yrs)	SD	p value
M	5.38	2.63	0.07
K	4.42	2.58	

Table no. 2. Mean weight (kg) in both groups

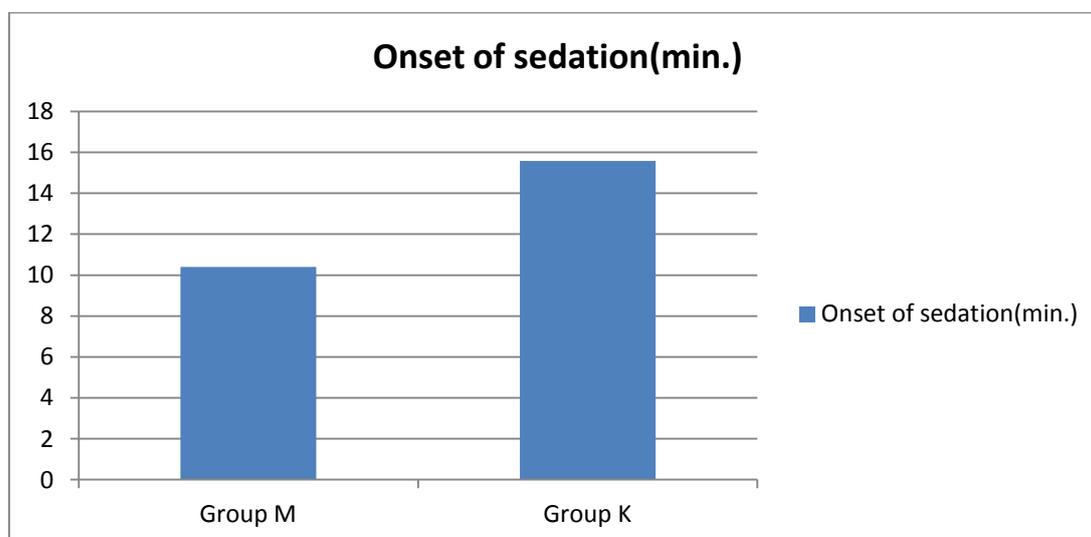
Group	Mean weight (Kg)	SD	p value
M	18.88	6.78	0.06
K	16.24	6.8	

Table no. 3. Types of surgery in both groups

Type of surgery	Group M	Group K
Herniotomy	40	41
Orchidopexy	4	6
Bone biopsy	2	3
Eye surgery	4	0

Table no. 4. Time of onset of sedation (min.) after premedication in both groups

Group	Mean time of onset of sedation (min.)	SD	p value
M	10.4	1.5	<0.0001
K	15.58	2.18	

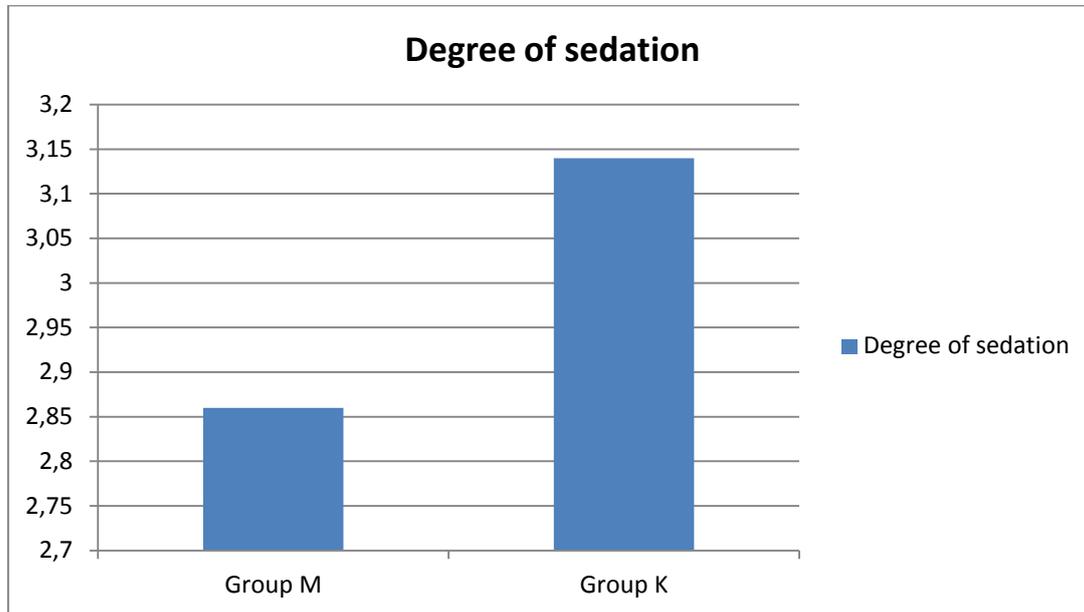


The mean time of onset of sedation in group M was 10.4±1.5 min., whereas in group K was 15.58±2.18 min. The mean time of onset of

sedation was faster in group M as compared to group K, which was statistically significant (p value <0.05).

Table no. 5 Degree of sedation after premedication in both groups

Group	Mean degree of sedation	SD	p value
M	2.86	0.99	0.17
K	3.14	1.1	

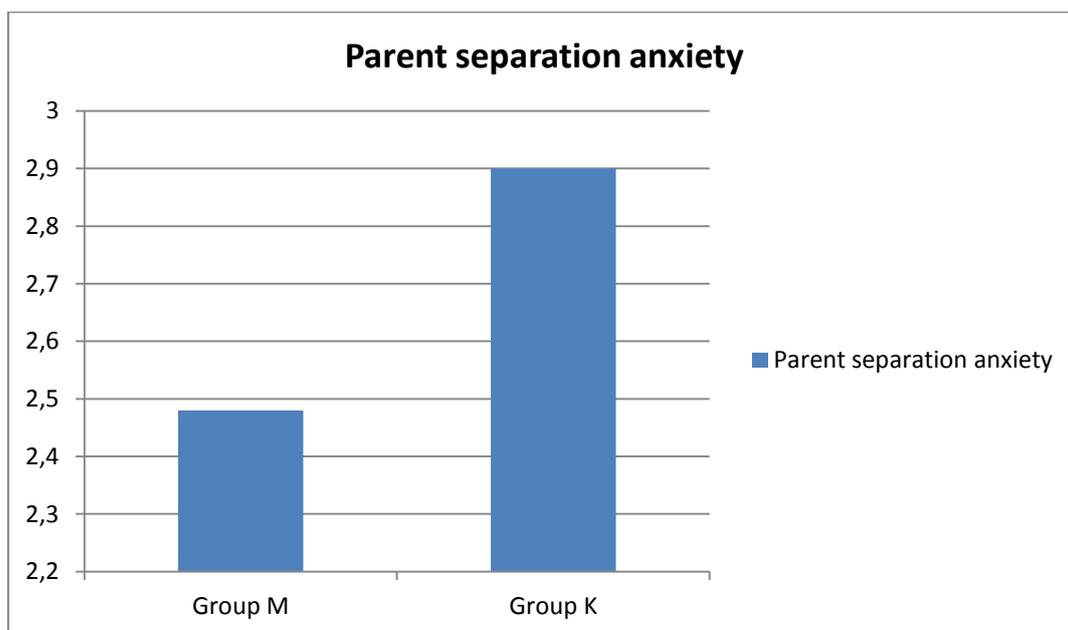


The degree of sedation in group M was 2.86 ± 0.99 and in group K was 3.14 ± 1.1 . The difference in

degree of sedation in both groups was statistically insignificant (p value >0.05).

Table no. 6. Parent separation anxiety scale after premedication in both groups

Group	Mean parent separation anxiety score	SD	p value
M	2.48	0.97	0.05
K	2.9	1.1	

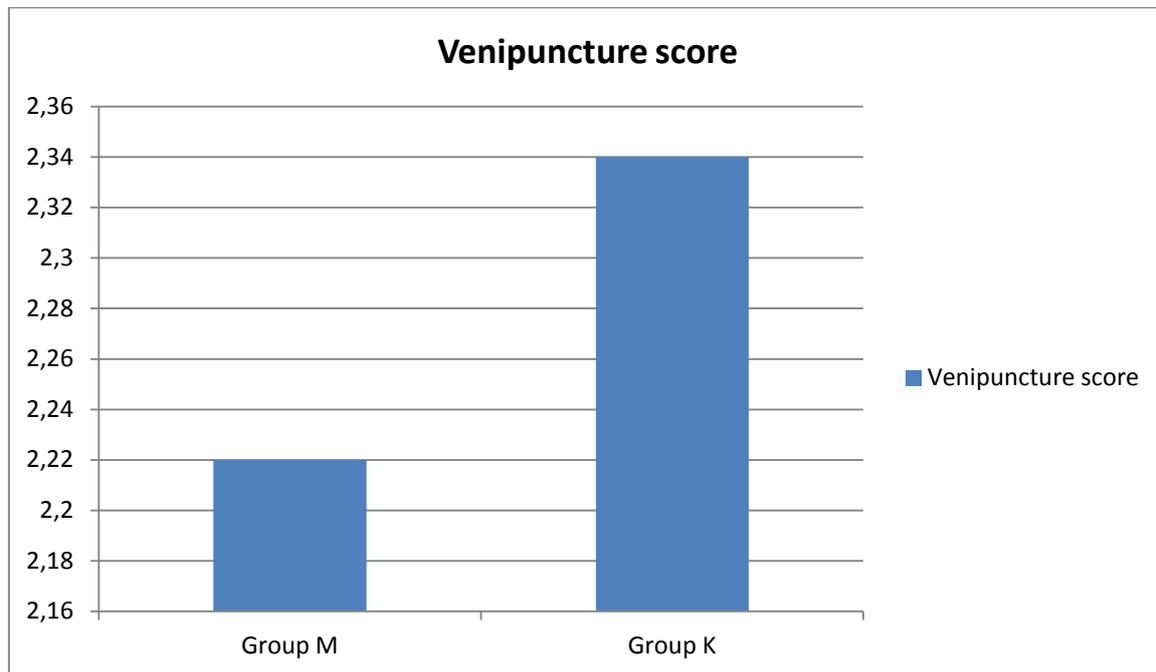


The parent separation anxiety score in group M was 2.48 ± 0.97 and in group K was 2.9 ± 1.1 . The difference in parent separation anxiety score in

both groups was statistically insignificant (p value =0.05).

Table no. 7. Venipuncture score after premedication in both groups

Group	Mean venipuncture score	SD	p value
M	2.22	0.68	0.4
K	2.34	0.7	

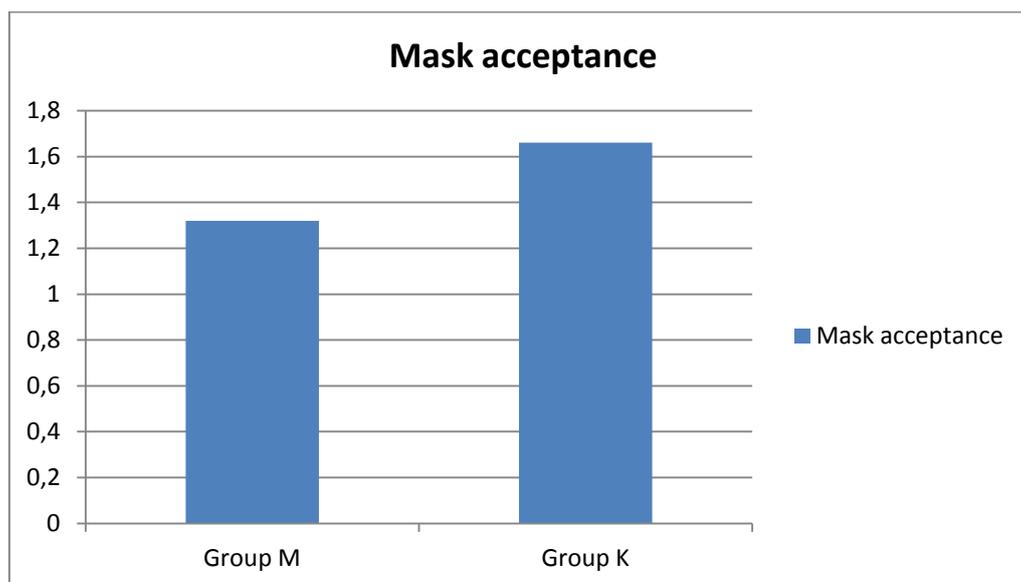


The venipuncture score in group M was 2.22 ± 0.68 and in group K was 2.34 ± 0.7 . The difference in

venipuncture score in both groups was statistically insignificant (p value >0.05).

Table no. 8. Mask acceptance after premedication in both groups

Group	Mean mask acceptance score	SD	p value
M	1.32	0.5	0.003
K	1.66	0.6	



The mask acceptance score in group M was 1.32 ± 0.5 and in group K was 1.66 ± 0.6 . Group M had better mask acceptance than group K and the

difference was statistically significant (p value < 0.05).

Table no. 9. Baseline vital parameters in both groups

Vital parameter	Group M (Mean±SD)	Group K (Mean±SD)	p value
HR (beat/min.)	123±10.8	127±13.9	0.17
SBP (mmHg)	102±6.8	102±8.3	0.9
DBP (mmHg)	65±7.3	64±6.1	0.2
SPO2 (%)	99.4±0.64	99.6±0.48	0.06

The baseline vital parameters in both groups were comparable (p value > 0.05).

Table no. 10. Vital parameters after premedication in both groups

Vital parameter	Group M (Mean±SD)	Group K (Mean±SD)	p value
HR (beat/min.)	117±12	136±15	0.0001
SBP (mmHg)	98.4±6.93	118±7.58	0.24
DBP (mmHg)	62±5.1	64±6.1	0.1
SPO2 (%)	97.96±1.01	98.2±0.95	0.222

After premedication, there was significant tachycardia noted in group K (p value < 0.05), which persisted throughout the study. Otherwise, both groups were comparable in vital parameters after premedication.

Discussion

Preoperative anxiety along with fasting is highly stressful in young children. It can have long lasting adverse effects on their personality development. Hence all paediatric patients should be pre-medicated in order to decrease preoperative anxiety, allow smooth induction and prevent postoperative psychological insult and behavioural changes.

Our study evaluated the efficacy of midazolam and ketamine as intranasal premedication in paediatric patients.

Demographic Data

The mean age in group M was 5.38±2.63 years and in group K was 4.42±2.58 years. The mean weight in group M was 18.88±6.78 kg and in group K was 16.24±6.8 kg. In group M, there were 44 males and 6 females, whereas in group K, there were 41 males and 9 females. Both groups were comparable demographically (p value >0.05).

Onset of Sedation

The mean time of onset of sedation in group M was 10.4±1.5min. and in group K was 15.58±2.18min., which was statistically

significant (p value <0.0001). This finding is consistent with those of Narendra et al⁵.

Degree of Sedation

The mean degree of sedation in group M was 2.86±0.99 and in group K was 3.14±1.1, which was statistically insignificant (p value >0.05).

Parent Separation Anxiety Score

The mean parent separation anxiety score in midazolam group was 2.48±0.97 and in ketamine group was 2.9±1.1, which was statistically insignificant. However, Shreyavathi et al⁴ noted that intranasal ketamine group achieved better quality of sedation and enabling easier parental separation of child than midazolam group.

Venipuncture Score

The mean venipuncture score in midazolam group was 2.22±0.68 and in ketamine group was 2.34±0.7, which was statistically insignificant (p value >0.05). These findings are consistent with those of Kazemi et al² and Gautam et al³.

In our study, both groups were comparable in terms of degree of sedation, parent separation anxiety and venipuncture score. These findings are consistent with those of Garcia et al¹ and Narendra et al⁵.

Mask Acceptance Score

The mean mask acceptance score in midazolam group was 1.32±0.5 and in ketamine group was 1.66±0.6, which was statistically significant (p value <0.05). However, Garcia et al¹ and Narendra et al⁵ did not find any significant difference in mask acceptance in both groups.

In our study, we noted significant difference in both groups in onset of sedation and mask acceptance. Midazolam group had faster onset and better mask acceptance than ketamine group. There was no significant difference found in both groups in terms of degree of sedation, parent separation anxiety and venipuncture score.

Hemodynamic Parameters

The heart rate (beats/min.) in midazolam and ketamine group were 123 ± 10.8 and 127 ± 13.9 preoperatively, after premedication 117 ± 12 and 136 ± 15 , intraoperatively 116 ± 11 and 137 ± 15.6 and postoperatively 120 ± 11.6 and 138 ± 16 . In our study, tachycardia was statistically significant in ketamine group after premedication (p value < 0.0001) and persisted throughout the study. These findings are consistent with those of Garcia et al¹ and Narendra et al⁵. There were no significant differences in other hemodynamic parameters in both groups in our study.

Complications

None of the children in both groups had untoward complications such as bradycardia, hypotension, hypertension and respiratory depression after premedication. These findings are consistent with those of Kazemi et al², Shreyavathi et al⁴, Garcia et al¹ and Narendra et al⁵.

Limitations of our Study

1. Study population was small.
2. It was not a placebo controlled trial of two nasal premedications, where superiority of these medications had been established.
3. Apart from drug absorption over nasal mucosa, significant part of drug will go to the pharynx where absorption via pharyngeal mucosa occurs and remaining volume will be swallowed. Thus we must emphasize that the term nasal premedication describes the mode of drug administration and not necessarily the single route of drug absorption.

Conclusion

We concluded that intranasal midazolam is a better premedication agent than intranasal ketamine in terms of faster onset of sedation, better mask acceptance and better hemodynamic stability.

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