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Research Article

EVALUATION OF EFFICACY OF INTRANASAL MIDAZOLAM AS PRE-ANAESTHETIC DRUG IN PAEDIATRIC PATIENTS

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ABSTRACT

Background & Aims: Most of the preschool children suffer from severe preoperative anxiety of parental separation; it may to predispose them to emergence delirium, behavioural changes and long lasting psychological trauma post operatively. Midazoalm has emerged as an ideal anxiolytic to remove fear and anxiety in children, it can be administered by various routes, oral and intranasal routes are preferred for pediatric sedation. So we designed current study to find out the efficacy of midazolam intranasally.

Material & Methods: Fifty paediatric patients of 2-5 years of age belonging to ASA I & II, scheduled for elective surgery under general anaesthesia were selected for this prospective, randomized double blinded observational study. Patients were divided in two groups, Group M received midazolam 0.2 mg/kg intranasally and Group C received normal saline. Outcomes measured include the haemodynamic parameters, level of sedation, emotional reaction, and response to parental separation, acceptance of intravenous cannulation and facemask application and adverse effects, if any.

Results: A statistically significant change in the level of sedation was found at10 min in group M as compared to control group. Parental separation was significantly easier in midazolam groups. The acceptance for intravenous cannulation and face mask was also found to be significantly better in midazolam groups. No significant difference was observed in incidence of adverse effects among both the groups.

Conclusion: we conclude that 0.2 $mgkg^{-1}$ intranasal midazolam is an effective premedication for producing anxiolysis and sedation in paediatric patients without any untoward adverse effects.

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INTRODUCTION

Induction of anaesthesia in preschool children is a challenge for anaesthetist as they suffer from severe preoperative anxiety of parental separation; it may to predispose them to emergence delirium, behavioural changes and long lasting psychological trauma post operatively. This stress response may be detrimental, neuro-endocrine hormones and cytokines provoke a negative nitrogen balance and catabolism, delay wound healing and cause postoperative immunosupression. [1] Various pharmacological and behavioural interventions have been in practice to reduce the preoperative anxiety. Midazoalm has emerged as an ideal anxiolytic to remove fear and anxiety in children; and makes child calm and sedated for smooth induction of anesthesia and rapid recovery in postoperative period.[2] Though it is administered by various routes, oral and intranasal routes are preferred for pediatric sedation.[3,4,5,6]Intranasal administration of midazoalm has the advantage of rapid absorption of the drug directly into the systemic circulation from an area of rich blood supply and bypassing the portal circulation.

The aim of this study was to evaluate the efficacy of intranasal midazoalm on preoperative anxiety, sedation and the ease of child-parent separation (as a primary outcome), and the haemodynamic changes, recovery profile and adverse effects, if any as secondary outcome variable.

MATERIAL AND METHODS

This prospective, randomized, double-blinded, observational study was conducted after the approval of the Institutional Ethics Committee and obtaining informed written consent from parents of all patients. Fifty children of either sex, American Society of Anesthesiologists physical status (ASA) I-II, 2 to 5 yrs of age, undergoing elective surgery under general anaesthesia were chosen for this study. Exclusion criteria included parent's refusal and respiratory tract infection. A thorough pre anaesthetic check-up, including history, general

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physical examination and necessary investigation were done one day prior to surgery. The essence of study with its advantage was explained and informed written consent was taken from all parents. The patients were randomized into two groups of twenty five patients in each using computer generated random number table and assigned group number was kept in a sealed opaque envelope.

Group M (n=25)-Patients received 0.2 mg/kg midazoalm nasally
Group C (n=25)-Patients received normal saline nasally

After confirming the fasting status, patient was shifted to operation theatre. Premedicant drug, as per group, was given nasally while child was accompanied with mother. Multipara monitor for heart rate (HR), oxygen saturation (SpO2) and respiratory rate was attached and baseline vital parameters were recorded. The child was monitored every 10 minutes after premedication, intraoperatively and 2 hr postoperatively for pulse rate, respiratory rate, oxygen saturation, sedation, emotional state, attitude towards surrounding people and any untoward effect like vomiting, apnoea, convulsion etc.

Sedation level was measured by using the five point sedation scale[7] [1(asleep)- arousable, does not respond to minor stimuli; 2(drowsy)- eyes closed, response to minor stimuli; 3 (calm)- sitting/lying comfortably with eyes open; 4(alert)- awake but not clinging to parents;5(agitated)-crying/clinging to parents]

Emotional reaction graded as [Thrashing (Th)-crying with limb movements; Crying (Cr)-crying without limb movement; Apprehensive (Ap)-not smiling, tentative behaviour withdrawn, Calm (Ca)-lying comfortably with eyes spontaneously open]

Grading of attitude was done as; Resistant-not ready to separate from parents, crying, throwing limbs; Anxious-crying but not moving limbs and Cooperative- calm, comfortably lying.

Patients were also observed for intravenous cannulation and face mask acceptance; Good (G)-accepts easily, requires persuasion (P)-grimaces and crying (Cr)-withdraws hand and cry.

Induction of anaesthesia was done with inj. thiopentone sodium intravenously 4-7 mg/kg, patient was intubated with appropriate sized tube after achieving muscle relaxation with inj succinylcholine 1-2mg/kg intravenously. Maintenance of anaesthesia was done using isoflurane in oxygen-nitrous mixture (50:50) and inj atracurium. At the end of surgery, isoflurane and nitrous oxide discontinued, patients ventilated with 100 percent oxygen. Reversal done with inj. neostigmine 0.05mg/kg and inj. glycopyrrolate 8mcg/kg and patient was extubated after fulfilling all criteria of extubation. All patients were observed for 2 hours postoperatively.

For statistical analysis, quantitative data were represented as mean =/-S.D. and qualitative data were expressed as number or percentage. Sedation level was analysed by Mann-Whitney test. Emotional reaction, attitude towards surroundings, separation reaction, and response to IV cannulation, facemask acceptance and incidence of adverse reaction were analysed by Pearson Chi-Square test. Hemodynamic changes and anesthesia recovery was assessed by standard error of difference between two means and *t*-test. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic variables like age, sex, ASA status and weight were comparable ($P > 0.05$) among both the groups. (Table 1)

Table 1 Distribution of demographic variables

Variables	Group M	Group C	*P* value	Significance
ASA(I/II)	1.16±0.374	1.12 ±0.332	0.691	**NS**
Age (yrs)	3.00 ± 1.00	3.52 ±1.085	0.084	**NS**
Weight (kg)	11.92± 2.44	12.44 ± 2.10	0.424	**NS**
Sex(M/F)	22/3	17/8	0.088	**NS**

Values presented as mean±SD, Group M-Midazolam; Group C- Control; ASA-American Society of Anesthesiologists; SD-Standard deviation, value <0.05 is taken as significant

When comparing the sedation score, baseline sedation level was 4.6 in midazoalm group and 3.96 in control group. There was statistically significant difference was observed in midazoalm group as compared to control group at 10, 20, 30 minutes. But no significant difference was observed at IPOP and 2HPOP. (Table 2)

Table 2 Level of Sedation (SED) in both Groups

Time of recording	Group	Mean Rank	Sum of Rank	Significance P value
Base SED	Midazolam	24.14	603.50	0.484
	Control	26.86	671.50	Not Significant
10 min SED	Midazolam	18.74	468.50	0.000
	Control	32.26	806.50	Significant
20 min SED	Midazolam	15.28	382.00	0.000
	Control	35.72	893.00	Significant
30 min SED	Midazolam	15.19	364.50	0.000
	Control	34.42	860.50	Significant
IPOP SED	Midazolam	22.64	566.00	0.114
	Control	28.36	709.00	Not Significant
2HPOP SED	Midazolam	22.64	566.00	0.114
	Control	28.44	709.00	Not Significant

SED-Sedation level; IPOP-Immediate post operative period; 2HPOP-2 Hours post operative period
Test applied-Mann-Whitney

The emotional reaction at 10, 20 &30 minutes, IPOP & 2HPOP was better in midazolam group than control group.(Table 3) (P value<0.05) Attitude towards surrounding was significantly better at 20, 30 minutes in midazolam group (P value <0.05)) but it showed no difference at 10 minutes, IPOP & 2HPOP in both the groups.

Table 3 Emotional reaction at various time intervals

Emotional reaction	Group	Base ER	At 10 min	At 20 min	At 30 min	IPOP	2 HPOP
Apprehension	M	10	7	5	13	10	11
	C	4	7	18	23	4	20
Calm	M	8	17	19	11	8	6
	C	0	0	0	0	0	2
Crying	M	7	1	1	1	7	8
	C	14	13	7	2	14	3
Thrashing	M	0	0		-	0	-
	C	7	5		-	7	-
P value		0.34 (NS)	0.000 (S)	0.000 (S)	0.001 (S)	0.000 (S)	0.032 (NS)

ER –Emotional reaction; IPOP-Immediate post operative period; 2HPOP-2 Hours post operative period; P value by Pearson Chi-Square test

Separation from the parents was much easier in midazolam group at 30 minutes as compared to control group.(Figure 1) Response to intravenous cannulation and face mask acceptance

was significantly better in midazolam group in comparison to the control group. (Figure 2) Haemodynamically patients were stable in both of the groups during the study period.

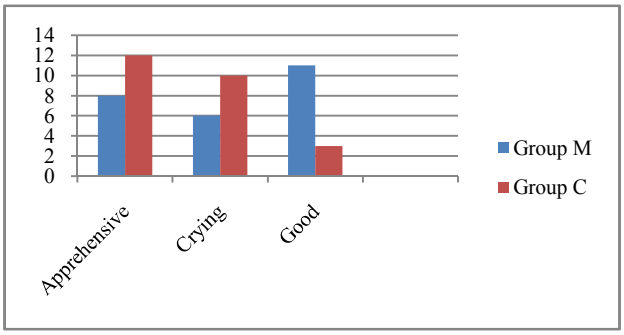

Figure 1 Separation Reaction after 30 minutes in Midazolam & Control group

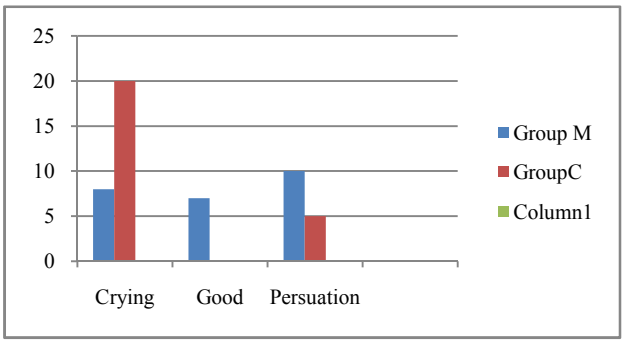

Figure 2 Response to IV Cannulation in Midazolam & Control group

DISCUSSION

In this study we evaluated the efficacy of intranasal midazolam as Premedicant in pediatric patients. We observed that intranasal midazolam 0.2mg/kg produced an effective anxiolytic and sedative response in paediatric patients, which is comparable with the other reported studies.[8,9] Children of 2-5 years of age were selected for the study as this age group is most susceptible to the separation anxiety, since their understanding is limited. [10]

We observed a significant change in sedation level in midazolam group by ten minutes, it was maintained till 30 minutes, these findings are in accordance with previous studies [8, 11, 12] Most of the patients in midazolam groups became either calm or drowsy (sedation scale score 3 or 4) which helped in easy separation of the child from their parents, and also in smooth induction of anaesthesia.

Better emotional reaction was observed in midazolam group, assessment of level of anxiety in children was done by observing response to parental separation, acceptance of intravenous cannulation and facemask application. We observed that separation reaction was better in midazolam group, these findings are comparable to Diaz J H *et al* [12] and Jungman *et al* [13], and they also observed better co-operation index and easy separation in intranasal midazolam group. Attitude towards surrounding people was comparable preoperatively in both of the groups, but it was better in midazolam group at 20, 30 minutes and during intraoperative period.

Facemask acceptance was improved in midazolam group; similar observation was made by Pradipta Bhakta *et al* [14]. Response to intravenous cannulation was also improved after administration of intranasal midazolam as 17 of 25patients allowed IV cannulation in comparison to only 5 patients in the control group.

No change in pulse rate was found after intranasal administration of midazolam, similar observation was made in previous study. [8]Oxygen saturation was within acceptable limits in both the groups, no case of apnoea, respiratory depression and excessive secretion was reported in midazolam group.

CONCLUSION

Hence, we conclude that intranasal midazolam in dose of 0.2mg per kg is an effective premedication for producing effective sedation and anxiolysis in paediatric patients without any untoward adverse effects. Intranasal midazolam provides optimal sedation at 20-30 minutes after administration, so we recommend using it 20-30 minutes prior to surgery.

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