



ORIGINAL RESEARCH PAPER

Anaesthesiology

COMPARISON OF ORAL MIDAZOLAM, ORAL DEXMEDETOMIDINE AND ORAL MIDAZOLAM KETAMINE COMBINATION FOR PREMEDICATION IN PAEDIATRIC SURGERY

KEY WORDS: ASA, HR, MAP, PONV

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ABSTRACT

Background: Children especially age group <10years undergoing operation may experience preoperative anxiety & may be uncooperative. This uncooperative behavior of children may be observed at the time of separation from parents, venipuncture or mask application. Untreated anxiety may lead to difficult induction, greater rescue analgesic needs, emergence delirium (ED), behavioural & postoperative psychological effects. An atraumatic premedication, calm separation from parents can minimize these problems and a smooth induction of anaesthesia can be achieved. **Method :** Prospective randomized double blind active controlled study was conducted in Government medical college & hospital, Aurangabad from 2018 to 2020 after Institution Ethics Committee approval. 75 ASA I & II subjects aged between 2 to 5 year weighing less than 15 Kg posted for elective paediatric surgery under general anaesthesia at tertiary care centre were selected. They were randomly allocated into 3 groups Group M ,Group M K & Group D with 25 subjects in each group using computer generated randomization list. Oral premedication was given in each group 30 minutes before surgery. Baseline heart rate, SBP and RR measured before administering premedication and at 10 minutes intervals up to 30 to 45 minutes after premedication. **Results:** Sedation & anxiolysis score at induction[S1] was significant higher in Group M K & Group D [p Value <0.05] compared to Group M. Sedation at the time of separation from parents [S2] was better in Group M K & Group D compared to Group M [p Value <0.05]. Sedation during Mask Acceptance[S3] was better in Group M K & Group D compared to Group M [p Value <0.05]. Wake up Behaviour [when the patient recovers from anaesthesia at end of surgery [S4]] was assessed & Subjects were more Sedated[post anaesthesia] in Group D when compared to Group m & Group M K [p Value <0.05]. Time taken for maximum change in vital parameters was more in Group D followed by Group M K and Group M respectively p Value 0.001]. There was significant changes in Vital parameters in Group D compared to Group M & Group M K .Bradycardia p Value 0.00044] & Hypotension [p Value 0.01] was more significant in Group D when compared to Group MK & Group M **Conclusion:** Oral Midazolam (0.2mg/kg) & Ketamine (2mg/kg) combination & oral Dexmedetomidine (0.5 g/kg) both provide satisfactory sedation levels & offers significant ease of separation from parents with satisfactory mask acceptance in children<10 years compared to oral Midazolam alone.

INTRODUCTION

Surgery and anaesthesia may cause considerable stress for both parents and children. The anticipation of pain, separation from family, and fear of surgery are few of the factors that trigger perioperative anxiety in children. [3]

The fear and anxiety associated with an anticipated operation can result in a variety of unwanted physiological changes and alteration in the hemodynamic profile of the patient, which can sometimes lead to disastrous intra-operative and postoperative consequences. [4]

An ideal pre-anaesthetic medication should ease separation from parents, facilitate patient's acceptance of intravenous cannula and face mask during induction of anaesthesia without prolonging recovery. It should promote good cardio respiratory stability along with minimization of postoperative complications. [4]

A wide variety of drugs and routes of administration has been described for paediatric patients, with each drug and each route having its own drawbacks. Oral route is the choice of most anaesthesiologists with a definite advantage of being less traumatic and easily acceptable. [4]

Therefore, the present study was undertaken to compare the efficacy of oral midazolam, oral dexmedetomidine and oral midazolam with oral ketamine combination as a premedication in children.

AIMS:

To compare the efficacy of oral midazolam, oral dexmedetomidine and oral midazolam with oral ketamine combination as a premedication in children.

OBJECTIVES:

Primary:

- 1.To compare level of sedation and anxiolysis after premedication with oral midazolam, oral dexmedetomidine and oral midazolam-ketamine combination for paediatric surgery under general anaesthesia.
- 2.To compare emotional state of child at the time of separation from parents, mask acceptance for smoother and safer induction of anesthesia.

Secondary:

- 1.To compare changes in vital parameters like pulse rate, blood pressure and oxygen saturation.
- 2.To compare post-operative complications like nausea, vomiting, restlessness, drowsiness, prolonged recovery.

Inclusion Criteria:

- ASA grade I & II
- Age between 2 to 5 years
- Weight <15 Kg
- Posted for elective paediatric surgery under GA at tertiary care centre

Exclusion Criteria :

- ASA grade III & IV
- Unwilling parents/guardians
- Known allergy to study drugs
- Premedication not completely ingested

METHODOLOGY:

75 ASA I & II subjects aged between 2 to 5 year weighing less than 15 Kg posted for elective paediatric surgery under general anaesthesia at tertiary care centre were selected. They were randomly allocated into 3 groups with 25 subjects

in each group using computer generated randomization list. Oral premedication was given in each group 30 minutes before surgery.

Group M- Midazolam 0.5mg/kg with atropine 0.02mg/kg.

Group MK- Midazolam 0.2mg/kg and ketamine 2mg/kg with atropine 0.02mg/kg.

Group D- Dexmedetomidine 0.5mcg/kg with atropine 0.02mg/kg.

The study drug will be given in pre-operative room by investigator blinded to the study medication when the children are with their parents. Baseline heart rate, SBP and RR measured before administering premedication and at 10 minutes intervals up to 30 to 45 minutes after premedication.

Sedation [S1] was assessed at 0, 10, 20, 30 minutes after premedication using Ramsay sedation scale. 30 minutes after premedication children are separated from their parents and emotional state [S2] was assessed at the time of separation from parents on the basis of a 4 points emotional state scale.

After shifting to operating room emotional state was recorded again after application of afacemask. Acceptance of Mask [S3] at Induction was on a scale of 1 to 4. 1 and 2 are considered satisfactory, 3 and 4 are considered unsatisfactory.

Preoxygenation was done with 100% oxygen, anaesthesia induced with propofol 1-2mg/kg & succinyl choline 1 - 1.5mg/kg & maintained with oxygen, nitrous oxide and Isoflurane/sevoflurane & with IV atracurium 0.5mg/Kg. Vitals parameters (PR, BP, haemoglobin oxygen saturation was be monitored). Muscle relaxation antagonized after surgery with IV Neostigmine 0.05 mg/Kg & glycopyrrolate 0.01 mg/Kg. Postoperative side effects such as PONV, giddiness, headache was recorded.

Wake up Behaviour [At end of surgery when the patient recovers from anaesthesia] [S4] was assessed in post-op recovery room on a scale of 1 to 4. Patients observed for 2 hours before shifted toward every 15 minutes for vitals, PONV & sedation level.

Sample size- Minimum 23 subjects in each group were required to be enrolled with confidence level 95% using software OpenEpi, Version 3. 25 subjects in each group were included to allow dropouts.

Statistical analysis- Descriptive variables presented as Mean (SD) & analysed by One way ANOVA, Chi square test used for categorical data.

Results

Table 1: Demographic Data-

Parameter Mean (SD)	Group M (N =25)	Group MK (N =25)	Group D (N =25)	P value
Age (Years)	3.42 (1.38)	3.10 (1.74)	3.16 (1.30)	0.712-NS
Weight (Kg)	11.27 (2.13)	10.89 (3.08)	11.18 (2.50)	0.865-NS
Duration of Surgery (Minutes)	58.64 (25.67)	62.40 (23.81)	67.96 (19.56)	0.364-NS
Duration of Anaesthesia (Minutes)	68.12 (24.45)	73.80 (25.06)	80.84 (21.12)	0.169-NS
Male (N)	22	23	22	0.869-NS
Female (N)	03	02	03	

Table 2: Distribution Of Study Participants Based On

Intraoperative Anaesthetic Requirement

Group	Number Of Subjects	Average	S.D	P Value
M	25	1.4	0.5	<0.05
M K	25	2.8	0.816	
D	25	3.28	0.737	

Table 3: Sedation & Anxiolysis Scores In Study Group [S1]

Anaesthetic Agent	Anaesthetic Concentration %	Group M (N)	Group MK (N)	Group D (N)	P value
ISOFLURANE	0.5-1%	4	14	4	0.000069
	1-1.5%	12	1	12	-S
SEVOFLURANE	1-1.5%	1	8	1	0.00709-S
	1.5-2%	7	1	7	
	>2%	1	1	1	
TOTAL		25	25	25	

Sedation & anxiolysis score at induction was significant higher in Group M K & Group D [p Value <0.05] compared to Group M.

Table 4: Emotional State [S2] At The Time Of Separation From Parents

Group	Number Of Subjects	Average	S.D	P Value
M	25	1.4	0.5	<0.05
M K	25	2.84	0.55	
D	25	3.12	0.60	

Sedation at time of separation from parents was better in Group MK & Group D compared to Group M.

Table 5: Mask Acceptance Score [S3] At The Time Of Induction

Group	Number Of Subjects	Average	SD	P Value
M	25	3.44	0.50	<0.05
M K	25	1.72	0.79	
D	25	1.68	0.74	

Sedation during Mask Acceptance was better in Group M K & Group D compared to Group M.

Table 6: Wake Up Behaviour [S4] At The End Of The Surgery

Group	Number Of Subjects	Average	SD	P Value
M	25	3	0.288	<0.05
M K	25	2.04	0.84	
D	25	1.72	0.73	

Wake up Behaviour was assessed after the procedure. Subjects were more Sedated [post anaesthesia] in Group D when compared to Group m & Group MK.

Table 7: Sedation, Emotional, Wake Up Behaviour Score:

Parameter Mean (SD)	Group M (N =25)	Group MK (N =25)	Group D (N =25)	P Value
Sedation Score	3.44 (0.50)	1.72 (0.79)	1.68 (0.74)	<0.05
Emotional State score	1.40 (0.50)	2.84 (0.55)	3.12 (0.60)	<0.05
Wake Up behaviour score	3 (0.288)	2.04 (0.84)	1.72 (0.73)	<0.05

Table 8: Maximum Change In Vital Parameters From Baseline In Study Groups

Parameter	Group M	Group MK	Group D	P Value
Heart Rate	↑ 0.35%	↓ 0.95%	↓ 16%	0.004
MAP	↑ 2.59%	↓ 0.94%	↓ 3.69%	
Time for maximum change in vital parameters from baseline in study groups in minutes Mean (SD)				
Heart Rate	33.28(2.49)	35.28(4.35)	50.92(5.55)	0.001
MAP	33.28(2.49)	36.15(4.23)	51.21(5.73)	

Time taken for maximum change in vital parameters was more in Group D followed by Group M K and Group M respectively. There was significant changes in Vital parameters in Group D compared to Group M & Group M K.

Table 9: Side Effects In Study Groups

Parameter	Group M (N%)	Group MK (N%)	Group D (N%)	P Value
Bradycardia	00	00	07 (28%)	0.00044
Hypotension + Bradycardia	00	00	04 (16%)	0.01
Delayed recovery	00	04 (16%)	07 (28%)	0.01

Bradycardia & Hypotension was more significant in Group D when compared to Group MK & Group M.

DISCUSSION:

This randomized prospective study was conducted as per guidelines of Helsinki declaration.

Most of children were oriented but tranquil & cooperative [S1] after oral midazolam-ketamine combination & dexmedetomidine compared to oral midazolam alone. This findings was comparable to study by **Moreira et al** [18]

EMOTIONAL SCORE [S2] at the time of separation from parents children in group MK & group D were calm to asleep whereas those in midazolam group were anxious to tearful . This findings was comparable to study by **Banerjee B et al** [26]

At the time of face mask application [S3] children in group MK & group D were cooperative or can be easily reassured as against moderate fear in midazolam group & their emotional state was found to be unsatisfactory. This findings was comparable to study by **DL Warner et al** [11]

Intraoperative inhalational anaesthetic requirement (Sevoflurane/isoflurane) was found to be significantly less with dexmedetomidine & midazolam-ketamine combination compared to midazolam alone.

Intra operative bradycardia & hypotension was more significant in Group when compared to Group MK & Group M. At end of surgery recovery from anaesthesia ,wake up behavior [S4] was calm in group D, they can be easily calmed in group MK whereas children in group M were combative, restless or moderately agitated . This findings was comparable to study **Sultan Keles et al** [25]

Basleine HR, MAP, SpO2 were recorded and later compared for the maximum changes in the vital paramteres. Group D showed 16% decrease in HR & 3.69% decrease in the MAP. Group MK showed 0.95% decrease in HR & 0.94% decrease in MAP. Group M didn't show any variations from vital parameters Saturation was unaffected in all the 3 groups.

Time for maximum changes in vital paramteres of all 3 groups showed Group M peak time was earliest (33.28 min) followed by Group MK (35.28 min) and Group D (50.92 min) respectively. Group D subjects were more sedated in post anaesthesia recovery room compared to Group MK and Group M. Significant bradycardia (28%) & bradycardia with hypotension (16%) was seen with dexmedetomidine as compared to none in other two groups [25]. Post operative delayed recovery from anaesthesia side effect after the surgery was more in Group D (28%) compared to Group MK (16%) & Group M.

Oral midazolam in a dose of 0.5 mg/kg for premedication showed no hemodynamic changes with less postoperative complications. [23]

With oral midazolam 0.5mg/kg with ketamine 3mg/kg

combination their were minimal side effects and no delayed recovery when compared with midazolam alone and ketamine alone groups. [11]

CONCLUSION:

Oral Midazolam (0.2mg/kg) & Ketamine (2mg/kg) combination & oral Dexmedetomidine (0.5 mg/kg) both provide satisfactory sedation levels & offers significant ease of separation from parents with satisfactory mask acceptance in children <10 years compared to oral Midazolam alone.

Oral dexmedetomidine is associated with more haemodynamic side effects and post operative delayed recovery compared to oral Midazolam & Ketamine combination.

Oral Midazolam & Ketamine combination provides satisfactory sedation & anxiolysis with minimum side effects compared to oral midazolam or dexmedetomidine.

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