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Original Article

Comparison of Efficacy of Oral Clonidine and Oral Midazolam as Premedication in Children

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Abstract

Background: Various drugs have been used as premedication in pediatric anesthesia practice. Clonidine, α-2 agonist has entered anesthesia practice and its efficacy as an oral premedication drug is to be evaluated.

Aim: The aim of this study is to evaluate and compare the clinical effects of oral midazolam and oral clonidine as premedication in children with regard to drug acceptance, pre-operative sedation, anxiolysis, acceptance of mask for induction of anesthesia, intravenous (IV) cannulation, and recovery profile.

Materials and Methods: A prospective randomized, double-blind comparative study in children, ASA physical Status I in the age group of 1-10 years, posted for elective lower abdominal surgeries (duration 30-45 min) was done. Patients were randomized into two groups, Group C and Group M of 50 each. Patients in Group C received powdered clonidine tablet (100 μg) dissolved in 100 ml of water in the dose of 4 μg/kg, 45 min before surgery. Patients in Group M received preservative free parenteral form of midazolam in the strength of 5 mg/ml in the dose of 0.5 mg/kg 45 min before surgery.

Results: All the children accepted the drugs very well without spitting (or) vomiting. 90% of patients in clonidine group have sedation scores of 2 and 3 when compared with midazolam group, 54% respectively. Anxiety level on separation from parents was high with midazolam group. Level of mask acceptance, response to IV cannulation was better with clonidine group. The post-operative agitation is higher with midazolam group compared to clonidine group.

Conclusion: Clonidine is a better oral premedicant drug in children producing higher sedation, decreased anxiety, improved mask acceptance and response to IV cannulation and diminished post-operative agitation.

Key words: Anesthesia, Clonidine, Lower abdominal surgery, Midazolam, Pediatrics

INTRODUCTION

Premedication plays a pivotal role in general anesthesia. Oral medication is well accepted by children than another route of administration. They are given to allay anxiety, to produce amnesia, sedation, analgesia, to facilitate smooth induction and to reduce secretion. They should be easily administered, should be safe for the patient, should not prolong the recovery from anesthesia, and should not produce undue depression of cardiovascular, respiratory and central nervous systems.[1] Clonidine is a centrally acting α-2 agonist commonly known as an antihypertensive drug. Due to its sedative, hypnotic and analgesic properties it is used in anesthesia. Its main site of action is on the locus ceruleus in the upper brainstem in the floor of the fourth ventricle.[2] Midazolam in parenteral form, due to bitter taste is mixed with cola. It has anxiolytic, sedative, hypnotic, anticonvulsant, muscle relaxant, and anterograde amnesic effects. If the receptor occupancy of the midazolam is 20%, it causes anxiolysis, 30 to 50% it causes sedation, more than 60% it causes unconsciousness. It produces dose-related ventilatory depression, decreases arterial pressure by decreasing systemic vascular resistance.[3] Oral clonidine premedication reduces the minimum alveolar concentration of sevoflurane in children.[4]

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MATERIALS AND METHODS

This prospective randomized double-blind comparative study was conducted in Department of Anesthesiology, Government Rajaji Hospital, Madurai, Tamil Nadu, India. After approved by the institutional ethics committee, this study was conducted in 100 ASA I patients in the age group 1-10 years. Undergoing elective surgeries such as inguinal herniorrhaphy, hydrocele repair, urethroplasty, and orchidopexy patient. Written informed consent was obtained from parents. Exclusion criteria: ASA III and IV, patients on other sedative narcoleptic drugs, A detailed preanesthetic check-up was done on all patients and relevant hematological, biochemical and radiological investigations were carried out for all patients as per surgical requirements. The patients were randomly allocated into two groups. Group C patients received. Clonidine premedication 4 μg/kg and Group M received midazolam 0.5 mg/kg orally 45 min before surgery. All the children were given general anesthesia and vital signs were monitored throughout the surgery. All the children were anesthetized in the sequence of preoxygenation, induction with thiopentone and atropine, intubation by using succinylcholine and maintenance with oxygen, nitrous oxide, Fentanyl, and atracurium. Neuromuscular blockade was reversed at the end of the surgery with neostigmine and atropine. The parameters observed were degree of sedation, level of anxiety for separation from mother, mask acceptance for preoxygenation, reaction to intravenous (IV) cannulation, post-operative agitation, and any side effects associated with these drugs.

Table 1: Demographic comparison of study group

Criteria	Clonidine Group I	Midazolam Group II	*P* value
Age (Years)	5.040	4.72	0.580
Sex (M/F)	44/6	45/5	0.749
Weight (kg)	16.3	17.16	0.486

RESULTS

50 patients in each group in mean age of 5.040 in clonidine group and 4.72 in midazolam group. Mean weight of Group I is 16.3 kg and Group II is 17.16 kg (Table 1). Surgeries performed in both groups are comparable the $P = 0.692$ (Figure 1). The mean values for clonidine group in 2.0 ± 0.452 mean value for midazolam is 1.56 ± 0.541. The Student's *t*-test is highly significant ($P = 0.000$). Thus, clonidine has better sedation score than midazolam group. The anxiety level on separation from mother was compared (Table 2). Mean value for clonidine group = 3.38 ± 0.69 for midazolam group = 2.04 ± 0.8 Student's *t*-test is highly significant ($P = 0.000$). Clonidine has better score. The mask acceptance was compared in both the groups (Table 2). The mean/standard deviation value for clonidine group = 2.5/1.015 and for midazolam group = 1.52/0.646. Clonidine group has better mask acceptance. Reaction to IV cannulation was compared between the two groups (Table 2). The mean value for clonidine group = 2.46 ± 0.61 and for midazolam group = 1.58 ± 0.609 Student's *t*-test is highly significant ($P = 0.000$). Hence, the clonidine has better score than midazolam group. Post-operative status was compared between the two groups (Table 2). The mean value for clonidine group = 2.5 ± 0.71 and for midazolam group = 1.8 ± 0.54 Student's *t*-test is highly significant ($P = 0.000$).

DISCUSSION

The efficacy of oral midazolam as premedication in children has been evaluated in previous studies that dose of 0.5 mg/kg is adequate for premedication in children.[5]

Table 2: Distribution variables in study groups

Variables	Score	Grade	Clonidine Group I	Midazolam Group II
Intensive of sedation	1	Awake	5	23
	2	Drowsy	40	26
	3	Asleep	5	1
Reaction to drug administration	1	Crying	0	14
	2	Anxious	5	21
	3	Calm, uncooperative	21	14
	4	Calm, co operative/asleep	24	1
Anxiety level on acceptance of mask	1	Combative/crying	9	28
	2	Moderate fear of mask	17	18
	3	Cooperative on assurance	14	4
	4	Calm/cooperative	10	0
Reaction to intravenous cannulation	1	Crying	3	24
	2	Withdrawal of hand	21	23
	3	Grimace	26	3
Post-operative status	1	Agitated/crying	6	13
	2	Crying, consolable	12	34
	3	Calm/asleep	32	3

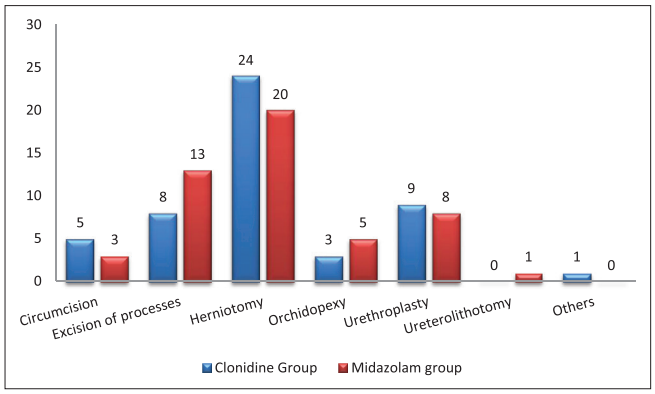

Figure 1: Distribution of surgeries in study group

Midazolam does not affect the recovery from anesthesia.[6] Oral midazolam has been well accepted by children than rectal midazolam.[7] The efficacy of oral clonidine in pediatric surgeries has been extensively studied. In our study, oral clonidine in the dose 4 μg/kg was given. Mikawa *et al.* compared the two doses of oral clonidine (2 and 4 μg) and concluded that 4 μg/kg is an effective dose. Hence, we decided to use 4 μg/kg of clonidine in our study.[8] McMillan *et al.* Compared different dose of midazolam (0.5, 0.75 and 1 μg/kg) and used the parental form of midazolam and concluded that 0.5 μg/kg is safe and effective. Hence, we decided to use parenteral form of 0.5 μg/kg of midazolam.[9] Nicole Almenrader *et al.* performed a prospective open study in 64 children who were randomly associated to receive either oral midazolam 0.5 μg/kg or oral clonidine 4 μg/kg as premedication. This study demonstrates the advantages of oral clonidine in both pre-operative period and during recovery compared with oral midazolam. Clonidine causes sedation similar to natural sleep where the patient can be easily aroused to perform the test. Clonidine acts by inhibition of spontaneous and evoked activity of central monoaminergic systems involved in modulation of sleep and cortical arousal.[10] In our study, 90% of clonidine group had sedation scores of 2 and 3 compared to 54% in midazolam group. Regarding anxiety level on separation from parents, 48% in clonidine group was calm and cooperative compared to 2% in midazolam group. Mask acceptance was 48% in clonidine group and only 8% in midazolam group. On comparing the response to IV cannulation, 48% of patients in midazolam group only 6% of patients in clonidine group are using. In our study, there was a trend towards an increased incidence of emergence agitation in midazolam group compared with clonidine group. In our study, the post-operative agitation is higher in midazolam group compared to clonidine group. 64% in clonidine group are calm/asleep while only 6% of patients in midazolam group are calm/asleep.

CONCLUSION

Oral clonidine can be used as a better premedicant drug to produce optimal sedation and emotional state than midazolam. The majority of the clonidine group children were calm and asleep during post-operative period compared to midazolam.

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