

EFFECT OF MIDAZOLAM AS ORAL PREMEDICATION IN CHILDREN

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Received:30/07/2018

Revised:22/09/2018

Accepted:28/09/2018

ABSTRACT

Background: Perioperatively in children, anaesthetic induction and adverse behavioral changes occurs, therefore to assess the efficacy of midazolam 0.5 mg/kg and triclofos sodium 100 mg/kg were compared as oral premedication in children undergoing elective surgery. **Material and Method:** A prospective controlled randomized study was undergone to assess the effectiveness of midazolam as oral premedication in children undergoing elective lower abdominal surgery. Patients were divided into oral midazolam group (Group MG 0.5 mg/kg 30 min before induction) and oral trichlophos sodium group (Group TG 100 mg/kg 60 min before induction). Each group consists of 20 children each in a total of 40 children. During induction of anesthesia level of sedation after premedication, behaviour at separation from parents and mask placement was evaluated. **Results:** After premedication, 90% of children of Group MG were adequately sedated (sedation score 4) compared to 55% in the Group TG. (P = 0.006) At the time of mask application 75% of children belonging to the Group MG were cooperative compared to 85% in the Group TG. (P = 0.164) **Conclusions:** Oral midazolam is a better sedative anxiolytic in children as compared to Trichlofos sodium. The midazolam can be recommended for use in children bearing in mind the more rapid onset, effectiveness, shorter duration of sedation, and less side effects of it.

Key words: Midazolam, premedication, Triclofos, sedation, behaviour

INTRODUCTION

During paediatric anesthesia perioperative anxiety and lack of cooperation is a common problem. (1) Sometimes, the pediatric anesthesiologist also very much concern about premedication in some children, to easy and smooth separation from their parents for relieving preoperative anxiety. (2, 3, 4) It avoids the postoperative behaviour problems like mood

disturbance and decreases the incidence of stress, eating disorders, nightmares, apathy, enuresis, and other forms of adverse postoperative behaviors. (5) Intravenous and intramuscular route is less favored by parents due to painful and frightening procedure as compared to oral form for premedication. (6, 7) Midazolam, can be used as premedication due to its

rapid onset and short duration of action, for controlling preoperative anxiety, rapid recovery, smooth induction of anesthesia and separation from parents with fewer unwanted side effects and produces hypnosis for 6-8 hours but further studies are required to evaluate. (8)

A stabilized form of Triclofos sodium, an older non-benzodiazepine, non-opiate, oral, sedative, hypnotic drug at a dose of 40-100 mg/kg 60 minute before induction, was used in children from years. (9) Therefore pre-operative planning should be made to minimize adverse psychological effects in children during peri-operative period. (10) The main aim to conduct the study was to assess the efficacy of midazolam 0.5 mg/kg and triclofos sodium 100 mg/kg as oral premedication for comparison individually in children undergoing elective surgery.

MATERIAL & METHODS

After obtaining approval from the Institutional Ethics Committee and taking written and informed consent from the parents of all children the study was started.

In this prospective controlled randomized trial 40 children of either gender were incorporated with 20 children in each group as per the guidelines of American society of anesthesiologist physical status I and II.

Inclusion criteria were children belong to 1-8 years of age underwent elective lower abdominal surgery.

Exclusion criteria include children less than 1 year of age with body weight more than 20 kg, children with difficult airway, CNS disorders, on drugs such as anticonvulsant, sedatives, antidepressants etc., mental retardation, or require additional sedative.

To assess the effectiveness of midazolam in children as oral premedication undergoing elective lower abdominal surgery, patients were divided into oral midazolam group (Group MG 0.5 mg/kg 30 min before induction) and oral trichlofos sodium group (Group TG 100 mg/kg 60 min before induction). Each group consists of 20 children each in a total of 40 children.

Oral premedication was prepared by mixing the specific drug to a fixed volume of fruit juice without

pulp (orange juice) to mask the bitter taste. In Group MG, placebo was given at 60 min before and preservative free injection form of midazolam was given at a dose of 0.5 mg/kg 30 min before induction of anaesthesia. In Group TG, syrup triclofos sodium was delivered at a dose of 100 mg/kg 60 min prior and placebo 30 min prior induction of anaesthesia. After giving oral premedication, the children were made to relax along with their parents in an undisturbed area with colourful toys, poster and bright objects in a room for diverting before starting of induction of anesthesia. The parameters assessed after premedication were level of sedation after premedication, behaviour at separation from parents and mask placement.

The level of sedation was measured by 5 point score (1 = asleep not readily arousable, 2 = asleep responds slowly to gentle stimulation, 3 = drowsy readily responds, 4 = awake calm and quiet, 5 = awake active). (11)

The behaviour at the time of separation from parents was evaluated when the child was separated from parents to shift to operating room using the separation score (1 = excellent-happily separated, 2 = good-separated without crying, 3 = fair-separated with crying, 4 = poor need for restraint). Score of ≤ 2 were considered successful while score >2 were considered unsuccessful. (11)

Behaviour during face mask placement was measured by cooperation score (1 = cooperative, 2 = mildly resistant, 3 = resists placement of mask). (11)

Ketamine 3 mg/kg IM with glycopyrrolate (10 μ g/kg) was administered if the separation was problematic. Inhalational induction with 33% oxygen in nitrous oxide and sevoflurane was made. Once the child was asleep an intravenous line and endotracheal intubation was made which was facilitated with vecuronium bromide 0.1 mg/kg. Anaesthesia was maintained with O₂ (33%), N₂O, isoflurane and vecuronium. Analgesia was provided with intravenous fentanyl (1-2 μ g/kg) and paracetamol suppository (20 mg/kg). The patients were transferred to postoperative recovery room and monitored. During the whole procedure respiratory rate, oxygen

saturation, blood pressure and pulse rate were monitored and recorded.

Different side-effects of oral premedication were observed during the entire procedure such as nausea, vomiting, airway obstruction, hiccups, anxiety, or slurring of speech.

Statistical analysis was performed using the SPSS 16.0 (Statistical Package for the Social Science for windows; Version 16.0, SPSS Inc., Chicago, USA). Results were analyzed using chi square test and P value. Significance level was set at $P < 0.05$.

RESULTS

The age and weight were comparable in both the groups. There was a male predominance in the triclofos group while female preponderance in midazolam group. After the premedication, at the level of sedation score 4, in the MG group about ninety present (18) of children were effectively sedated compared the Group TG in which fifty present (11) ($P = 0.002$). The differences in sedation between the two groups were found to be statistically significant with a $P = 0.006$ (Table 1). None of the children had oxygen saturation below 95%.

Table 1: Comparison of sedation scores post premedication

Sedation score	Group MG (n=20)	Percentage (%)	Group TG (n=20)	Percentage (%)	P
1	0	0 %	0	0 %	0.006
2	1	5 %	8	40 %	
3	1	5 %	1	5 %	
4	18	90 %	11	55 %	
5	0	0 %	0	0 %	

n = number of cases

On comparison of separation score, both groups had an equal number of children with successful separation (score 1 and 2 clubbed together as successful).

At the time of mask application 75% of children belonging to the Group MG were cooperative

compared to 85% in the Group TG. ($P = 0.164$) The difference found between the two groups was statistically not significant with a $P = 0.164$ (Table 2). No adverse effects initiated by premedication were seen in both groups.

Table 2: Comparison of co-operation score (face mask acceptance by the child)

Sedation score	Group MG (n=20)	Percentage (%)	Group TG (n=20)	Percentage (%)	P
1	15	75 %	17	85 %	0.164
2	5	25 %	3	15 %	
3	0	0 %	0	0 %	

n = number of cases

DISCUSSION

In pediatric day care anesthesia, premedication is widely used in children orally (12) due to easiness, acceptability and not cause any traumatic damage, has an important role as it minimizes the psychological stress to the family, make the child calm and quiet and has no adverse cardiac and pulmonary effects as it is a pre-requirement of anesthesia. It provides rapid recovery, early discharge from recovery room, minimizes amnesia during transport to operation theatre as well as smooth induction. (13) , Triclofos sodium is frequently applied for sedation in children for different purposes as preoperatively, diagnostic procedures and other possibly uncomfortable procedures (14) but in our study midazolam was the potential source recommended for premedication.

Excellent anxiolysis was obtained in 80-90% of children with oral midazolam 0.5 mg/ kg 30 min before induction of anesthesia at the time of separation as it is a safe and effective pre-medication. (15) More dose of Midazolam (>0.5 mg/ kg) does not provide additional effect but causes side effect such as blurred vision, dysphoria and loss of balance and head control. However mixing of drug with fruit juice causes pH changes which will affect absorption in the stomach, was not under consideration was a pitfall in the study. Intravenous preparation prepared for administration orally was more effective compared to readymade oral preparation.

Sedation score, separation anxiety and co-operation during placing face mask were assessed at the peak effect of the drug. Some investigator have assessed that in children receiving placebo/ oral midazolam anxiety score and behavior at induction was same but addition of chloral hydrate caused more calm and asleep behavior at the induction. (16)

In our study, sedation score (awake, calm and quiet) was better in Midazolam group as compared to Triclofos group which was statistically significant. In a similar study observation was similar when compared midazolam group with trimeprazine group. (17) The time interval from premedication to separation of children from parent was 30 – 40 min.

as seen in a similar study. (15) Therefore it was presumed that both the drugs i.e. midazolam and triclofos sodium are good agent for premedication in children but midazolam can be used potentially.

Oral midazolam having short half life ($t_{1/2}$) provide little sedation, fast anxiolysis and early separation from parents, is ideal drug for short/ day care procedures in children. Our study showed that midazolam is a better drug as compared to triclofos while other study in concordance with other, showed midazolam is better as compared to triclofos or promethazine for anxiolysis and sedation. (18) In contrast to our study one study found triclofos to be better (19) while the showed that both are equally effective. (20) No side effect was found in our study.

Therefore oral midazolam is a better drug for premedication in children as it provides better sedation, less separation anxiety, improved quality of induction, no adverse effect and most importantly safe in children.

CONCLUSION

Oral midazolam is superior to oral triclofos sodium in relation to sedation, anxiolytic and separation from parents in paediatric population. The midazolam can be recommended for use in children bearing in mind the more rapid onset, effectiveness, shorter duration of sedation, and less side effects of it. Thus oral midazolam is a valuable additive to the anaesthesiologists' armamentarium in pediatric patients as premedication.

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How to cite this article: Kapoor J., Hussain A., Effect of midazolam as oral premedication in children, *Int.J.Med.Sci.Educ* 2018;5(4):573-577