

Oral Midazolam for Premedication in Children Undergoing Various Elective Surgical procedures

E-mail – gauripanjabi@yahoo.co.in

1st Author: Dr Panjabi Gauri M., M.D., D.A., Senior Assistant professor.

2nd Author: Dr Pandya Charu J., M.D. Associate Professor

Department Of anesthesia, Smt SCL General Hospital, Smt. NHL Municipal Medical College, Ahmedabad.

Corresponding Author:

Phone numbers (91) 9377244003

E-mail address gauripanjabi@yahoo.co.in

Abstract

Background; This study was done to compare oral midazolam 0.5 mg/kg versus 0.75 mg/kg as a premedication in children with regard to sedation and anxiolysis.

Material and Methods: Study was done in 90 children (ASA I & II), aged 4 to 8 years who were scheduled for various elective surgeries. Patients were randomly divided into three groups (No=30 each). Group A was control and Group B and C received an oral administration of 0.5mg/kg, 0.75mg/kg respectively, of injectable midazolam (Preservative free) mixed with orange syrup, 45 minutes before surgery.

Results: The acceptance of drug was very good. All children in Group A (without premedication) were extremely anxious and crying or thrashing while in Group B and C, 80% and 90% patients respectively were calm and sleepy at the time of separation from parents, on arrival at OR and at the time of venipuncture and induction of anesthesia. Midazolam did not impact the overall recovery time in children.

Conclusion: A dose of 0.75mg/kg of injectable midazolam given orally as premedication for children undergoing various elective surgical procedures offers effective sedation and better emotional control facilitating better separation and cooperation during venipuncture and induction of anesthesia.

Keywords: Oral midazolam, Children, Premedication.

“Oral Midazolam for Premedication in Children Undergoing Various Elective Surgical procedures.”

Introduction:

Surgical intervention causes Psycho-trauma to children as well as parents. Most children are fearful, anxious and uncooperative.

A multimodal approach consisting sedative drugs, parental presence, play therapy, familiar environment and effective pain therapy is necessary to reduce pre-operative anxiety.

Premedication is best given by an oral route in children as children exhibit an exaggerated psychological response to a needle, and it is easier to give medication

orally than to use nasal or rectal routes^[1]. At physiological PH, it becomes highly lipophilic which causes rapid absorption of midazolam from GIT.

Midazolam has rapid onset and relatively short duration of action. It has several beneficial effects such as sedation, anxiolysis and amnesia. Midazolam in children decreases preoperative anxiety and facilitate separation from parents with fewer unwanted side effects.^[2] Doses of injectable midazolam mixed with orange syrup were used in this study as an oral premedication.

The objectives of this study were to assess the efficacy and safety of oral injectable midazolam (Preservative free) in different doses and to determine the optimal dose as a premedication in children undergoing Surgery.

Material and methods:

The study was done in 90 children (ASA I & II), aged 4 to 8 years within normal range of weight who were scheduled for various elective surgeries. Preoperative assessment was done and written informed consent was obtained from parents. Children were excluded from the study if they had any mental retardation or physical disabilities, were under treatment with sedatives or anticonvulsants, or if their parents refused to allow them to participate.

Patients were randomly divided into three groups (No=30 each). Group A was control group and Group B and C received an oral administration of 0.5mg/kg, 0.75mg/kg respectively, of injectable midazolam 5mg/ml preparation (Preservative free) mixed with orange syrup, 45 minutes before surgery.

Acceptance of drug by patient and incidence of vomiting was noted. Time of onset of action of drug noted and after 45min, patients were separated from parents and shifted to O.T. Degree of sedation / anxiolysis noted as per sedation and anxiolysis scores when the child was first seen in the operating room (OR). Patient's heart rate, blood pressure, respiratory rate, oxygen saturation (SaO₂), reaction to separation from parents, and sedation scores including ease of venipuncture and induction of anesthesia were noted.

All children received a standardized GA by the same anesthesiologist. Induction was done by Inj Pentothal 6-7mg/kg, Inj Glycopyrolate 0.004 mg/kg and Inj Scoline 1.5-2mg/kg. Oral Intubation was done by appropriate size of endotracheal tube. Maintenance was done with O₂, N₂o and Sevoflurane. Patient Ventilation was assisted to maintain normocapnia (EtCO₂ 32–38mmHg).

Patients' electrocardiogram, noninvasive arterial blood pressure, pulse oximetry, capnography were monitored as part of standard GA procedure. Analgesia was given by IV Inj. Diclofenac. Tracheal extubation was performed when normoventilation was achieved and the patients regained gag or cough reflex. Recovery time to painful stimulation and Verbal command noted.

Observation and Results:

All groups were comparable with respect to ASA status, gender, age, weight, and duration of anesthesia.

Acceptance of the medication was defined as swallowing without immediate vomiting. The acceptance of drug was very good and similar across the groups. All children liked the taste very well and none of the patients in any of the groups vomited soon after swallowing the premedication.

The degree of sedation and anxiolysis was noted when the child was first seen in the operating room (OR) as given in Table 1. Score 2 or less was considered as satisfactory sedation and anxiolysis.

Table 1 Sedation and Anxiolysis scores

| Score | Sedation | Score | Anxiolysis |
|-------|----------------------|-------|--------------|
| 1 | Asleep | 1 | Calm |
| 2 | Drowsy – less active | 2 | Apprehensive |
| 3 | Awake | 3 | Crying |
| 4 | Agitated | 4 | Thrashing |

Table 2 : Satisfactory sedation and Anxiolysis (Percentage of patients)

| Time(Min) | Satisfactory sedation | | | Satisfactory Anxiolysis | | |
|-----------|-----------------------|-----|-----|-------------------------|-----|-----|
| | A | B | C | A | B | C |
| 15 | 0% | 10% | 20% | 0% | 15% | 25% |
| 30 | 0% | 50% | 40% | 0% | 55% | 50% |
| 45 | 0% | 80% | 90% | 0% | 80% | 90% |

Satisfactory sedation and anxiolysis was noted in 80% and 90% of patients in Group B and C respectively after 45 min of premedication.

Time taken for score to be 2 or less was considered as onset of action of drug. The onset of action was 20±5 and 18±5 minutes in Group B and C respectively.

Reaction to Separation from Parents was noted from sedation and anxiolysis scores. All children in Group A (without premedication) were extremely anxious and crying or thrashing while in Group B and C, 80% and 90% patients respectively were calm and sleepy at the time of separation from parents, on arrival at OR and at the time of venipuncture and induction of anesthesia.

This difference was statistically significant ($P < 0.05$)

Vital parameters

During the premedication time, none of the patients in Group B and C had an incidence of bradycardia (heart rate $< 20\%$ baseline), hypotension (mean blood pressure $< 20\%$ of baseline) or desaturation episodes (O_2 saturation $< 95\%$) while Group A patients shows tachycardia and rise in B.P.

Table 3 : Recovery Time

| Recovery time(Min) | A | B | C |
|-------------------------------|-----------|-----------|-----------|
| Responding to painful stimuli | 5 ± 2 | 5 ± 2 | 6 ± 3 |
| Following verbal command | 6 ± 5 | 8 ± 2 | 9 ± 5 |

The recovery time was short in both the Groups B and C. Patients were responding to painful stimuli within 5-6 minutes and following verbal commands within 8-10 minutes in Group B and C. Midazolam dose did not impact the overall recovery time in children.

Statistical Analysis

Demographic variables and duration of anesthesia were compared using ANOVAs test, whereas the results were compared within groups using Chi Square analysis. A P-value of < 0.05 was considered statistically significant.

Discussion

The population of children has special characteristics; they are extremely uncooperative, fearful, anxious, and physically resistant. Midazolam is the most commonly used drug for premedication and is used in greater than 90% of surgical cases involving premedication in the United States ^[3].

The combination of the sedative and anxiolytic characteristics is believed to create a calming effect which makes children less anxious when they are separated from their parents and during induction of anesthesia. Finley et al. ^[4] showed that a midazolam decreases anxiety which was more pronounced for children with higher baseline levels of anxiety.

Oral midazolam was found to be superior when compared with other commonly used premedications. Oral midazolam was reported to give a more predictable and effective sedation than oral diazepam^[5]. The problem with injectable midazolam is that it is very bitter. In this study we used orange syrup as a carrier. We found that it is easily available and convenient to use.

Mishra et al.^[6] mixed IV midazolam with honey which was well accepted by most of their subjects. However, since this mixture is not transparent and not a liquid, there is a question if its use violates the fasting protocol for children^[6].

Feld et al.^[7] also reported a superior anxiolysis 30 minutes after a 0.75mg/kg dose of oral midazolam as compared to 0.25mg/kg and 0.5mg/kg doses or placebo. Clinical sedative effects are seen within 5 to 10 minutes of oral midazolam administration; the peak effect is achieved in 20 to 30 minutes. Similar results were seen even when separation time was set to 45 minutes.

Cox et al.^[8] reviewed 30 papers regarding the use of oral midazolam for premedication and concluded that it is effective in reducing both separation and induction anxiety in children, with minimal effect on recovery times. We did not observe any significant delay in recovery time after 0.5 and 0.75mg/kg doses.

Preoperative oral midazolam has proved effective in treating preoperative anxiety. In this study, injectable midazolam given orally as premedication was acceptable, effective, and safe. The onset of action was 20±5 and 18±5 minutes in Group B and C respectively. Satisfactory sedation and anxiolysis was noted in 80% and 90% of patients in Group B and C respectively after 45 min after premedication. All children in Group A (without premedication) were extremely anxious and crying or thrashing while in Group B and C, 80% and 90% patients respectively were calm and sleepy at the time of separation from parents, on arrival at OR and at the time of venipuncture and induction of anesthesia. Midazolam did not impact the overall recovery time in children.

We concluded that oral Midazolam is well suited, acceptable, effective, and safe as premedication in pediatric patients and it did not impact the overall recovery times in children. A dose of 0.75mg/kg of injectable midazolam given orally as premedication for children undergoing various elective surgeries offers effective sedation and better emotional control facilitating better separation and co-operation during venipuncture and induction of anesthesia.

References:

- 1) K. Connors and T. E. Terndrup, "Nasal vs oral midazolam for sedation," *Annals of Emergency Medicine*, vol. 24, no. 6, pp. 1074–1079, 1994. View at Publisher · View at Google Scholar
- 2) J. W. Dundee, N. J. Halliday, K. W. Harper, and R. N. Brogden, "Midazolam. A review of its pharmacological properties and therapeutic use," *Drugs*, vol. 28, no. 6, pp. 519–543, 1984.
- 3) Z. N. Kain, A. A. Caldwell-Andrews, D. M. Krivutza, M. E. Weinberg, S.-M. Wang, and D. Gaal, "Trends in the practice of parental presence during induction of anesthesia and the use of preoperative sedative premedication in the United States, 1995–2002: results of a follow-up national survey," *Anesthesia and Analgesia*, vol. 98, no. 5, pp. 1252–1259, 2004. View at Publisher · View at Google Scholar
- 4) G. A. Finley, S. H. Stewart, S. Buffett-Jerrott, K. D. Wright, and D. Millington, "High levels of impulsivity may contraindicate midazolam premedication in children," *Canadian Journal of Anesthesia*, vol. 53, no. 1, pp. 73–78, 2006.
- 5) C. A. Pywell, Y.-J. Hung, and J. Nagelhout, "Oral midazolam versus meperidine, atropine, and diazepam: a comparison of premedicants in pediatric outpatients," *Journal of the American Association of Nurse Anesthetists*, vol. 63, no. 2, pp. 124–130, 1995.
- 6) L. D. Mishra, G. K. Sinha, P. Bhaskar Rao, V. Sharma, K. Satya, and R. Gairola, "Injectable midazolam as oral premedicant in pediatric neurosurgery," *Journal of Neurosurgical Anesthesiology*, vol. 17, no. 4, pp. 193–198, 2005. View at Publisher · View at Google Scholar
- 7) L. H. Feld, J. B. Negus, and P. F. White, "Oral midazolam preanesthetic medication in pediatric outpatients," *Anesthesiology*, vol. 73, no. 5, pp. 831–834, 1990.
- 8) R. G. Cox, U. Nemish, A. Ewen, and M.-J. Crowe, "Evidence-based clinical update: does premedication with oral midazolam lead to improved behavioural outcomes in children," *Canadian Journal of Anesthesia*, vol. 53, no. 12, pp. 1213–1219, 2006.