A comparative evaluation of oral midazolam with other sedatives as premedication in pediatric dentistry

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The purpose of present study was to evaluate the safety and efficacy of orally administered midazolam in children as a sedative agent and to compare it with two other older agents, triclofos and promethazine. The study was conducted on ninety child patients requiring some short dental procedure. All the patients were with a good physical status (ASA-I). The ages ranged between 3 and 9 years. The patients were randomized into three study groups: Group 1, midazolam, Group II, triclofos and Group III, promethazine, on the basis of the drugs to be administered. After administration of drugs in each group, the effects were evaluated in terms of onset of action, sedative effect, ease of treatment completion, recovery time and postoperative amnesia. Midazolam was found to be the best drug among the three to produce conscious sedation in children.
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INTRODUCTION

Pain and fear are two most dreaded enemies of human psyche and the fear of dental treatment is one of the worst of fears among the common fears experienced by human beings. Due to pain and fear associated with dentistry, a number of patients try to avoid dental treatment until the pathology becomes very severe and no home remedies are effective. Thus, one of the primary duties of the dentist is to allay the anxiety and fear of the patient visiting the dental clinic. This duty becomes more important for the pediatric dental practitioner, because the children are in a very impressionable age. Certain retrospective studies have attributed the adult dental fear to unpleasant treatment received during early childhood.[1,2]

The majority of pediatric dental patients can be managed by conventional approach of behavioral management. But still, there is a fair number of children for whom this psychological approach alone is not sufficient. For these children, the role of pharmacological intervention becomes very important.

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In the past a number of sedative agents have been used to achieve conscious sedation by pediatric dental practitioners, but none of them as a sole agent proved to be an ideal sedative especially when administered through oral route. Combined drug therapy has been in much use to sedate the child patients. However, polypharmacy must be avoided due to known hazards in the form of adverse reactions.

Midazolam is a newer, short acting, water-soluble benzodiazepine having sedative/hypnotic, anxiolytic and amnesiac properties, which make it suitable for premedication both in adults and children. This drug can be administered through most of the routes available for drug administration. Many of the workers are continuously working on this drug, but still there is paucity of literature on the oral use of this drug. So the present study was designed to evaluate the efficacy and safety of oral midazolam as premedication in child patients and to compare it with two other commonly used oral sedatives, namely, triclofos and promethazine.

Triclofos is a chloral derivative and has proved to be safe and effective sedative in children.[1,4] Promethazine is a phenothiazine derivative, which has a dose-response curve, so it can be used over a wide range of dosages. It has been used alone or in combination by various workers.[5-7]

MATERIALS AND METHODS

Ninety child patients, aged between 3 and 9 years were enrolled in this double blind study. All the patients were with ASA-I health status and requiring short dental procedures like extraction, restorations, and endodontic treatment with or without local anesthesia.

Patients were randomized in to three groups of thirty each and labeled as Group I, II and III. Different sedative agents were allotted to the three groups as:

Group I	Midazolam: oral dose of 0.5mg/kg body weight.
Group II	Triclofos: oral dose of 70mg/kg body weight.
Group III	Promethazine: oral dose of 1.2mg/kg body weight.

The patients reporting to the Pedodontic Clinic were examined and those requiring extractions, restorations and endodontic treatment were selected. The physical status was assessed and only those patients with ASA Class-I were chosen. Informed consent was obtained from the parents. The weight was recorded and dose of the drug to be given was calculated. Arterial BP, pulse rate and respiratory rate were recorded before the administration of drug.

As midazolam is very bitter in taste, it cannot be given as such orally to a child patient. To make it palatable, it was mixed with a flavored, sweet fruit juice and the child was asked to drink it.

In this form it was reasonably accepted by most of the children. As this study was double blind, the other two agents were also administered after mixing in the same juice in order to maintain uniformity and to eliminate the possibility of any error due to distinction. The time of drug administration was noted.

After the administration of the drug, patients were placed to a calm and comfortable room. There they were continuously under observation by the operator. When sedative effects started to appear, the time of onset was noted.

Arterial blood pressure, pulse rate and respiratory rate were recorded at definite intervals. Any change in them was noted.

The degree of sedation was rated on a rating scale consisting of scores ranging from 1 to 7. Score 1 was asleep and 7 was excited.

The ease of treatment completion was rated as 1, 2 and 3, when it was excellent, difficult and impossible respectively.

The time of recovery was recorded when patient became able to sit and stand alone or with minimal assistance.

The anterograde amnesia was assessed after 24 hours by a recall questionnaire, which included the questions about events, which took place after the administration of sedative. The quality of anterograde amnesia was rated as good, fair or poor.

RESULTS

The three treatment groups (I, II, III) were comparable with respect to patient numbers, age, sex, body weight and health status. The various parameters under consideration were observed, recorded and results were summarized as follows:

Onset of sedative action

The time of onset of sedative action was shortest for group I (midazolam group) and longest for group III (promethazine group) with group II (triclofos group) lying in between.

The difference of time of onset was highly significant between groups I and II ($p<0.001$) and groups I and III ($p<0.001$), and the difference between groups II and III was also significant ($p<0.05$) (Figure 1).

Sedation Scores	Behavioral Signs	Classification
1.	Sleeping, no response to patting the Shoulder	Asleep
2.	Sleeping, no response to calling by name 2 or 3 times. Responds to patting on the shoulder	Asleep
3.	Eyes closed, dull reaction, Responds to verbal stimulus as above.	Drowsy
4.	Eyes open and closed by turns, dull reaction. Responds to verbal stimulus	Sedated
5.	Eyes open dull reaction. Responds to verbal stimulus.	Sedated
6.	Normal reaction	Normal
7.	Irritable with body movement	Excited
8.	Highly irritable with considerable body movement	Excited

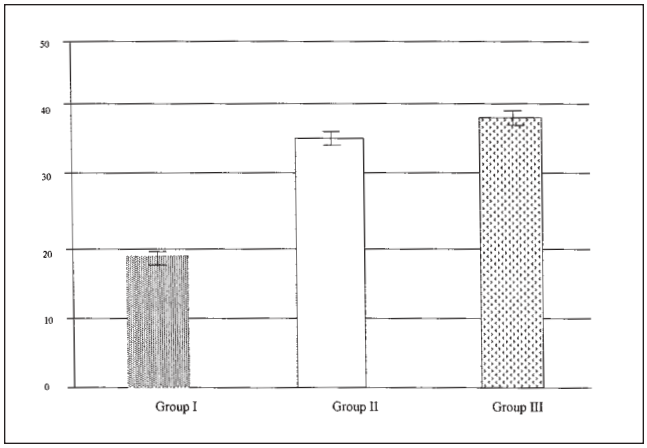

Figure 1. Mean Time of Onset in Different Groups

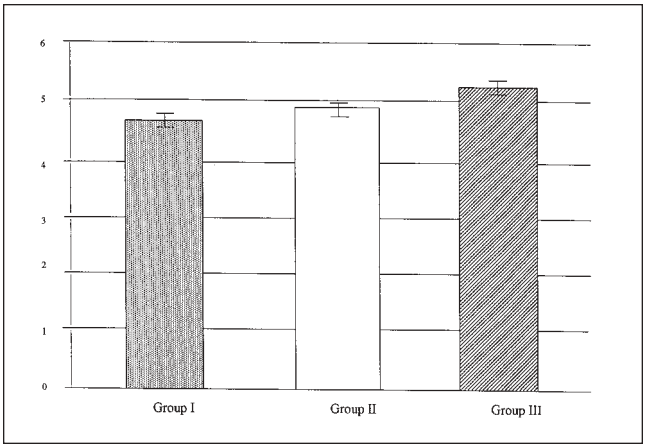

Figure 2. Mean Sedative Scores in Different Groups

Sedative scores

The sedative scores were best for group I followed by groups II and III. The variation of sedative scores was highly significant between groups I and III ($p<0.001$) and significant between groups II and III ($p<0.05$) (Figure 2).

Ease of treatment completion

The treatment was most convenient for group I followed by groups II and group III. The difficulty in treatment was significantly more for group III in comparison to group I ($p<0.01$) and group II ($p<0.05$).

Recovery time

The recovery from sedation was most rapid for group I and slowest for group III. The variation in recovery time between both groups I and II and groups I and III were highly significant ($p<0.00l$) (Figure 3).

Anterograde amnesia

Anterograde amnesia was much more pronounced for patients of group I in comparison to groups II and Ill. Seventy percent patients of group I showed good amnesiac effect in comparison to 30% patients of group II and only 10% patients of group III.

Change in vitals

All the three drugs were well tolerated by the patients. There was no significant change in blood pressure, pulse rate and respiratory rate in any of the groups.

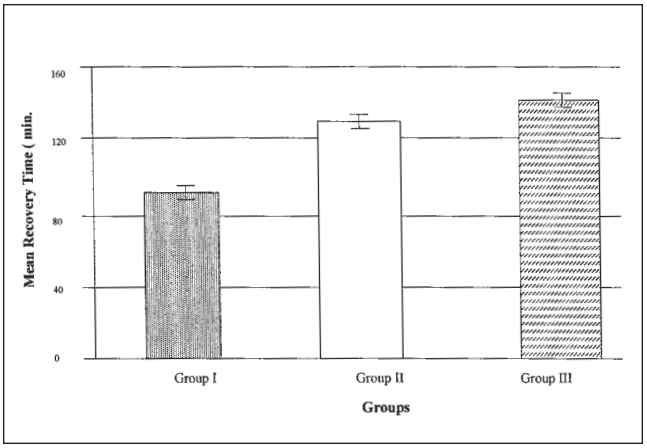

Figure 3. Mean Recovery Time in Different Groups

DISCUSSION

To perform dentistry at chair side, the state of conscious sedation may be desired in a number of cases, because it reduces the fear of pain and anxiety associated with dental procedures and makes patient cooperative for future dental appointments.

The state of conscious sedation can be achieved through variety of pharmacological agents adminis-

Table I. Table showing mean values of time of onset, time of recovery and sedative scores

	Group I	Group II	Group III
Mean time of onset ± S.E. (mm)	19.12 ± 0.68	35.22 ± 0.77	37.93 ± 0.74
Mean recovery time ± S.E. (mm)	92.88 ± 2.53	131.11 ± 2.31	142.67 ± 2.58
Mean sedative scores ± S.E.	4.70 ± 0.12	4.93 ± 0.11	5.27 ± 0.09

tered through various routes, but the oral route is usually the most preferred one for pediatric dental patients. Combination of drugs have been in practice for a long time, but polypharmacy has its own hazards. So it was decided in the present study to give all the drugs orally as sole agent.

A few workers have already worked on oral midazolam as an agent to produce conscious sedation. They found it safe and effective[8,9] with rapid onset of sedation.[10,11] But still there is not much literature available on the oral use of midazolam. So, in the present study it was compared with two other oral sedatives, triclofos and promethazine in an attempt to find out an appropriate agent for conscious sedation.

Regarding the duration of action, it was seen in the present study that the duration of sedative effect of midazolam was significantly shorter as compared to that of triclofos and promethazine. However, this time period was sufficient for the dentist to perform the required dental procedures.

In a few earlier studies the lower doses of midazolam (0.2 mg/kg and 0.3 mg/kg) were not found to effective.[12,13] The results of present study showed that oral midazolam administration at a recommended dose of 0.5 mg/kg body weight is a suitable premedication for children in ASA class 1. Significantly better sedative and anterograde amnesiac effects were achieved with midazolam than triclofos (70 mg/kg) or promethazine (1.2 mg/kg). The high grade of amnesia with midazolam, was also observed by other workers.[14,15]

From the results of present study, it can be stated that oral midazolam, at the dose used in the study reliably and rapidly produces an appropriate degree of sedation in child patients.

A close observation on all the patients was kept throughout the post drug administration period, because adverse reactions are reported by many investigators with the drug used in the present study.[16-20] However, in present study the alteration in pulse rate, blood pressure and respiratory rate were within physiological limits and no adverse reactions were observed in any patient in all the three groups.

CONCLUSION

In conclusion oral midazolam in a dose of 0.5mg/kg of body weight is a suitable premedication for child patients during short dental procedures of ASA class 1. It may be preferred over triclofos and promethazine owing to the rapid and better sedative effect and good quality of post-operative amnesia.

REFERENCES

1. Stouthard MBA, Hoogstratin, J. Prevalence of dental anxiety in Netherlands. Comm Dent Oral Edpidemiol 18: 139–42, 1990.
2. Milgrom P, Mane L, King B. Origins of childhood dental fear. Belzav Res Fiber 33: 313–9, 1995
3. Lindgren L, Saarnivaara L, Hiinberg JJ. Comparison of oral triclofos, diazepam and flunitrazepam as premedicants in childrden undergoing otolaryngological surgery. Brit J Anaesth 52: 283–90, 1980.
4. Jackson EA, Rabbette PS, Dezateux C, Hatch DJ, Stocks J. The effect of triclofos sodium on respiratory rate, oxygen saturation and heart rate in infants and young children. Pediatric Pulmonology 10: 40–5, 1991.
5. Solomon AL, Lowell RJ. Promethazine as an adjunct to the treatment of the problem dental patient. NY State Dent 24: 348–353, 1958.
6. Stuebner EA, Sandove MS. The use of promethazine for premedication. J Am Dent Soc Anesth 5: 12–18, 1958.
7. Weiss WA, Mc Cree JP, Jr. Promethazine as adjunct to preoperative medication. Ann Surg 144: 861–864, 1956.
8. Roelofse JA, Loun IR, Roelofse PG. A double blind randomized comparison of oral triineprazine-methadone and ketamine-midazolam for sedation of paediatric dental patients for oral surgical procedures. Anaesthesia Progress 45: 3–11, 1998.
9. Silver T, Wilson C, Webb M. Evaluation of two dosages of oral midazolam as a conscious sedation for physically and neurologically compromised paediatric dental patients. Pediatr Dent 16: 350–9, 1994.
10. Gallardo F, Cornejo G, Bode R. Oral midazolam as premedication for the apprehensive child before dental treatment. J Clin Pediatr Dent 18:123–7, 1994.
11. Levine MF, Spahr-Schopfer TA, Hartley F, Derman J, Mac Pherson R. Oral midazolam premedication in children: the minimum time interval for separation from parents. Canadian J Anaesthesia 40: 726–9, 1993.
12. Davies FC, Waters M. Oral midazolam for conscious sedation of children during minor procedures. J Accident Emerg Med 15: 244–8, 1998.
13. Talksdorf W, Bremerich D, Nordmeyer U. Midazolam for premedication of infants: A comparison of the effect between oral and rectal administration. Anaesthesie Intensivtherapie Notfallmedizin 24: 355–61, 1989.
14. Balakrishnan K, Panchal ID, Talwalkar L, Kamath SK, Suri YV, Jalali RK, Singh B, Gowrishankar R, Bagati A. A comparative evaluation of midazolam and diazepam as preoperative medication. Ind J Ana 42: 33, 1998.
15. Zuora KL. Midazolam in emergency surgery - a pilot study on adult Nigerian patients. West African J Med 13: 70–2, 1994.
16. Malinovsky JM, Populaire C, Cozain A, Lepage JY, Lejus C, Pinand M. Premedication with midazolam in children. Effect of intranasal, rectal and oral routes on plasma midazolam concentrations. Anaesthesia 50: 35–4, 1995.
17. Shane SA, Fuchs SM, Khine H. Efficacy of rectal midazolam for the sedation of preschool children undergoing laceration repair. Annals Emergency Med 24: 1065–73, 1994.
18. Van Eugelen BG, Gimbrere JS, Booy IH. Benzodiazepine withdrawal reactions in two children following discontinuation of sedation with midazolam. Annals Pharmacotheraphy 27: 579–81, 1993.
19. Orwin JM, Schroeder JD. Safety of choral. Br Med J 3: 187, 1968.
20. Chan-Tack, KM. Nueroleptic malignant syndrome due to promethazine. S Med J 92: 1017–8, 1999.