Efficacy of nitrous oxide-oxygen inhalation versus oral midazolam-promethazine as sedative agents in pediatric patients: a comparative study

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Background
Managing difficult and uncooperative pediatric dental patients is a challenging task. Conscious sedation has been propagated as a pharmacological means for handling such situations.
Objective
To evaluate the effects of sedation using nitrous oxide-oxygen inhalation versus oral midazolam-promethazine in pediatric patients.
Patients and methods
A total of 100 pediatric patients were selected and divided into two equal categories: group 1 (midazolam-promethazine) and group 2 (N_2O-O_2). Ethical committee approval was obtained, and patients were assessed. Data collected were analyzed using an unpaired *t* test.
Results
Duration of sedation was found to be statistically significant, and a higher duration was found for group 1. No significant differences were noted in the behavior rating scale with either of the combinations and in pulse oximeter readings.
Conclusion
Midazolam/promethazine is better in inducing longer sedation than N_2O/O_2.

Keywords:
children, conscious sedation, midazolam, nitrous oxide, oxygen, promethazine

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Introduction

Managing pediatric patients for a variety of dental treatment procedures while within a dental setup is a highly challenging task. Behavioral issues that are most commonly noted among children may be because of reasons such as lack or incomplete reasoning, limited coping capability, and anxiety or fear [1]. Conscious sedation is an effective and documented therapeutic adjunctive approach that can be of assistance in these situations.

Conscious sedation has been defined as 'a controlled state of low level of consciousness that helps in conserving various protective as well as unconditional reflexes and permits continuation of functioning of patient's airway and at the same time allowing a patient for communicating appropriately using both physical and verbal means' [2].

Conscious sedation is a technique that can be used for allaying anxiety, uneasiness, and feeling of fear, and it minimizes any uncooperative child's attempts against treatment [3,4].

Drugs used for sedation may be administered via different routes, for example, oral, inhalational, intramuscular, subcutaneous, and intravenous routes [5].

A wide variety of agents are available for conscious sedation in dental clinical procedures. Midazolam is a water-soluble benzodiazepine drug that has nonirritating nature and is anxiolytic, causes sedation and hypnosis, and also has amnesia-inducing properties [6].

It has a short-acting time of activity [7,8]. Hence, it is used for performing procedures that require a very short time [9–12]. Additionally, midazolam has been shown to upregulate anterograde amnesia when used preoperatively in young children [13–15].

It has been hypothesized that combining anesthetic agents for achieving conscious sedation may help in preserving sedation efficiency while at the same time, lowering the adverse effects. This is mainly because of

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the fact that most potentially deleterious effects rely on the dose used for drug measurement and whenever they are used in combination, subsequent, reduction in the dose of drugs used benefits by reduction of adverse effects [16].

Nitrous oxide (NO), an anesthetic agent, is used primarily for achieving preoperative sedation and for maintaining anesthesia as an adjunctive tool to intravenously administer anesthetic drugs in dental settings [17].

NO is a safe, easy-to-use, and effective agent with the least adverse effects during emergency-performed dental treatment of uncooperative pediatric patients. It is aided by the use of specifically designed vaporizers that are capable of transforming liquid into a gaseous state. This agent decreases or when administered at high doses completely eradicates the consciousness of a particular patient [18].

Conscious sedation is a highly useful tool for adding to the armamentarium that is used for treating teeth diagnosed with symptomatic irreversible pulpitis [19].

Nitrous oxide may be administered along with oxygen among patients with any behavior-related disorders, among mentally retarded, or in patients who experience excessive anxiety regarding dental treatment. The use of nitrous oxide as an inhalational sedative agent has been shown to cause improvement in patient behavior during the treatment process [20,21].

Hence, by keeping into consideration various pros and cons of various sedative agents, this study was planned to compare and evaluate the effects of sedation using nitrous oxide-oxygen inhalation versus oral midazolam-promethazine in pediatric age group patients.

Patients and methods

This prospective study was conducted after obtaining approval from the institute's Ethical Committee (IEC/22/234/MM). Inclusion criteria were (a) an informed written parent consent form, (b) children with ASA status I, (c) age range from 7 to 12 years, (d) bodyweight: 21–33 kg, (e) children indicated for extraction of primary teeth, and (f) definite negative behavior as per Frankl scale [22].

Exclusion criteria for the study were (a) if a patient refused the use of a nasal hood for inhalational anesthesia; (b) children who had not received anesthetist clearance for sedation procedure; (c) any previously known allergies and/or hypersensitive reactions toward any of the drugs that were used throughout in this study; (d) children who were given analgesic agents 6 h before performing sedation; and (e) children who had been recently administered with medications like erythromycin and/or anticonvulsive agents, which may be interfering with midazolam pharmacokinetics.

Levels of sedation were assessed and grading was done as per the Observer's Assessment of Alertness/Sedation Scale [23].

A total of 100 children were included in the study who were then divided equally into two groups: (a) group 1 (oral midazolam with promethazine) patients received a combination of 0.25 mg/kg of midazolam along with 3 mg/kg of promethazine and (b) group 2 patients received nitrous oxide-oxygen.

Procedure for obtaining sedation

Selected pediatric patients were asked to fast 2 h before sedation. Patients have not been prescribed any other medications. All patients were then monitored by a pulse oximeter.

(1) Group 1: drug vials of 5 ml of midazolam and 10 ml of ketamine were procured for this study. Drug dosage was determined on the basis of the weight of patient. The drug was then taken out from the respective vials by using a 27-G disposable syringe. Both drugs after drawing were then transferred within disposable cups containing a flavored fruit juice.

Timing of administered drug was then noted, and the patient was then observed by an anesthetist. At least a waiting period of 30 min was then provided between administering the medicine and separation from parents.

(1) Signs for the onset of sedation, which included a dazed eye look, delayed movement of eyes, lack of coordination of muscles, slurring of speech, were analyzed. The efficacy of the sedative agent was then assessed by making use of Houpt's sedation scale. All patients were discharged on achieving a score of ten according to Aldrete Recovery Scoring criteria (which involved physical activity, respiration rate, rate of circulation, and conscious levels). The operating clinician was in constant contact with the children's parents for 24 h for the determination of adverse effects such

as vomiting, changes in sleep pattern, and alertness.

Sedation using nitrous oxide-oxygen inhalation: patients were sedated in a standardized procedure using a nasal hood for inhalation of 40% nitrous oxide in oxygen, and inhalation was then continued using 40–60% nitrous oxide in oxygen with the high gas flow at a rate of 5 l/min.

Toward the end of the tooth extraction procedure, discontinuation of nitrous oxide (N_2O) inhalation was done, and 100 % inhalation using O_2 was given for 2 min. Nasal hoods, as well as monitoring devices, were removed when the patient exhibited alert behavior, and the values of heart rate and SpO_2 scores were found to be within the normal range. However, in case of any type of complication, proper documentation of the same was done.

Before performing extraction of the tooth, a topical anesthetic agent (20% Benzocaine) was applied onto the dried mucosal surface adjacent to the indicated tooth. 2% Lignocaine in 1:80 000 adrenaline was injected in the selected area. After the analgesic effect was achieved, indicated primary teeth were then extracted after the beginning of N_2O/O_2 inhalation.

The patient's peripheral saturation levels of oxygen (SpO_2) were observed before, that is, T0 (initial baseline values), during sedation, that is, T1 (after 3 min), and T2 (postoperatively).

Results

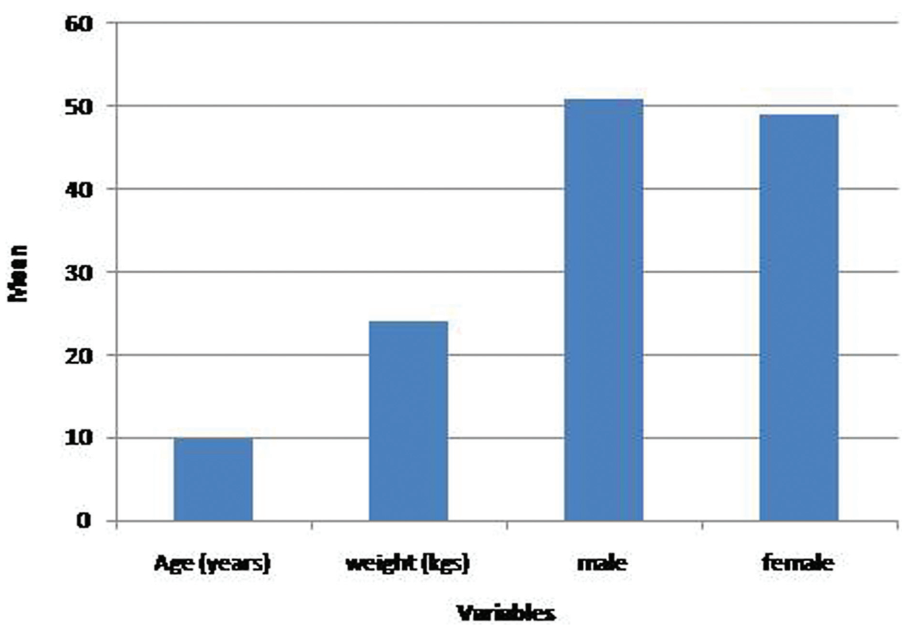
The studied patient's sample comprised 36.3% males and 63.7 females in group 1. The mean age in this group was 6.4±1.9years. Group 2 comprised 42% females and 58% males. The average age was found to be 6.5±1.7 years. No statistically significant difference was found between both the groups. Figure 1 shows the mean value of all the variables.

Although statistical significance (P<0.001) was obtained between both groups in the time required for reaching the maximum level and duration of the sedation, time required for obtaining maximum sedation was found to be longer in group 1 (35 ±9.8 min) than in group 2 (25±3.1 min). Duration of sedation was observed to be higher in group 1 (200.1 ±25 min) when compared with group 2 (90±2.9 min). On comparison of behavioral rating scale (Frankl), no significant difference was observed between the two groups (P=0.54) (Tables 1 and 2), whereas on pulse oximeter readings, the median SpO_2 level in group 1 was 98, whereas in group 2, it was found to be 97 (Table 3).

Discussion

Fear of dentistry is a normal emotion to a single or more than one specific stimuli in dental clinics, whereas dental anxiety is the apprehension of some dreadful occurrence during dental treatment. Children exhibit greater anxiety and noncooperation between 3 and 7 years of age. Anxiety reduces as a child becomes old.

Figure 1



Mean values of variables.

Sedation with N_2O and O_2 may be useful to provide tolerability to dental treatment in fearful patients, helping to control anxiety and pain, as well as improving patient cooperation [23].

Pharmacological management of anxious or difficult children is an important means for performing the treatment in such children. In the present study, midazolam/promethazine was found to have higher sedative potential when compared with nitrous oxide//oxygen.

Most pediatric dentistry clinics prefer midazolam as a drug of choice for achieving conscious sedation [24]. However, clinical use of oral midazolam must be done by physicians who have considerable experience and knowledge in the management of pediatric airways along with resuscitation [25]. Bhanot *et al.* [26] showed that both 0.3 and 0.5 mg of midazolam can reduce identical levels of conscious sedation. Ilasrinivasan *et al.* [27] in their study reported no statistical significance between ketamine/midazolam sedation against nitrous oxide/oxygen sedation.

Cheng *et al.* [28] found that an oral solution of midazolam is equally effective as in intravenous injectable form and also has better efficacy when compared with ketamine. These investigators found that a 0.5–1 mg/kg dose in a midazolam solution can be recommended in children.

Naraosualitehrani *et al.* [29] found no statistically significant difference between sedation scores, working conditions, along with recovery times of midazolam in combination with propofol or ketamine plus propofol combination ($P>0.05$). For both combinations, the intravenous route for achieving conscious sedation was found to be effective in regulating and guiding behavioral patterns of children aged between 4 and 6 years for receiving dental treatment. However, in the present study, no statistically significant difference was observed between both study groups.

Silay *et al.* [30] in their study found significantly less levels of oxygen saturation ($P<0.001$) and a shorter duration of treatment ($P<0.001$) in conscious sedation with midazolam when compared with general anesthesia. However, in our study, no statistically significant difference was noted in SpO_2 levels between the study groups.

Vallogini *et al.* [31] evaluated the role of conscious sedation in autistic pediatric patients and found that midazolam proved to be a better sedative agent compared with diazepam.

Sakshi *et al.* [32] reported midazolam as a drug of choice for in-office sedation procedures in an Indian scenario.

Conclusion

Conscious sedation is required during dental procedures for managing uncooperative and difficult children. In the present study, midazolam/

Table 1 Demographic variables and period of tooth extraction

Variables	Mean±SD
Age (years)	9.9±1.6
Weight (kg)	24.1±2.8
Sex (male/female)	51/49
Period of extraction (in min)	4.9±1.6 (nitrous oxide-oxygen inhalation)
	4.8±1.4 (oral midazolam-promethazine)

Table 2 Comparison of behavioral scales

	Overall behavioral scale							
Group	Aborted	Fair	Good	Very good	Excellent	Total score	χ^2 value	*P* values
Midazolam/promethazine	24%	7.1%	42%	24.6%	2.3%	100%	3.564	0.54
Nitrous oxide/oxygen	23.5%	15.1%	27.2%	32%	2.2%	100%		

Table 3 Comparison between pulse oximeter readings in both groups

Groups	Measurement time	Mean±SD	Median	Minimum	Maximum
Midazolam/promethazine	Preoperative	98.7±1.5	98	95	100
	Operative	98.6±1.7	98		
	Postoperative	98.5±1.6	98		
Nitrous oxide/oxygen	Preoperative	97.1±1.6	97	95	100
	Operative	97.9±1.5	97		
	Postoperative	97.5±1.6	97		

promethazine was found to be superior to N_2O/O_2 combination and must be preferred in clinical settings. However, on analysis, no statistically significant differences were obtained either on the behavioral rating scale or in SpO_2 levels.

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Conflicts of interest

There are no conflicts of interest.

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