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# Oral Midazolam Vs Promethazine as Pre Sedation Medication in Pediatric Dentistry

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**Objectives** Pre- and post-sedation effect of oral Midazolam to promethazine in2-6 yrs old fearful children for dental treatment

**Methods** This randomized clinical trial was carried out on a group of 26 children aged 2-6 years referred to the dental school due to their fear and multiple dental needs. Patients were selected from ASA I or II classification and scored 1 in Frankl Behavior scale. Each patient was scheduled for two subsequent visits to receive one of the two pre medications before IV sedation. Each patient served as self-control and randomly assigned to either group A: receiving Midazolam oral as premed in 1st visit or group B: receiving Promethazine oral as the premed in 1st visit. Six hour NPO was instructed prior to sedation visit. Monitoring vital signs were conducted at every 15 minutes starting with base line before any drug administration. Sedation score was recorded using Houpt Sedation scale. Post sedation problems were recorded by operator. Data were analyzed using Student t test and Kruskal Wallis.

**Results** No significant difference was noted between the patient perceptions at the two different visits. Children did not show a significant difference on symptoms such as Crying, Movement, Sleep and overall behavior in two visits at the first 15 minutes of sedative injection. Post-operative complications were having no significant difference. Lower sickness and vomiting were reported following promethazine intake.

**Conclusion** Promethazine seems to be as effective and as acceptable premedication as Midazolam in pediatric dentistry.

**Keywords** Promethazine, Midazolam, Oral premedication, IV Sedation, Children, teeth

## Introduction

Treatment of anxious children remains to be a big challenge for pediatric dental profession.[1] It is proved to be difficult and in certain cases even impossible to treat these fearful young children on a routine setup dental chair.[2] In these circumstances, the use of pharmacological methods comes to light in order to enable certain cases to be seen effectively. These include the conscious sedation (CS), deep sedation and general anesthesia (GA). Since administration of GA has several short comes including necessity of special training, hospital setup, high cost and longtime taken, CS is nowadays advocated as an acceptable replacement while cheaper and more convenient to both patient and operator in many instances.[3] Varying methods are employed for sedation induction with the oral route as being at the top of the list for its ease of use and high patient acceptance[4] In fact oral sedation is acknowledged as the oldest known yet effective, economic, and easy to use among all routes of CS[5] Nasal, Rectal, IV and IM routes are also other ways of induction routinely used in certain cases with their own advantages and limitations.[5] High patient acceptance is the key advantage of the oral routes in children of the families not interested in forced treatment.

Midazolam is widely and readily available in an oral dosage as a sedative hypnotic agent. Peak action occurs after 30 minutes of oral administration. It has been employed orally as the sole sedative agent as well as in combination as premedication prior to other sedative agents before medical and dental surgical procedures for adults and children.[6-8] Promethazine is a Phenothiazine derivative commonly used as an antiemetic for management of nausea and vomiting, for preoperative sedation, main sedation as to relief the apprehension and anxiety, light sleep with easily aroused and management of allergy Midazolam is a short -acting but fast and effective benzodiazepine and its sedative and anxiolytic effects begin 20 minutes after oral administration. Promethazine, in the other hand is a long acting antihistaminic and anti-vomiting agent.

Ketamine hydrochloride is a Cyclohexane derivative closely related chemically and pharmacologically to phencyclidine, a veterinary anesthetic and drug abuse known as “angel dust”.[1]

This clinical trial was designed to evaluate the post sedation side effects of oral Midazolam and Promethazine premedication in an IV ketamine sedated pediatric dental service.

## Materials and Methods

This randomized cross over clinical trial was designed in a double blind manner (IRCT Reg No: 2016120516106N3). A total of 26 uncooperative children aged 2-6 years were included who were judged by an anesthesiologist as

medically fit for conscious sedation and stand in ASA I. Dental behavior scaling was conducted and only those in Frankl I score were included in this investigation. Cases were divided into two groups randomly in order to enable evaluation of the carry over effect by having each case act as self-control receiving medications in different orders. Attempts were made to ensure each case has at least 2 similar dental needs on similar teeth of the other side on the same jaw to simulate the treatment sessions.

Informed consent was sought from individuals prior to each treatment session. Randomly assigned cases into one of the two groups of A and B were subjected to premedication as follows:

Group A: received Midazolam (Amsed, UK) Atropine (Alborz Daroo, Iran) (0.5mg/kg, 0.25mg, respectively) as oral premed at their1st session and Promethazine (1 mg/kg) at their 2nd session

Group B: received the same regimen but in an opposite order

Patients were instructed to observe a 6 hour NPO prior to the sedative drugs administration step. The oral sedative drug's onset time was expected to be at and around 30-45 min of intake. A clinical evaluation of the sedation level was carried out prior to the main IV sedative administration of Ketamine (Rotex medica, Germany) & Midazolam (Abooreihan, Iran) (2mg/kg, 0.1 mg/kg) and treatment completed. Evaluation steps were continued at treatment end, one, two and six hours post-operative through the phone interviewing Mum.

Physiologic signs were recorded and parameters evaluated were: Heart Rate, Respiratory Rate, $SPO_2$, Blood Pressure changes throughout the procedure. These signs were recorded at start, During LA injection, at 15 min and 30 min of starting dental procedure.

HOUPT scale was used to evaluate and classify each cases Behavior parameters with the following details: Crying (C), Sleepiness (S), Movement (M) & Overall Behavior (O).Side effects were recorded in 1st, 2nd and 6 hours post operatively which include possible any possible: Vomiting, Nausea, Dizziness, Sleepiness. Collected data were analyzed using student t-test (s) and the level of significance was ($p<0.05$). Non parametric Kruscal Wallis test was used to analyze the level of sedative effect on each case session as well as the rate of post-operative complications.

## Results

In total 26 uncooperative children aged 2-6 years who scored as Frank l I, with weight ranged 8-20kg were included in this study (Tables 1).

Differences were not statistically significant ($P>0.05$) for child's Behavior Parameters, Physiologic Parameters, Recovery time, and side effects when their first and second visits were compared (Figures 1 and 2).

However there was a significant difference between the two groups when nausea and sleepiness were compared ($p<0.05$) in 1and 2 hours post operatively. No Significant differences were found between the two groups ($p>0.05$) for their side effects. There was however minimal difference in favor of Promethazine for reduce vomiting rate

.Table 1- **Distribution of Age and Weight among children of this investigation**

| Age/ Weight | Ages | Number of Patients | Percentage |
|---|---|---|---|
| **Age** | 2 - 3 | 16 | 64 |
| | 3- 4 | 5 | 20 |
| | 4 - 5 | 4 | 16 |
| **Total** | | 25 | 100 |
| **Weight** | 8 - 12 | 3 | 12 |
| | 12 - 16 | 16 | 64 |
| | 16 - 20 | 6 | 24 |
| **Total** | | 25 | 100 |

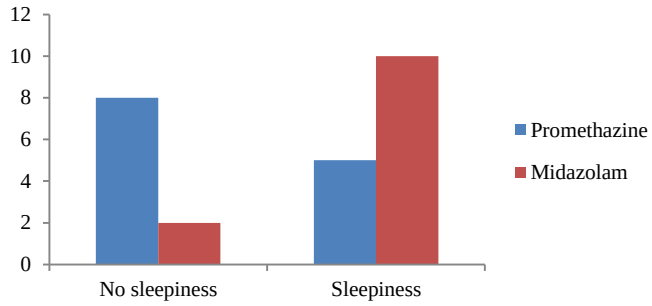


**Figure 1- Bar Chart showing the rate of various side effects following the use of both premedication regimens**

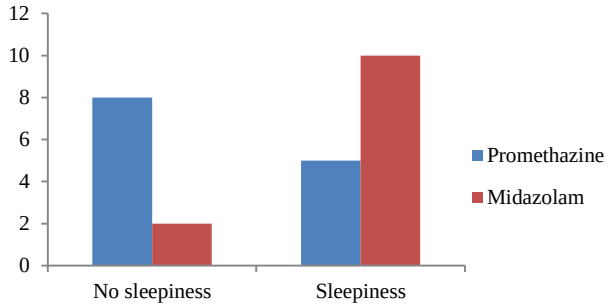


**Figure 2: Bar chart showing the difference between sleepiness at discharge time of the two premedication regimens**

## Discussion

Every day growing preference for sedation and GA dental treatment emerges for treatment of highly anxious and very young children.[5, 9-11] To date, a large number of researches have reported the necessity as well as safety, efficacy and potential side effects of the techniques and drugs involved in various sedation approached at the dental practices. Mathai *et al.* (2014) looked at the rapid onset in intranasal midazolam and oral Promethazine in preschool children with higher results in favor of Midazolam.[12] Fallah *et al.* (2014) stated that side effects of Promethazine and chloral hydrate as being little when checked by EEG with no

significant difference between groups.[13] Behetwar *et al.* (2011) reported slower onset and faster recovery in children receiving midazolam or ketamine alone compare to those received combination of the two.[14] Bui and Ronald (2002) evaluated the efficacy of oral ketamine versus oral Ketamine and Promethazine with Ketamine alone proved to be more efficient than their combined administration.[15] Dolman *et al.* (2001) evaluated the efficacy and safety of intranasal midazolam and oral chloral hydrate and oral Promethazine. Lower systolic pressure were reported in Promethazine and chloral hydrate and a delayed recovery in midazolam.[16] In current trial, the side effects of oral Midazolam and Promethazine premedication were almost similar and ignorable.

There was no significant differences between the two groups when HOUPT scale was compared for children's sedative reactions ($p>0.05$).Similarly no significant differences was found between the physiologic parameters and side effects of each pre-medications regimen at the two intervals. Mathai *et al.* (2014) and Derakhshan *et al.* (2013) reported no significant difference between the levels of sedation induced by oral midazolam and oral Promethazine. Although they referred to rapid onset as a pharmacologic advantage of midazolam beside shorter duration to maximal sedation which accelerates patient's recovery.[12, 17]

Surprisingly no such differences were observed by Singh *et al.* (2002).[18] It was concluded that oral midazolam is a preferred sedative drug when compared to Promethazine and oral Triclofan.[18] A significant difference was noted between the rate of sleepiness after 2 hours (more sleepiness in Promethazine group) and nausea after the 1st hour of treatment (less nausea in Promethazine group) in this investigation.

Derakhshan *et al.* (2013) stated that except nausea and vomiting there was no significant difference between complications following the introduction of two drugs with both having a similar sedative effect in children. Shorter onset of sedation and short duration to peak sedation were considered as Midazolam advantage in an out-patient setting, while a quick recovery with lesser nausea and vomiting were associated with antiemetic Promethazine prescriptions.[17]

Promethazine is one of the most frequently used drugs for the treatment of nausea and vomiting while it has some degree of potential sedative effects.[19-21]

Mathai *et al.* (2014), Derakhshan *et al.* (2013) and Pfeil *et al.* (2008) indicated that there were no significant differences in hemodynamic changes between various groups when they received similar drugs through different routes of administration.[12, 17, 19] There are also concerns over the safe administration of many of these sedative agents including antihistaminic agents such as Promethazine for under the age of three.[22]

However there were several limitations to the current investigation include sample selection and compliance, behavior variations, parents being the responders.

## Conclusion

Based on the findings of this investigation, it is concluded that both medications could be used for reduction of the anxiety before and during certain medical and dental treatment processes.

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## Conflict of Interests

None Declared ■

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