Comparison of Oral Midazolam and Triclofos in Conscious Sedation of Uncooperative Children

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Objective: *To compare the safety and efficacy of two orally administered conscious sedation agents, Triclofos 70mg/kg and Midazolam 0.5mg/kg in pediatric dental patients.* ***Study Design:*** *In this cross over study twenty four sedation sessions were carried out with twelve children between the age group of 3 to 9 years. Children exhibiting negative behavior according to Frankl behavior rating scale (Rating No.2) were selected. Patients were randomly assigned to receive oral midazolam 0.5mg/kg or triclofos 70mg/kg. The alternate drug was administered at the next appointment. Patients' behavioral responses were recorded using a scoring system established by Houpt et al and modified by Badalaty et al considering the degree of sleep, body movement, crying and overall behavior. Scoring was done for both midazolam and triclofos session as well as for the session which was tried without medication. Ratings were made during all the procedures like injection of LA, extraction, cavity preparation, restoration and pulp therapy. Statistical analysis was done using Friedman test and Wilcoxon sign rank test.* ***Results:*** *Both the drugs showed significantly higher scores when compared to the session which was tried without medication although the scores for midazolam were significantly higher than triclofos.* ***Conclusion:*** *Oral midazolam in a dose of 0.5mg/kg is more effective in regulating patient behavior when compared to triclofos.*

Keywords: *Conscious sedation, Midazolam, Triclofos, Dental treatment*
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INTRODUCTION

To perform the highest quality dental care for the pediatric patient, the practitioner may need to use pharmacologic means to obtain a cooperative patient. Techniques that use drugs to induce a cooperative yet conscious state in an otherwise uncooperative child are most commonly referred to as techniques of conscious sedation.[1]

Conscious sedation has been used as a behavior management technique for uncooperative pediatric dental patients using either a single agent or agents in combination. The use of conscious sedation is preferred because it can be performed without the risk of general anesthesia. The objectives of conscious sedation are to improve the patient's behavior, reduce apprehension, minimize the negative psychological response towards treatment by reducing anxiety, maximize amnesia potential and control behavior during dental pediatric rehabilitation.

A variety of methods are available for producing sedation or alteration of mood in the pediatric patient which include inhalation, oral, nasal, submucosal, intramuscular, intravenous and rectal. The most universally accepted and easiest method of drug administration is the oral route.

The pediatric dental literature contains numerous reports on various medications (e.g., nitrous oxide, benzodiazepines, chloral hydrate, barbiturates, antihistamines and opioids like fentanyl and meperidine) which have been administrated alone or in combination.[2-7] However, the search for a predictable, safe and efficacious sedative protocol is still the main goal of therapeutic health care procedures for children.[8-11]

Midazolam, is a popular medication in pediatric dentistry. It is a highly water soluble, short acting benzodiazepine which is more potent than diazepam,[12] and can be administered through intramuscular, intravenous, rectal and oral routes.[13] Oral administration is indicated primarily for anxious dental patients requiring relatively short dental procedures and is the most favorable way to administer this med-

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ication in pediatric dentistry. However the onset of action when given orally is slower compared to other routes.[14]

Triclofos (trichloroethanol) is a derivative of chloral hydrate with an onset of action of about 30 - 45 minutes and produces good anxiolysis and permits smooth induction of anesthesia especially in children below 5 years of age.[15]

This study was done to compare the clinical success of two orally administered conscious sedation regimens, Midazolam 0.5mg/kg and Triclofos70mg/kg in pediatric dental patients.

METHODS AND MATERIALS

The study sample consisted of children exhibiting negative behavior according to Frankl[16] behavior rating scale (Rating No.2) reporting at the Department of Pediatric and Preventive Dentistry at Yenepoya Dental College, Mangalore.

Only normal healthy uncooperative children who refused treatment with non pharmacologic behavior management techniques were included in the study. Any child with any systemic/chronic disease, respiratory tract infection, mental retardation and nasal obstruction were excluded from the study. Informed consent was obtained from parents after informing them about the procedures, possible discomforts or risks as well as the possible benefits.

Ethical clearance for the study was obtained by the Ethical committee of Yenepoya dental college and hospital. Twenty four sedation sessions were carried out with twelve children between the age group of 3 to 9 years in this cross over study.

Children exhibiting negative behavior according to Frankl behavior rating scale were selected to be treated under conscious sedation and were recalled on a scheduled appointment day.

Procedures were preferably scheduled for early morning appointments and necessary indications and preoperative instructions were given to the parents. Patients were instructed to be on an empty stomach for 6 hours in case of solid food and 3 hours in case of liquid foods prior to reporting time on the day of appointment for sedation.

Patients were randomly assigned to receive oral midazolam 0.5 mg/kg or triclofos 70mg/kg. The alternate drug was administered at the next appointment. The two sedation appointments were separated by at least 1 week.

Pre-operative recording of vital signs of the patient - heart rate, blood pressure, respiratory rate and body temperature was done. Patient was administered with midazolam 0.5 mg/kg or triclofos 70 mg/kg after mixing it with honey. The time of drug administration was noted and following drug administration, the child remained with the parent in a calm room for approximately 30 minutes where he or she was kept under continuous observation. Vital signs were again monitored before starting the dental treatment. When the sedative effects started appearing the time of onset was recorded and the treatment was started with the administration of local anesthesia (if required).

Patients' behavioral responses throughout the treatment were recorded using a scoring system established by Houpt[17] *et al* and modified by Badalaty[2] *et al*, considering the degree of sleep, body movement, crying and overall behavior. Scoring was done for both midazolam and triclofos session as well as for the first session which was tried without administering any medication. Ratings were made during all the procedures like during injection of LA, extraction, cavity preparation, restoration and pulp therapy.

Vital signs were again recorded after completing the dental procedure. Once treatment was completed patient was kept in a quiet room free from disturbance for recovery. Time of recovery was noted when the patient was well oriented to the surroundings, could sit and stand unaided with minimal assistance. Patient was discharged 2 hours postoperatively.

Statistical analysis was done using the Friedman test and Wilcoxon sign rank test to determine whether the mean scores of the session with triclofos were significantly different from the scores of the session with midazolam.

Behavior rating criteria[2]

Sleep
1. Fully awake, alert
2. Drowsy, disoriented
3. Asleep

Body movement
1. Violent movement that interrupts treatment
2. Continuous movement that makes treatment difficult
3. Controllable movement that does not interfere with treatment
4. No movement

Crying
1. Hysterical crying that interrupts treatment
2. Continuous persistent crying that makes treatment difficult
3. Intermittent, mild crying that does not interfere with treatment
4. No crying

Overall behavior
1. Aborted – no treatment rendered
2. Poor – treatment interrupted, only partial treatment completed
3. Fair – treatment interrupted but eventually all completed
4. Good – difficult but all treatment performed
5. Very good – some limited crying or movement
6. Excellent – no crying or movement.

RESULTS

Evaluation of behavior during administration of Local Anesthesia

During the administration of local anesthesia, body movement and crying was significantly reduced with both the drugs when compared to the session which was carried out without any medication. The overall behavior while administering local anesthesia had significantly improved with both triclofos and midazolam, however it was observed that midazolam when compared with triclofos was significantly better with a p value of 0.003. However both the drugs midazolam and triclofos did not have any significant effect on sleep while administering local anesthesia (Table 1, Figure 1).

Evaluation of behavior during extraction

The results indicated that there was no statistically significant difference between the session with triclofos and the session which was tried without medication indicating that triclofos did not have any significant effect for the extraction procedure. In the session with midazolam, there was no statistically significant difference for sleep and crying when compared to the session which was carried out without any medication meaning that the child did not sleep and crying was always present disturbing the procedure. However during extraction, the body movement had significantly reduced and the overall behavior during extraction had significantly improved with midazolam with a p value of 0.039 (Table 2, Figure 2).

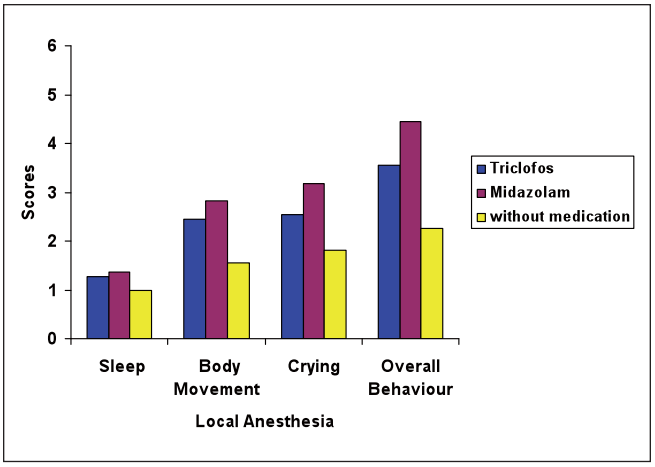

Figure 1. Graphic representation of scores for behavior during administration of local anesthesia.

Table 1. Evaluation of behavior during administration of local anesthesia

		Mean	Std. Deviation	P	Triclofos vs Midazolam P	Triclofos vs without medication P	Midazolam vs without medication P
LA SLEEP	Triclofos	1.27	.467	.102	.655	.069	.051
	Midazolam	1.36	.505				
	Without medication	1.00	.000				
LA Body movement	Triclofos	2.45	.820	.002	.317	.009	.002
	Midazolam	2.82	.874				
	Without medication	1.55	.522				
LA crying	Triclofos	2.55	.688	.001	.053	.019	.001
	Midazolam	3.18	.751				
	Without medication	1.82	.603				
LA overall behavior	Triclofos	3.55	1.036	.001	.003	.005	.001
	Midazolam	4.45	1.214				
	Without medication	2.27	1.009				

Table 2. Evaluation of behavior during extraction

		Mean	Std. Deviation	P	Triclofos vs Midazolam P	Triclofos vs without medication P	Midazolam vs without medication P
Extraction sleep	Triclofos	1.13	.354	.112			
	Midazolam	1.43	.535				
	without medication	1.00	.000				
Extraction Body movement	Triclofos	2.13	.835	.049	.160	.196	.020
	Midazolam	2.86	.900				
	without medication	1.57	.787				
Extraction Crying	Triclofos	2.75	.463	.298			
	Midazolam	2.71	.951				
	without medication	2.14	.900				
Extraction overall behavior	Triclofos	3.13	1.356	.048	.164	.058	.039
	Midazolam	3.86	2.035				
	without medication	1.71	1.254				

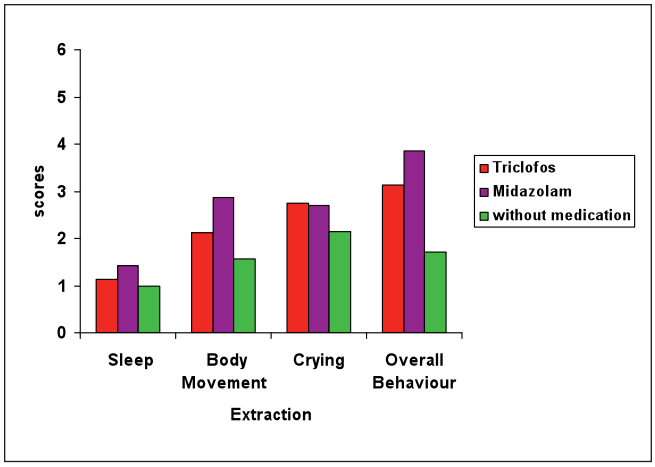

Figure 2. Graphic representation of scores for behavior during extraction.

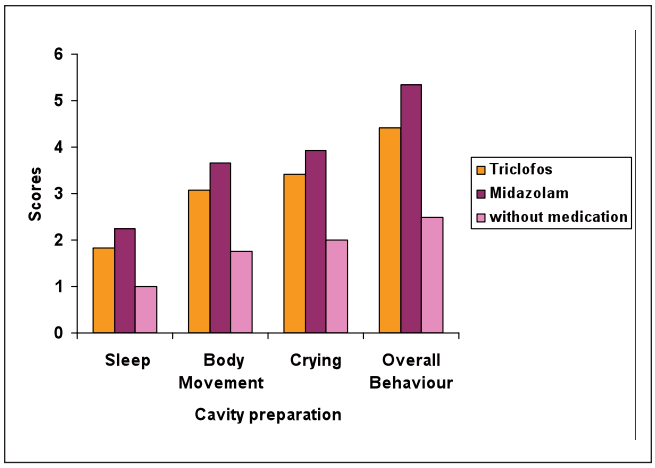

Figure 3. Graphic representation of scores for behavior during cavity preparation.

Evaluation of behavior during cavity preparation

The results indicate that there was a statistically significant difference with both triclofos and midazolam session when compared to the session which was carried out without medication for sleep, body movement, crying and overall behavior. However it was also observed that midazolam was significantly better than triclofos to control body movement and crying, but there was no statistically significant difference between both the drugs in the scores for sleep. The scores for overall behavior were significantly higher with midazolam when compared to triclofos indicating it to be a better drug with a p value 0.004 (Table 3, Figure 3).

Evaluation of behavior during restoration

Statistically significant difference was observed with both the drugs compared to the session which was tried without medication indicating that with both the drugs the child was drowsy with controlled body movement and no crying. However there was no statistically significant difference between triclofos and midazolam session in the scores for sleep, body movement and crying. But for overall behavior the scores were significantly higher with midazolam when compared to triclofos with a p value of 0.011 (Table 4, Figure 4).

Evaluation of behavior during Pulp therapy

For pulp therapy, the scores for both midazolam and triclofos sessions were significantly higher compared to the session which was tried without medication. This indicates that during pulp therapy, both drugs had significant effect on sleep, controlled body movement, reduced crying and overall behavior was improved with both the drugs. However, it was also observed that midazolam was significantly better than triclofos in controlling body movement and sleep,

Table 3. Evaluation of behavior during cavity preparation

		Mean	Std. Deviation	P	Triclofos vs Midazolam P	Triclofos vs without medication P	Midazolam vs without medication P
Cavity preparation Sleep	Triclofos	1.83	.835	.001	.182	.002	.001
	Midazolam	2.25	.622				
	without medication	1.00	.000				
Cavity preparation Body movement	Triclofos	3.08	.515	.001	.012	.001	.001
	Midazolam	3.67	.492				
	without medication	1.75	.754				
Cavity preparation Crying	Triclofos	3.42	.669	.001	.027	.001	.001
	Midazolam	3.92	.289				
	without medication	2.00	.739				
Cavity preparation Overall behavior	Triclofos	4.42	.669	.001	.004	.001	.001
	Midazolam	5.33	.651				
	without medication	2.50	1.168				

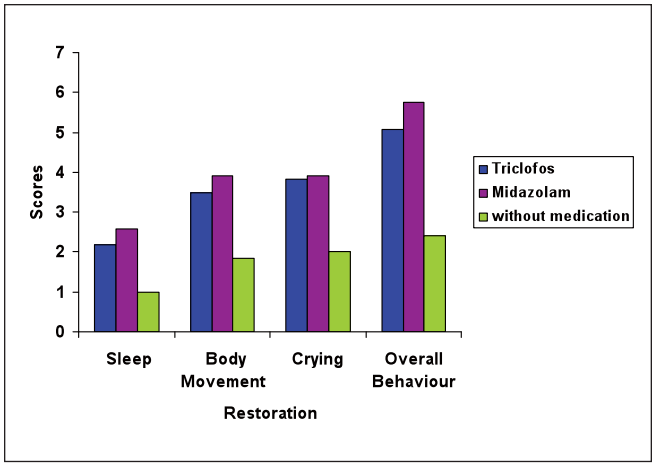

Figure 4. Graphic representation of scores for behavior during restoration

though for crying there was no statistically significant difference between triclofos and midazolam sessions. Overall, the scores with midazolam were significantly higher than the scores with triclofos indicating that midazolam was significantly better than triclofos for pulp therapy with a p value of 0.009 (Table 5, Figure 5).

Evaluation of Vital signs after drug administration (Table 6,7)

Statistical analysis showed that there was a decrease in heart rate by a mean value of less than 1 beat/min with triclofos, although the respiratory rate and BP did not show any statistically significant difference. With midazolam the respiratory rate was decreased but no statistically significant difference was observed with heart rate and BP after drug administration.

Table 4. Evaluation of behavior during Restoration

		Mean	Std. Deviation	P	Triclofos vs Midazolam P	Triclofos vs without medication P	Midazolam vs without medication P
Restoration Sleep	Triclofos	2.17	.835	.001	.214	.001	.001
	Midazolam	2.58	.515				
	without medication	1.00	.000				
Restoration Body movement	Triclofos	3.50	.674	.001	.061	.001	.001
	Midazolam	3.92	.289				
	without medication	1.83	.835				
Restoration Crying	Triclofos	3.83	.389	.001	.546	.001	.001
	Midazolam	3.92	.289				
	without medication	2.00	.853				
Restoration Overall behavior	Triclofos	5.08	.793	.001	.011	.001	.001
	Midazolam	5.75	.622				
	without medication	2.42	.996				

Table 5. Evaluation of behavior during Pulp therapy

		Mean	Std. Deviation	P	Triclofos vs Midazolam P	Triclofos vs without medication P	Midazolam vs without medication P
Pulp therapy Sleep	Triclofos	1.50	.527	.001	.030	.012	.001
	Midazolam	2.10	.568				
	without medication	1.00	.000				
Pulp therapy Body movement	Triclofos	2.60	.516	.001	.002	.010	.0005
	Midazolam	3.70	.675				
	without medication	1.80	.632				
Pulp therapy Crying	Triclofos	3.30	.483	.001	.081	.001	.0005
	Midazolam	3.70	.483				
	without medication	2.00	.816				
Pulp therapy overall behavior	Triclofos	4.20	.919	.001	.009	.0005	.0005
	Midazolam	5.30	.949				
	without medication	1.90	.738				

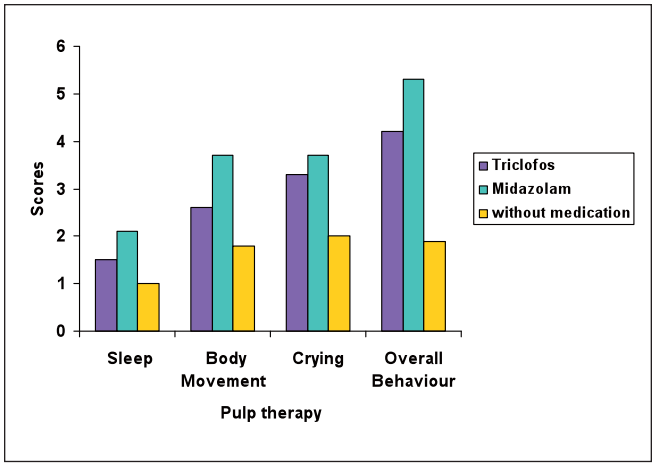

Figure 5. Graphic representation of scores for behavior during pulp therapy.

Table 6. Evaluation of vital signs after administering Triclofos

ANOVA

Heart Rate

	Mean	Std. Deviation	N
Heart rate before drug is administered	73.50	2.680	12
Heart rate after drug is administered	72.67	2.015	12
Heart rate after completing dental treatment	72.25	2.768	12

F=3.1313 P=.05

Pairwise Comparisons

(I) factor1	(J) factor1	Mean Difference (I-J)	P
1	2	.833	.526
	3	1.250(*)	.005
2	3	.417	1.000

Respiratory Rate

	Mean	Std. Deviation	N
Resp rate before drug is administered	18.58	1.379	12
Resp rate After drug is administered	18.08	1.379	12
Resp rate after completing dental treatment	17.92	1.084	12

F=3.48 P=.056

Systolic BP

	Mean	Std. Deviation	N
Systolic BP before drug is administered	100.50	1.243	12
Systolic BP after drug is administered	100.83	1.801	12
Systolic BP after completing dental treatment	101.17	1.801	12

F=.846 P=.443

Diastolic BP

	Mean	Std. Deviation	N
Diastolic BP before drug is administered	69.83	1.586	12
Diastolic BP after drug is administered	70.33	1.875	12
Diastolic BP after completing dental treatment	70.33	1.875	12

F=.579 p=.569 ns

Table 7. Evaluation of vital signs after administering Midazolam

Heart rate

	Mean	Std. Deviation	N
Heart rate before drug is administered	71.92	1.881	12
Heart rate after drug is administered	71.92	2.193	12
Heart rate after completing dental treatment	72.58	2.151	12

F=3.14 P=.063

Respiratory rate

	Mean	Std. Deviation	N
Resp rate before drug is administered	18.42	1.165	12
Resp rate After drug is administered	17.50	1.087	12
Resp rate after completing dental treatment	17.50	1.000	12

F=10.1 P=.001

Pairwise Comparisons

(I) factor1	(J) factor1	Mean Difference (I-J)	P
1	2	.917(*)	.014
	3	.917(*)	.006
2	3	.000	1.000

Systolic BP

	Mean	Std. Deviation	N
Systolic BP before drug is administered	100.83	1.586	12
Systolic BP after drug is administered	100.17	1.337	12
Systolic BP after completing dental treatment	100.67	1.557	12

F=.799 p=.462

Diastolic BP

	Mean	Std. Deviation	N
Diastolic BP before drug is administered	70.33	1.435	12
Diastolic BP after drug is administered	70.17	1.337	12
Diastolic BP after completing dental treatment	69.83	1.992	12

F=.30 p=.744

DISCUSSION

The important purpose of sedation is to prevent negative experiences for the dental care patient, as well as for the family and the dental team.[18] It is also to encourage change in the child's behavior, to help children develop their own coping skills and to promote acceptance of the dental environment.[19] It reduces the fear of pain and anxiety associated with dental procedures and makes patient co-operative for future dental appointments.[20]

The state of conscious sedation can be achieved through variety of pharmacological agents administered through various routes, but the oral route is usually the most preferred for pediatric dental patients. Combination of drugs have been in practice for a long time, however it has its own hazards.[20] For example apnea is more likely to occur when midazolam is used with narcotics. Hypotension also occurs more frequently with this combination.[21] Hence it was decided in the present study to administer the drugs orally as sole agent.

Midazolam, a water-soluble benzodiazepine, is a popular medication in pediatric dentistry. It is more potent than diazepam,[12] and can be administered through intramuscular, intravenous, nasal, rectal, and oral routes.[13] The oral route is the most favorable way to administer this medication in pediatric dentistry, due to the discomfort associated with other routes. The onset of drugs given orally or rectally, however, is slower than if administered nasally. [14,22]

In this study, midazolam was selected for the reason that it has sedative effects on patients undergoing surgical procedures. Oral administration is indicated primarily for anxious patients requiring relatively short dental procedures.[1] The intravenous liquid is bitter to taste and so the preparation is often mixed with a fruit flavored drink or honey. However recently the oral form of midazolam has become available and holds great promise for pediatric conscious sedation. Oral route is the most common method of administration in pediatric dentistry. It is more common than intravenous due to fear of injection in children; or intranasal administration, which gives a nasal burning sensation and poor and irregular absorption via rectal administration.[23]

Triclofos (Trichloroethanol) is a primary metabolite of Chloral hydrate which is an extremely well known and widely used drug for pediatric sedation.[1] Triclofos was chosen in this study because when given orally at a dose of 70mg/kg it has been reported to produce good sedation[24] and has probably been the most popular of the non barbiturate hypnotics for pediatric use.[15] Trichloroethanol produces good anxiolysis and permits smooth induction of anesthesia especially in children under 5 years of age and also has an antisialogogue effect.[15,25] Although it has been a commonly used sedative in pediatrics, the advantages of triclofos as a sedative agent in pediatric dentistry have been largely underutilized.

This study demonstrated that both midazolam and triclofos provided conscious sedation of anxious children with some significant differences. In this study, in order to verify if the cooperation was associated with the kind of procedure that was being performed, the correlation was done with the rating scores in all the clinical procedures with both the drugs and in the session which was tried without medication in all children.

The findings of this study showed that the ratings for sleep were significantly higher rendering the children calm and drowsy during cavity preparation, restoration and pulp therapy with both midazolam and triclofos, whereas while administering local anesthesia and during extraction both these drugs did not have any significant effect on sleep thus allowing the patients to be alert. These findings could be explained by the kind of procedures, as with local anesthesia and extraction which involve pain and discomfort thus keeping the child alert.

Body movement and crying had significantly reduced with both the drugs while administering local anesthesia, during cavity preparation, restoration and while performing pulp therapy although midazolam was found to be significantly better than triclofos.

In the studied sample triclofos did not contribute to behavior management while extraction was being performed whereas midazolam did help in reducing the body movement and improving the overall behavior during extraction when compared to the session which was tried without the use of any medication.

Both the drugs improved the overall behavior during cavity preparation, restoration, administering local anesthesia and during pulp therapy. The results also showed midazolam resulted in greater success which was statistically significant when compared to triclofos in improving the overall behavior during all the procedures.

In a few earlier studies the lower doses of midazolam (0.2 mg/kg and 0.3mg/kg) were not found to be effective.[26,27] The results of the present study showed that oral administration of midazolam at a recommended dose of 0.5mg/kg body weight is a suitable conscious sedation agent for normal anxious children. This is consistent with findings of past studies.[25,28,29] In the present study significantly better sedative effects were achieved with midazolam when compared to triclofos. The predictable responses of midazolam found in this study are similar to previous reports of its effects in normal children.[20,30,31,32,33]

Recovery was uneventful and none of the children experienced nausea or vomiting during or after the procedure. A close observation on all patients was kept throughout the post drug administration period because adverse reactions have been reported by some investigators with the drugs used in the present study.[13, 34, 35] Midazolam may produce respiratory depression with higher doses. There is also a dose-related risk of apnea, which is believed to be influenced by the rapidity with which the drug is administered.[36] Although hypoventilation and hypoxemia are major risks associated with high doses of midazolam, there are few reports of respiratory depression in children.[37] Unlike diazepam, midazolam metabolites are inactive: therefore, patients can be discharged immediately after the dental procedure with midazolam sedation.[38]

However in the present study the alteration in pulse rate, blood pressure and respiratory rate were within physiological limits and no adverse effects were observed in any patient at any time during the procedure with both the drugs.

From the results of the 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.

CONCLUSION

Based on the results of the present study, it can be concluded that both the drugs, oral midazolam 0.5 mg/kg and oral triclofos 70 mg/kg appear to be safe and effective sedative agents for anxious child patients during short dental procedures. However, oral midazolam in a dose of 0.5 mg/kg of body weight is more effective in regulating patient behavior when compared to triclofos 70mg/kg owing to the better sedative effect.

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