Sedation in Uncooperative Children Undergoing Dental Procedures: A Comparative Evaluation of Midazolam, Propofol and Ketamine.

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Dentists usually face a common problem dealing with pediatric patients due to their high levels of anxiety and fear, associated with dental procedures. Such children are usually managed by various pharmacological methods. The efficacy and safety of conscious sedation, using intravenous short acting group of drugs (midazolam, propofol and ketamine) in uncooperative children, requiring oral rehabilitation was thus evaluated in this study. A total of 30 uncooperative children, aged 3-6 years, belonging to ASA I, II category formed the study group. The efficacy of the three group of drugs was evaluated on the basis of the onset of sedation, duration of action, side effects encountered, and the overall cooperative behavior of the child throughout the course of the procedure, after obtaining parental consent. Results showed that propofol was highly effective in terms of onset of sedation, although increased body movements and crying, pain on injection and intermittent cough was observed as the main side effects of the drug. Midazolam showed the longest duration of action, but was not very effective in terms of treatment completion due to increased movements and crying. Maximum cooperation during the procedure was obtained with ketamine and no adverse effects were encountered. We preferred ketamine from the results of our study and recommended future evaluation of ketamine in combination with other sedatives.

Keywords: *conscious sedation, uncooperative children, midazolam, propofol, ketamine.*
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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 experienced by human beings. Due to pain and fears associated with dentistry, it is challenging to deliver dental treatment in the pediatric patients. Thus, one of the primary duties of the dentist is to alley 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.[1]

The majority of pediatric dental patients can be managed by conventional approach of behavioral management, but still, there is a fair number of children, requiring pharmacological intervention, either by conscious sedation (C.S) or general anesthesia (G.A).[2]

In the past a large number of sedative agents [such as – short acting benzodiazepines, barbiturates, inhalational agents, opoids][3] have been tried out, but none of them could be rated as a ideal sedative agent, in terms of safety and efficiency for children.

Midazolam is a newer, short acting, water – soluble benzodiazepine having sedative/hypnotic, anxiolytic and amnestic properties, which make it suitable for chidren.[4,5] Propofol is a very short acting sedative, introduced by Kay and Rolly[6] in 1977, and was widely accepted for pediatric sedation regimens due to its minimally reported systemic effects and fast recovery post-operatively. Ketamine is a non-barbiturate anesthetic agent that produces a clinical state of amnesia with a wide safety margin, maintenance of cardiovascular and respiratory function and intact laryngeal reflexes.[7]

Although these three drugs have been used in past, there is scanty literature for their use as intravenous (IV) sedative agents for the pediatric patients.

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Hence, this study was undertaken to evaluate the safety and effectiveness of these three commonly used sedative drugs in pediatric dental practice.

MATERIALS AND METHODS

30 healthy children requiring oral rehabilitation, belonging to ASA I and II category, who were anxious, uncooperative and apprehensive, reporting to the Department of Pedodontics and Preventive Dentistry in A.B. Shetty Memorial Institute of Dental Sciences were enrolled in the study. They were randomly divided into three groups of 10 children each, and their complete oral rehabilitation was planned under conscious sedation using the three selected drugs i.e. group I: midazolam, group II: propofol and group III: ketamine respectively.

After obtaining the parental consent they were subjected to pre-anesthetic and physical evaluation and were made to follow NPO guidelines.[8]

One hour prior to the procedure, all the children were premedicated with oral midazolam (0.5 mg/kg) and atropine (0.6mg) and their vital statistics were recorded. The anesthetist did the supervised administration of the bolus and the infusions of the chosen drug as given in Table I. A baseline measurement of the patient's vital signs was recorded at every 5 minutes interval during the sedation procedure. Various dental procedures (not exceeding 45 minutes to one hour duration) were performed which included: oral prophylaxis and fluoride gel application, dental restorations, dental extractions, composite fillings and pulp therapies.

During the whole course of the sedation procedure, the overall response of the sedative drug was assessed on the basis of Houpt's *et al* sedation rating score[9] (Table II).

After the compilation of the procedure, the patients were shifted to the post operative ward where vitals were continuously monitored at 10 minutes interval and recorded. The recovery time of each patient was recorded using Aldrete's recovery rating score[8] (Table III). Any associated post operative complications such as vomiting, fever or pain was also noted in accordance to that particular sedative drug used. Finally the patient was discharged only after he/ she fulfills the discharge criteria.[8]

The obtained results were subjected to statistical analysis using Kruskal-Wallis test.

Table I. Drugs and Their Dosages Used in the Study

Drugs	Bolus dose	Infusion dose
Midazolam	0. 1 mg kg^{-1}	0.004 mg $kg^{-1}min^{-1}$
Propofol	1 mg kg^{-1}	0.06 mg $kg^{-1}min^{-1}$
Ketamine	0.5 mg kg^{-1}	0.01 mg $kg^{-1}min^{-1}$

Table II. Houpt's et al sedation rating score[9]:

RATING SCALE	SCORE
(a)**SLEEP**	
Awake, but responsive	4
Drowsy, disoriented	3
A sleep, easily aroused	2
Asleep, difficulty to arouse	1
(b)**MOVEMENT**	
No movement	4
Intermittent movement affecting treatment	3
Continuous movement affecting treatment	2
Violent Movement that Interrupted or prevented the treatment	1
(c)**CRYING**	
No crying	4
Intermittent crying	3
Continuous crying	2
Hysterical crying	1
(d)**OVERALL BEHAVIOR**	
Excellent, no disruption	6
Very good, limited disruption	5
Good, some difficulty	4
Fair, Much difficulty but treatment done	3
Poor, partial treatment done	2
aborted	1

RESULTS

Assessment of the level of sedation (immediately, after 5 minutes of the drug administration and at the end of the sedation procedure) with the three group of drugs was made. Midazolam showed the lowest level of sedation (Houpt's score being 3.9,3.2, 1.6 respectively), while propofol showed the highest level of sedation (Houpt's score being 2.9,2.9,1.7 respectively) Ketamine remained intermediate of the two drugs (Houpt's score being 3.3, 2.2, 1.6 respectively) (Table IV).

Bodily movements of various degrees was encountered with all the three drugs when sedation procedure was carried out. The results showed minimal bodily movements following ketamine administration, slightly more with midazolam while propofol showed continuous movements (Table V).

Table III. Alderate Recovery Score[8]:

Activity	Scores
• Moves 4 extremities voluntarily or on command.	2
• Moves 2 extremities voluntarily or on command.	1
• Does not move any extremity	0
Respiration:	
• Able to deep breath, couch or cry.	2
• Dyspneic or limited breathing	1
• Apneic	0
Circulation:	
• BP +- of the pre anesthetic value	2
• BP +- 20-50% of the pre anesthetic value	1
• BP +-50% of the pre anesthetic value	0
Consciousness:	
• Fully awake	2
• Arousal to stimuli	1
• Unresponsive	0
Color:	
• Pink	2
• Pale, Dusky, Blochy	1
• Cyanotic	0

Table IV. Mean values for Houpt's et al Sedation rating score for "SLEEP"

		N	Mean	Std. Deviation	H	p
	Midazolam	10	3.9	0.31623		
Immediately	Propofol	10	2.9	0.31623	13.27	.001 vhs
	Ketamine	10	3.3	0.82327		
After 5	Midazolam	10	3.2	0.42164		
Minutes	Propofol	10	2.6	0.96609	7.46	.024 sig
	Ketamine	10	2.2	0.91894		
	Midazolam	10	1.6	0.69921		
At the end	Propofol	10	1.7	0.48305	.92	.63 ns
	Ketamine	10	1.6	0.96609		

Table V. Mean values for Houpt's et al sedation score for "MOVEMENT"

		N	Mean	Std. Deviation	H	p
	Midazolam	10	2.1	0.56765		
Immediately	Propofol	10	2.2	0.78881	12.82	.002 hs
	Ketamine	10	3.4	0.69921		
After 5	Midazolam	10	3.2	0.42164		
Minutes	Propofol	10	2.7	0.48305	15.89	.001 vhs
	Ketamine	10	3.8	0.42164		
	Midazolam	10	3.2	0.78881		
At the end	Propofol	10	3.7	0.48305	6.21	.045 sig
	Ketamine	10	3.9	0.31623		

On assessing the "crying" it was seen that, children sedated with propofol and midazolam encountered continuous crying throughout the sedation procedure. However, with ketamine children were calm, comfortable and without crying (Table VI).

Maximum level of cooperation was obtained with ketamine throughout the procedure. Immediately on drug administration, due to inadequate sedative effect the overall behavior was poor with midazolam than with propofol. After 5 minutes and at the end of the sedation procedure, almost equal cooperation level was observed with both the other two drugs (Table VII).

Propofol showed the fastest post operative recovery with the score of 2.0 followed by ketamine with the score of 1.5. Midazolam took the longest time for recovery with the score of 0.3 (Table VIII).

DISCUSSION

Traditional non-pharmacologic behavioral management techniques and prevention, coupled with local anesthesia when required, form the foundation of the delivery of pain free dentistry. But for highly anxious uncooperative children as well as children lacking in cooperative ability due to immature cognitive skills, behavior management is needed to be augmented with sedation techniques.[10.]

Although it is generally accepted that general anesthesia is relatively safe when administered in a hospital setting, it is not without risk of complications, especially for the pediatric

Table VI. Mean values for Houpt's et al Sedation score for "CRYING":

		N	Mean	Std. Deviation	H	p
	Midazolam	10	2.2	0.78881		
Immediately	Propofol	10	2.2	1.0328	13.11	.001 vhs
	Ketamine	10	3.6	0.5164		
After 5	Midazolam	10	3.3	0.67495		
Minutes	Propofol	10	2.8	1.0328	12.91	.002 hs
	Ketamine	10	4	0		
	Midazolam	10	3.7	0.67495		
At the end	Propofol	10	2.8	1.31656	7.52	.023 sig
	Ketamine	10	4	0		

Table VII. Mean values for Houpt's et al Sedation score for "overall Behavior"

		N	Mean	Std. Deviation	H	p
	Midazolam	10	2.5	0.52705		
Immediately	Propofol	10	3.2	0.42164	23.41	.001 vhs
	Ketamine	10	4.9	0.56765		
After 5	Midazolam	10	3.3	0.48305		
Minutes	Propofol	10	3.6	0.5160	22.21	.001 vhs
	Ketamine	10	5.9	0.31623		
	Midazolam	10	3.2	0.42164		
At the end	Propofol	10	3.5	1.08012	20.36	.001 vhs
	Ketamine	10	5.8	0.42164		

Table VIII. Alderete's recovery score for " ACTIVITY"

		N	Mean	Std. Deviation	H	p
	Midazolam	10	0.3	0.48305		
Immediately	Propofol	10	2	0	22.14	.001 vhs
	Ketamine	10	1.5	0.52705		

patients. Major life-threatening complications are allergic reactions and bronchospams.[11]

Increasing awareness of the potential risks of general anesthesia has led the researchers to develop alternative methods and led parents to accept perhaps controversial but safer methods to treat their child.[12]

Usually the decision of the sedative technique is subjected to parent's bias regarding its safety, cost and practicality[13]. Because children are provided single session treatment under general anesthesia, parents opt for it, in comparison to prolonged and numerous treatment sessions and ignore concerns about safety of each mode of treatment. Dental phobic parents are unable to comprehend the advantages of conscious sedation.[14]

This study was undertaken as an attempt to evaluate the safety and efficacy of conscious sedation. Following 30 minutes of premedication, children were sedated with midazolam, propofol or ketamine, intravenously, in doses given in Table I.

No side effects were encountered at the site of drug injection with either of the three drugs, except pain on injection

which was observed with propofol in 90% of the cases. The painful stimulus or the allergic reaction has been attributed to the drug solvent present in propofol preparation i.e. 10% intralipid, which does not contain any preservatives as stated by Parworth *et al*.[15]

Immediately after propofol administration none of the patients were awake, while with ketamine most of the patients were drowsy and disoriented. Almost all of the children sedated with midazolam were awake and responsive. Similar observations were also obtained by Godambe *et al,*[16] Seigler *et al,*[17] Vardi *et al*[18] and by Ostreikov *et al*.[19]

Propofol showed the shortest duration of anesthetic effect due to its very high clearance rate- 1.5-2.2 l/min and repeated bolus of drugs had to be administered every 2.5 minutes. Whereas, ketamine and midazolam showed the longest duration of sedative effect and no additional bolus dosages were required to maintain the desired level of sedation. But according to Bennett *et al*, bolus administration of propofol should be best avoided as it tends to produce variable plasma concentration, thereby, increasing the amount of drug to be administered.[20]

Continuous movements and crying were encountered with propofol immediately and after 5 minutes of drug administration and intermittent movements at the end of the procedure which made the commencement of the treatment with propofol very difficult throughout. Movements and intermittent crying was also high with midazolam but comparatively less than that of propofol. Treatment procedures were very comfortable with Ketamine sedation, were children showed least movements and no crying throughout the procedure. These findings were in accordance with the findings of Ostreikov *et al*,[19] but not in accordance with the findings of Tamminga *et al*,[21] who reported a better acceptance of midazolam as compared to ketamine by uncooperative children.

Systemic side effects such as cardiorespiratory depression or stimulation, nausea, vomiting, shivering, perspiration etc were not encountered with either of the three group of drugs, except intermittent cough with propofol which was seen in about 70% of the cases throughout the procedure. This unusual side effect encountered with propofol can prove to be hazardous for the commencement of short oral procedures without intubations, hence, it has to be evaluated by further investigations. Pyrexia was observed post operatively in 2% of cases with midazolam. This is not reported in any acceptable literature, hence may be due to some other systemic or local cause.

All the three group of drugs used as short acting sedatives offered a fast post operative recovery of the patient and was uneventful. Hence, the patients were discharged the same day of the procedure.

CONCLUSION

Conscious sedation is safe and cost effective in facilitating routine dental care of short duration for the anxious and uncooperative children.

Propofol was found to be superior drug due to its rapid onset of sedation, while ketamine was the drug of choice when compared with respect of ease of dental treatment completion and the patient's level of cooperation during the sedation procedure, followed by midazolam.

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