

## CURRENT METHODS OF SEDATION IN DENTAL PATIENTS – A SYSTEMATIC REVIEW

SK Srinath<sup>1\*</sup> and Chandralekha<sup>2</sup>

<sup>1</sup>Prof and HOD, <sup>2</sup>Post Graduate, Dept. of Pediatric Dentistry, Government Dental College and Research Institute, Bangalore 560002, Karnataka, India.

Corresponding Author: - **SK Srinath**  
E-mail: [srinath.krishnappa@yahoo.com](mailto:srinath.krishnappa@yahoo.com)

<b>Article Info</b> <i>Received 15/08/2016</i> <i>Revised 27/08/2016</i> <i>Accepted 02/09/2016</i>  <b>Key words:</b> Conscious sedation, Pediatric dentistry.	<b>ABSTRACT</b> Objective: The main objective of this systematic literature review is to identify the safest and most effective sedative drugs so as to ensure successful sedation with as few complications as possible. Study Design: A systematic literature review of the PubMed MEDLINE database was carried out using the key words “conscious sedation,” “pediatric” and “dentistry.” A total of 381 scientific articles were found, and these were narrowed down to 140 articles after applying inclusion and exclusion criteria. These 140 studies were then individually assessed for their suitability for inclusion in this literature review. Results: A total of 9 studies were selected due to their rigorous study design and conduciveness to further, more exhaustive analysis. The selected studies included a total of 4,467 patients classified as ASA I or II. Midazolam was the drug most frequently used for successful sedation in dental surgical procedures. Ketamine also proved very useful when administered intranasally, although some side effects were observed when delivered via other routes of administration. Both propofol and nitrous oxide (N <sub>2</sub> O) are also effective sedative drugs. Conclusions: Midazolam is the drug most commonly used to induce moderate sedation in dental surgical procedures, and it is also very safe. Other sedative drugs like ketamine, dexmedetomidine and propofol have also been proven safe and effective; however, further comparative clinical studies are needed to better demonstrate which of these are the safest and most effective.
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### INTRODUCTION

Conscious sedation is an effective method of reducing preoperative anxiety in children and in adult patients who suffer from anxiety, especially prior to surgical procedures requiring general anesthesia. When administered before dental treatments, conscious sedation methods have been shown to aid in the reduction of patient pain and anxiety. Conscious sedation is very useful in encouraging patient cooperation and improving overall patient satisfaction with dental treatment. However, conscious sedation methods do involve some level of risk for patients and dental practitioners[1]. It is well known that conscious sedation allows dental practitioners to treat uncooperative patients[2]. Some patients simply cannot be treated with local regional anesthesia alone for various reasons, generally due to behavioral problems resulting

from some form of disability or because the patient is a child. In these cases, procedures must be performed with the patient under conscious sedation[3]. However, in some cases requiring very complex dental procedures, or if the patient is in poor condition, conscious sedation may be inadvisable or the class of drugs used may be contraindicated. The adverse effects associated with conscious sedation are a result of the class of drugs used, with hallucinations being the most frequently observed adverse reaction [4,5] linked to the use of benzodiazepines, propofol and nitrous oxide. Nitrous oxide may also cause damage to immune and hematologic systems, and it can cause fertility problems in women[6-9]. However, the biggest disadvantage of conscious sedation is that it can mask symptoms of a medical emergency, so clinicians



should remain very conscious of proper methods of sedation for dental procedures and their importance[10]. Clinics that employ methods of conscious sedation are required to have the equipment necessary to handle medical emergencies such as hypoventilation or central nervous system depression[11-13]. The most important consideration when dealing with a potential emergency is to have a highly qualified team capable of handling any issues that may arise, especially any respiratory complications. Today, there are a wide variety of drugs that can be used to sedate patients[14]; however, there are relatively few studies that compare the safety and effectiveness of different kinds of sedatives. Therefore, the main objective of this systematic literature review is to identify the safest and most effective sedative drugs so as to ensure successful sedation with as few complications as possible.

## MATERIAL AND METHODS

To fulfill the given objectives, a systematic literature review was undertaken using the PubMed MEDLINE database, with a view to identifying the safest and most effective sedative drug in order to provide dental practitioners with updated information on whichever drugs were found to be the most suitable. A total of 381 scientific articles were found by entering the key words “conscious sedation”, “pediatric dentistry” into the PubMed MEDLINE database.

The search was then further limited to date 2010 till 2016, which narrowed the results down to 102 studies. These 102 studies further narrowed based on clinical trials filter to 46 studies. Results were then individually assessed for their suitability for inclusion in this literature review, with a total of 9 studies being selected due to their rigorous study design and conduciveness to further, more exhaustive analysis; in this case, only prospective randomized studies were classified as rigorous. The only studies selected were prospective randomized studies; any studies that were not prospective were discarded. Other inclusion criteria stipulated that studies focus on sedative

drugs administered to either healthy patients or patients with specialized treatment needs, including need for buccal or cervicofacial surgical intervention, or studies that compared and assessed different drugs used to induce light or moderate sedation. Figure 1 shows a diagram detailing how this literature review was carried out.

## RESULTS

The selected articles studied a total of 4,467 patients classified as ASA I or II. Table 1 and 1 continue provides an overview of each of the selected articles: Authors, year of publication, number of patients treated, drugs administered, route(s) of administration, medical speciality, and conclusions reached. Upon analyzing the different kinds of sedative drugs used, it appears midazolam was used 7 times in 6 studies, at concentration of 0.5mg/kg. It was administered orally in 5 studies, and intranasally in 1 study. In 2 study it was administered in combination with ketamine. On one study, it was administered as midazolam hydroxyzine. All of the studies showed that midazolam can be used safely and effectively to induce light or moderate sedation.

Ketamine was administered at concentration of 5mg/kg over 4 different studies. It was administered orally in 2 studies, intravenously in 1 study and intranasally in 1. It was administered in combination with N20/O2 in 2 studies. The drug proved to be a highly effective sedative in all of these studies.

One study administered dexmedetomidine intranasally 1µg/kg and it resulted in profound sedation and exhibited relatively stable hemodynamic parameters.

Chloral hydrate was administered orally in 1 articles, in concentrations 50 mg/kg, with favorite juice and 1mg/kg hydroxyzine. The drug provided good results.

The following drugs were used in only one study: 2mg/kg of tramadol administered orally; 70mg/kg of triclofos administered orally; 0.4mg/kg of zolpidem administered orally.

Cognitive behavioral therapy was used in one study.

**Table 1. Authors, year of publication, number of patients, drugs administered, route of administration, medical speciality, and conclusions of each of the analyzed articles**

Authors	Date	Type of study	No of patients	Drug usage and dosage	Route of administration	Speciality	Conclusion
Shabbier et al	2011	Randomized controlled cross over study.	12	Midazolam 0.5 mg/kg and triclofos 70mg/kg	oral oral	Dentistry	Oral midazolam in dose of 0.5mg/kg is more effective in regulating patient behavior when compared to triclofos
Bahetwar SK et al	2012	3 stage cross over trial	45	Midazolam 0.5mg/kg; ketamine 5mg/kg	Nasal Nasal	Dentistry	M, K and MK are safe and effective by IN route to produce moderate sedation for providing dental care to pediatric dental patients

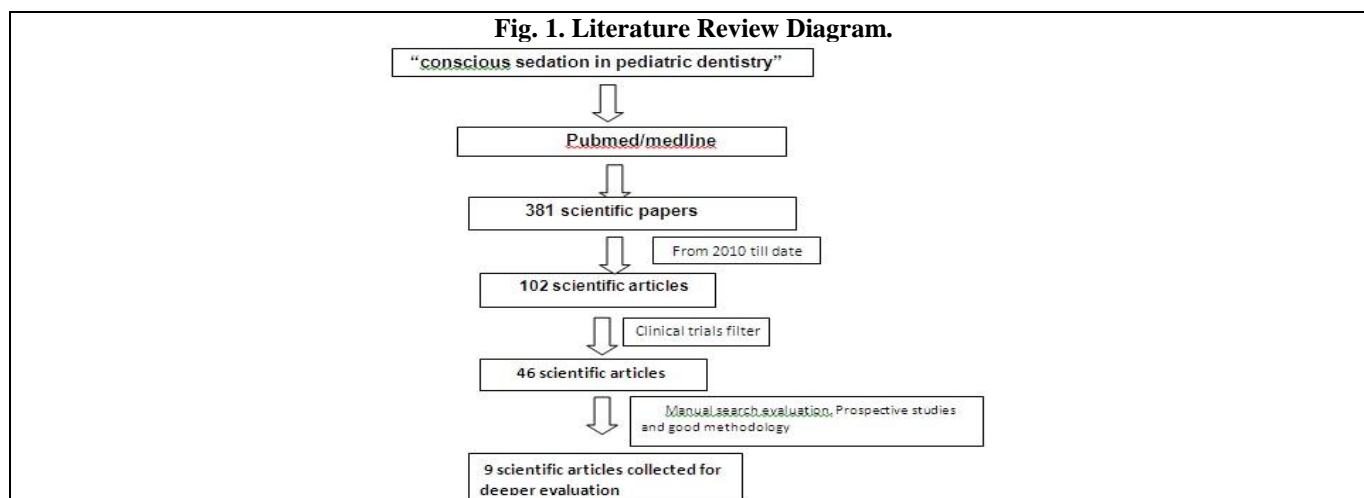


							who have been otherwise indicated for treatment under general anesthesia.
Bhatnagar S, Das UM et al	2012	Randomized control trail	60	Midazolam 0.5 mg/kg; Tramadol 2 mg/kg; Triclofos 70 mg/kg; Zolpidem 0.4 mg/kg.	oral oral oral oral	Dentistry	this study concluded that midazolam is the best drug for producing conscious sedation followed by tramadol and triclofos. Zolpidem was not able to produce a sufficient level of sedation and it cannot be supported as a sedative agent at the present dosage
Masoud Fallahinejad Ghajari et al	2013	Randomized Clinical Trial	16	Midazolam 0.5mg/kg; chloral hydrate 50mg/kg; 1mg/kg hydroxyzine	Oral Oral Oral	Dentistry	Midazolam/hydroxyzine showed a significantly higher sedative effect than chloral hydrate/hydroxyzine in this study.
F. Kebriaee et al	2014	Randomized Clinical Trial	45	N2O/O2 gases.	Nasal	Dentistry	Both test methods were effective in reducing dental anxiety in preschoolers. Considering the adverse effects and necessity of equipment and trained personnel when using nitrous oxide and oxygen inhalation sedation, cognitive behavioural therapy is preferable because of its better applicability.
M. N. Wood et al	2015	Randomized Clinical trail	3,751	Ketamine 0.41 mg/kg	Intravenous	Dentistry	This study demonstrated the safety and effectiveness of using intravenous ketamine for conscious sedation and implications for training and appropriate service delivery were discussed
VaSanthi Done et al	2016	In vivo study clinical study	30	Midazolam 0.5mg/kg; ketamine 5mg/kg; N2O-O2	Oral Oral Nasal	Dentistry	Both the drugs were effective in reducing the patient anxiety while undergoing dental extractions. Though the t-test results were not statistically significant with respect to physiological parameters. Oral midazolam-N2O showed marginally better results compared to oral ketamine-N2O with respect to psychomotor effects
Parul	2016	Double-blind	36	midazolam	Oral	Dentistry	Oral midazolam-ketamine



Uppal Malhotra et al		randomized controlled trial		0.5 mg/kg; ketamine 5 mg/kg; dexmedetomidine 1 µg/kg	Oral Nasal		combination and intranasal dexmedetomidine evaluated in the present study can be used safely and effectively in uncooperative pediatric dental patients for producing conscious sedation
Angela Galeotti et al	2016	In vivo study clinical study	472	nitrous oxide-30%	Inhalation	Dentistry	.Inhalation conscious sedation represented an effective and safe method to obtain cooperation, even in very young patients.

**Fig. 1. Literature Review Diagram.**



**DISCUSSION AND CONCLUSION**

There are a wide range of drugs, routes of administration, and varying clinical protocols that can be used to induce conscious or deep sedation. 86. Conscious sedation in dentistry Benzodiazepines are the class of drugs most often used to induce a state of anxiolysis, sedation, or amnesia[15]. Of the articles selected for this review, midazolam is the most frequently used benzodiazepine[16-18-22,23-29]. Midazolam can be used to induce a safe and effective state of sedation without risk of cardiopulmonary complications. This conclusion has been reached after comparing midazolam with other sedative drugs such as ketamine, tramadol, triclofos, zolpidem and dexme detomidine in double- and triple-blind randomized studies. In these studies, midazolam provided the best results in terms of onset time of action, depth of sedation, and anxiolysis[16-20,27]. Midazolam can be delivered in various ways, including via intravenous, intramuscular, submucosal, oral, or intranasal routes of administration. The most commonly used routes of administration of midazolam are intranasal, oral, or intravenous. Intranasal administration of a midazolam spray is also an effective method of inducing sedation and fast-onset anxiolysis. A level of moderate sedation can be achieved with this drug and route of administration after about 30 minutes[16,17].

However, the spray may cause symptoms such as bitter taste or burning sensations or pain within the nose. These side effects can be avoided by opting for a buccal midazolam spray applied to the oral mucosa, which is well tolerated by uncooperative patients[19,24]. However, midazolam can be used in conjunction with other sedatives like ketamine to help decrease the overall dosage needed, which also aids in minimizing any adverse effects and may promote quicker recovery times and a faster onset of sedative action[29]. While this was demonstrated by one of the clinical trials evaluated as part of this systematic literature review, there is a need for additional double-blind studies in order to obtain more concrete evidence. Other diazepamines such as diazepam or alprazolam have also been successfully used to sedate patients[15,18,21,30]. Diazepam and midazolam exhibit similar sedative effects, but the latter provides a better anxiolytic effect as well as a minimally higher level of sedation; therefore diazepam does not offer any sedative advantage over midazolam[18,21]. Ketamine is a dissociative anesthetic and analgesic that is also used as a sedative drug, maintaining the patient’s muscle tone and the respiratory system’s protective reflexes[29,31]. However, in adults, ketamine may also cause hallucinations and nightmares



during the recovery period, and as such it sees limited use in adults; these side effects are rarely seen in children<sup>31</sup>. Intravenous ketamine has been shown to have a powerful sedative effect; some researchers actually preferred ketamine to midazolam due to increased patient cooperativeness and because it carried less side effects; more double- and triple-blind studies are necessary to compare its effectiveness with that of other drugs in order to obtain sufficient scientific evidence for this claim[32]. On the other hand, when comparing oral midazolam and oral ketamine, while they exhibit similar sedative effects, midazolam is more conducive to anxiolysis, and orally administered ketamine results in a slower recovery period post-sedation. These drugs were compared in a well-designed, double-blind randomized clinical trial[27]. Ketamine can be delivered safely and effectively via an intranasal route of administration[16,26,29]. A combination of oral ketamine and oral midazolam results in safe and effective sedation [22,23,29].

Dexmedetomidine target the  $\alpha$ -2 adrenergic receptor agonists, and their potential use as preoperative premedications has been studied extensively. Dexmedetomidine appears to function just as well as

midazolam, providing a safe, moderate, and effective sedation. Additionally, some studies suggest it may even increase patient cooperation[16,20]. Chloral hydrate is another safe and effective sedative drug, but it does not appear to have any advantages over midazolam[28,30]. A combination of chloral hydrate and hydroxyzine only results in more side effects, and therefore this combination should not be administered to patients[28]. Triclofos was shown to have a less powerful sedative effect than midazolam.

In conclusion, Midazolam is the most commonly used sedative drug in dental procedures (light sedation). It is a very safe sedative, and it is most often administered either intranasally or orally. Ketamine also proves very useful when administered intranasally, inducing a high level of sedation (deeper than that of midazolam); however, when delivered via other routes of administration, various side effects have been observed. Dexmedetomidine have also been proven effective in inducing a state of conscious sedation. However, further clinical trials are needed to compare these drugs and obtain more evidence in order to determine which of these are the safest and most effective.

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