10.5005/jp-journals-10028-1119

REVIEW ARTICLE

Pediatric Dental Sedation Practice: Evolution and Current State-of-the-Art

[1]Neeti Mittal, [2]Krishan Gauba, [3]Ashima Goyal, [4]Aditi Kapur

ABSTRACT

The practice of the pediatric dental sedation has evolved continuously during the past few decades. Newer agents continuously seem to replace older agents and the pediatric dentists need to update themselves timely to efficiently administer sedation to their young and anxious patients. The practice and the research of pediatric dental sedation is very diverse throughout the world. In this paper, we attempt to review the diversity of pediatric dental sedation research through a systematic review. Further, we review the pharmacopoeia of pediatric dental sedation with brief description of commonly used agents. We also touch upon evolution of pediatric dental sedation guidelines in different countries and international variation in pediatric dental sedation practice. Lastly, we review the future perspective of research pertaining to field of pediatric dental sedation research.

Keywords: Dental sedation agents, Dental sedation guidelines, Dental sedation practice, Pharmacological behavior management, Pediatric dental sedation.

How to cite this article: Mittal N, Gauba K, Goyal A, Kapur A. Pediatric Dental Sedation Practice: Evolution and Current State-of-the-Art. J Postgrad Med Edu Res 2014;48(3):139-147.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Contrary to the revolutionary upward shift in dental technology and material sciences, children's behavior seems to have undergone a retrograde qualitative transformation; being less cooperative or even unreceptive these days. The evolving contemporary parenting which is more protective with inability to control children's behavior is probably accountable for this.[1,2] Further, the fear of needles, drills and white collars is not uncommon in pediatric population.[3] When an uncooperative child with a backdrop of fear toward dentistry steps in office, successful delivery of dental care might become a patience testing procedure for dentist and his/her staff. Although pediatric dentist is having so many conservative behavior management techniques such as 'tell-show-do', 'modeling', 'contingency management', etc. in his munitions store; these fail to gain cooperation from difficult children at many instances.[4] This situation tends to become worse when the intervention is urgently needed. These are the circumstances when pharmacotherapeutic means of behavior management, such as general anesthesia and sedation are called in for.[4,5] Former is generally avoided because of associated greater risk and higher cost and sedation is the commonly chosen modality.[6] Further, sedation has also shown to improve behavior and lessen anxiety for future visits (Sadana K, Chawla HS, Gauba K, Goyal A. Master's Thesis, Punjab University, 2007 unpublished).

[1]Assistant Professor, [2]Professor and Head
[3]Professor, [4]Associate Professor

[1]Department of Pediatric and Preventive Dentistry, Santosh Dental College and Hospital, Ghaziabad, Uttar Pradesh, India

[2-4]Department of Pediatric and Preventive Dentistry, Oral Health Sciences Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Neeti Mittal, Assistant Professor Department of Pediatric and Preventive Dentistry, Santosh Dental College and Hospital, Ghaziabad, Uttar Pradesh, India Phone: 08860817917, e-mail: dr.neetipgi@gmail.com

PEDIATRIC DENTAL SEDATION RESEARCH AND PRACTICE

Pediatric Dental Sedation Research: Trends till Date

For the purpose of getting an insight into the trends in the type of research papers published addressing pediatric dental sedation, a search through search engine PubMed with Mesh keywords 'sedation and dentistry' with limits set for age (birth-18 years) was conducted. Abstracts were assessed for content and type of study and in case of doubt original articles were referred to. The studies were selected if the exclusive pediatric age group (0-18 years) had been included and the outcome measures were either 'completion of procedure' or 'adverse effects during intraoperative or postoperative period' or 'cardiopulmonary parameters' without considering the study design. Both prospective trials (randomized as well as nonrandomized) and retrospective audits were included. Studies conducted on a variety of drug regimen, for example sedative agents such as midazolam, nitrous oxide, ketamine, propofol, chloral hydrate, fentanyl, sevoflurane, hydroxyzine, promethazine, diazepam and meperidine, etc. were included.

A total of 226 research papers, conducted from 1970 to 2012 were found to be eligible. A comparative bar diagram was drawn for 'number of studies conducted in past decade, such as 2003 to 2012: Time frame I' and 'number of studies

conducted from 1970 to 2007: Time frame II'. Seventy-eight trials were reported from 2003 to 2012 and 148 trials were reported from 1970 to 2002.

Results depicted that a variety of regimens (>65) were tested in various combinations and dosages in trials reported on pediatric dental sedation research (Table 1). Thirty-two regimens were tested only once (Table 2). Midazolam alone and nitrous oxide alone were most commonly tested agents with these two being additionally tested in combination with various agents. Another popular drug used in various combinations was chloral hydrate. A variety of routes were explored with oral route being the most common one. Various routes were reported in frequency order; oral> inhalation> intravenous> intranasal> intramuscular> rectal> submucosal>sublingual (Graph 1).

Midazolam dominated the pediatric dental sedation research in both the time periods studied with a greater proportion in recent years when compared to yester years (50/78; 64.10% of trials in 2003-2012 and 58/148; 39.19% in 1970-2002) (Table 3, Graphs 2 and 3). Almost equal proportion of trials were reported for nitrous oxide, ketamine, propofol, and hydroxyzine (Table 3 and Graph 3). Frequency of reporting increased multifold for sevoflurane and fentanyl in 2003 to 2012 when compared to 1970 to 2002, while a clear decline was seen in number of trials reported on diazepam and chloral hydrate in past decade when compared to previous years (Table 3 and Graph 3). Interestingly, use of promethazine seemed to have ceased completely with no trial being reported in past decade while it appeared in 12.16% of total trials reported in 1970 to 2002 (Table 3 and Graph 3). Though few trials on intravenous sedation utilizing dexmedetomidine, an α2 agonist, have been

Table 1: Commonly and uncommonly used regimen in pediatric dental sedation

S. no.	*Regimen*	*Frequency of reporting*
1	Midazolam	94
2	Nitrous oxide	44
3	Chloral hydrate	17
4	Diazepam	14
5	Ketamine	13
6	Propofol	12
7	Chloral hydrate and hydroxyzine	12
8	Chloral hydrate, hydroxyzine and meperidine	9
9	Chloral hydrate and nitrous oxide	9
10	Midazolam and ketamine	8
11	Midazolam and nitrous oxide	7
12	Hydroxyzine	6
13	Meperidine and promethazine	6
14	Chloral hydrate and promethazine	6
15	Chloral hydrate, hydroxyzine and nitrous oxide	5
16	Hydroxyzine, nitrous oxide	5
17	Meperidine	5
18	Sevoflurane and nitrous oxide	4
19	Triazolam	4
20	Temazepam	4
21	Midazolam and fentanyl	4
22	Triclofos	3
23	Flunitrazepam	3
24	Midazolam, nitrous oxide and sevoflurane	2
25	Ketamine, midazolam and nitrous oxide	2
26	Triazolam and nitrous	2
27	Trimeprazine and methadone	3
28	Promethazine	2
29	Diazepam and nitrous oxide	2
30	Meperidine and hydroxyzine	2
31	Midazolam and sulfentanil	2
32	Meperidine, promethazine and chloropromazine	2
33	Pentobarbital, meperidine and scopolamine	2
34	Midazolam, fentanyl, sevoflurane and nitrous oxide	2

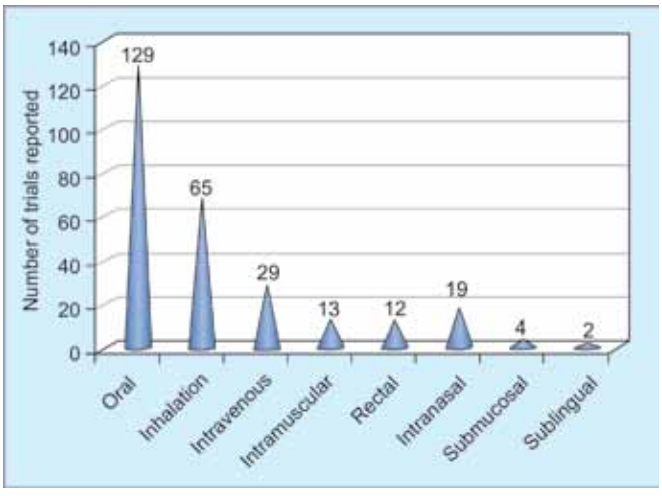
Table 2: List of regimen reported only once in pediatric dental sedation

S. no.	*Regimen*
1	Alphaprodine, hydroxyzine and nitrous oxide
2	Alphaprodine and promethazine
3	Chloral hydrate + diazepam, nitrous oxide,
4	Chloral hydrate, meperidine, hydroxyzine and nitrous oxide
5	Chloral hydrate, midazolam and nitrous oxide
6	Chlormezanone
7	Diazepam, suprofen and fentanyl
8	Hydroxyzine and diazepam
9	Hydroxyzine and metaclopramide
10	Ketamine, meperidine and promethazine
11	Ketamine and promethazine
12	Lorazepam
13	Melatonin
14	Meperidine and nitrous oxide
15	Meperidine, promethazine and nitrous oxide
16	Meperidine, hydroxyzine and nitrous oxide
17	Meperidine, hydroxyzine, diazepam and nitrous oxide
18	Methohexital
19	Midazolam, fentanyl and propofol
20	Midazolam, hydroxyzine and nitrous oxide
21	Midazolam and hydroxyzine
22	Midazolam, meperidine and hydroxyzine
23	Midazolam and nalbuphine
24	Midazolam, nalbuphine, droperidol and nitrous oxide
25	Morphine and promethazine
26	Midazolam and remifentanil
27	Midazolam and tramadol
28	Remifentanil
29	Sulfentanil
30	Triclofos and promethazine
31	Zolpidem and tramadol
32	Clonidine, diazepam and meperidine

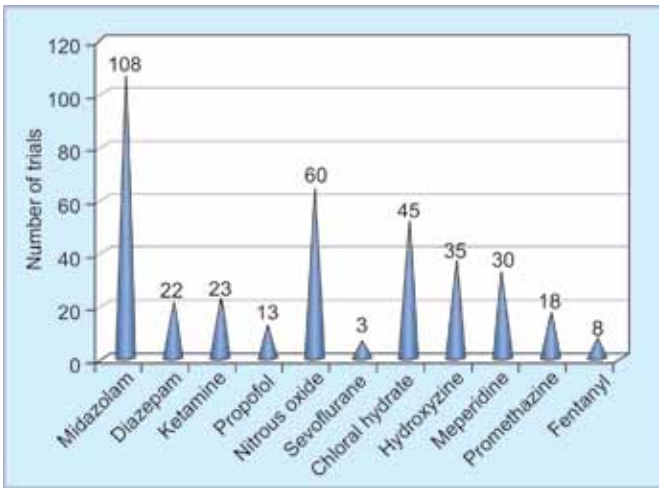
Table 3: Trends in number of reported trials on commonly used agents in pediatric dental sedation

Agent	*Number of trials (%) reported from 1970-2012*	*Number of trials (%) reported from 2003-2012*	*Number of trials (%) reported from 1970-2002*
Midazolam	108 (47.79)	50 (64.1)	58 (39.19)
Diazepam	22 (9.73)	3 (3.85)	19 (12.84)
Ketamine	23 (10.18)	7 (8.97)	16 (10.81)
Propofol	13 (5.75)	5 (6.41)	8 (5.41)
Nitrous oxide	80 (35.4)	29 (37.18)	51 (34.46)
Sevoflurane	8 (3.54)	6 (7.69)	2 (1.35)
Chloral hydrate	45 (19.92)	8 (10.26)	37 (25)
Hydroxyzine	35 (15.49)	12 (15.38)	23 (15.54)
Meperidine	30 (13.27)	8 (10.26)	22 (14.86)
Promethazine	18 (7.96)	0 (0)	18 (12.16)
Fentanyl	8 (3.54)	4 (5.13)	4 (2.7)
Total	226	78	148

reported on adult population undergoing minor oral surgical procedures in recent years from 2006, [7,8] only one trial[9] has been reported on its usage in pediatric population for dental intervention from Egypt. But, we did not include this trial in our analysis as it is included in database of Scopus, while here we are presenting the data from PubMed.



Graph 1: Number of trials reported on various routes of administration



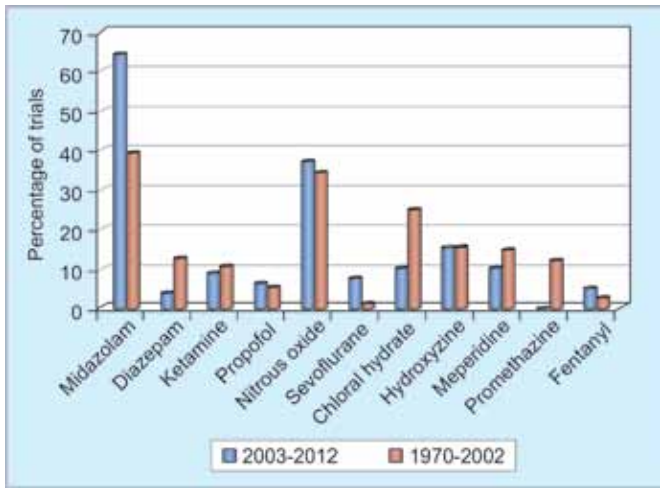
Graph 2: Trials reported from 1970-2012

PEDIATRIC DENTAL SEDATION PRACTICE: PHARMACOPOEIA FOR PEDIATRIC DENTAL SEDATION

Evolution in research arm of any medical field paces the evolution of clinical practice in that particular field, while the curiosity in the clinics gives rise to newer plateaus of research. Same holds true for pediatric dental sedation. Pediatric dental sedation practice in eighties was dependent on agents such as hydroxyzine, promethazine, meperidine, morphine, diazepam and chloral hydrate.[10] In late 1980s, dentists started preferring midazolam[11,12] to other agents and its popularity rose possibly due to variety of routes offered by this safe drug. In 1990s, existing pharmacopoeia of pediatric dental sedation welcomed the addition of older agents, such as ketamine and nitrous oxide in it.[10] Toward the end of this decade, ultrashort-acting agents used for total intravenous anesthesia, such as propofol, were incorporated.[13]

CHLORAL HYDRATE

Chloral hydrate,[14-17] has long enjoyed great popularity in the pharmacological management of the pediatric dental



Graph 3: Proportion of trials published in percentage from '1970-2002' *vs* '2003-2012'

patients, is usually administered orally or rectally in a dosage of 25 to 75 mg/kg body weight.[18] One of the main attributes of drug is its minimal effect on respiration, though respiratory depression[19,20] and deaths have also been reported.[21] It shows a delayed peak effect of around 60 minutes or longer, and its bitter taste makes it less acceptable to some children. Rectal absorption is erratic and might result in unpredictable effects. Its main disadvantage, however, is that it can result in prolonged sedation and the peak effect sometimes occurs well after the intended time of desired treatment. Further, it is not very reliable in children older than 3 years of age. Deaths due to oversedation in children at home following discharge from hospitals have also been reported.[18] There exists no known dosage threshold for these potential impending complications.[22,23] Moreover, concerns have been raised about possible carcinogenicity and genotoxicity[18] restricting its routine use. Although American Academy of Pediatrics (AAP) has cleared the drug[24] as the evidence to label this agent as a mutagen/carcinogen is insufficient, countries like France have banned it. Despite being widely used agent, the efficacy of chloral hydrate as a perioperative medication for dental procedures has not been clearly demonstrated and the optimal dose and combination of medication is still unknown.

HISTAMINE (H_1) BLOCKERS (ANTIHISTAMINES)

The two histamine blockers most frequently used for their sedative-antianxiety properties are promethazine and hydroxyzine. These drugs have proven to be quite useful additives to other sedatives, commonly used as an antiemetic, as a preoperative sedative and to augment sedative effect of other agents. Both of these drugs have a very high therapeutic index and remarkable safety.[25] Anyhow, the main reason for their declining use in pediatric dental practice is poor efficacy when used alone or possibly the availability of better agents.

Hydroxyzine, a diphenylethane has been one of the most popular psychosedative agents in pediatric dental practice. It is given orally in a dose of 3.7 mg/kg body weight,[26] 45 minutes to 1 hour before the appointment or in divided doses. It is a very mild respiratory depressant and has a wide margin of safety. Its dose can therefore be adjusted according to the clinical effect rather than age and body weight. It is, however, somewhat unpredictable in its action and paradoxical hyperexcitability has been noted,[26] thus limiting its use.

Promethazine, a phenothiazine derivative, commonly known by its trade name as phenargan, is administered in a dose of 1 to 1.2 mg/kg body weight,[27,28] 1 hour prior to the appointment. Promethazine is not particularly effective as a sole agent for sedation, though it does help in calming lesser degree of anxiety. It is, therefore, most commonly employed in combination with other sedative drugs, such as chloral hydrate, hydroxyzine, meperidine, etc. Side effects include paradoxical hyperexcitability, hallucinations and mild hypertension.[29]

BENZODIAZEPINES

Diazepam was the first benzodiazepine used for pediatric dental sedation,[30] midazolam quickly replaced it following its introduction because of its faster and potent action and multiple routes of administration. Various other benzodiazepines such as flunitrazepam,[31] temazepam,[32] and triazolam[33] have been used in few isolated reports. However, midazolam has been quite popular as depicted by a vast majority of the research papers on this agent in various dosages and combinations administered by a variety of routes.

Midazolam is a short acting benzodiazepine with rapid onset of action, adequate duration[34,35] of effect to outlast the procedure and rapid recovery when compared to other benzodiazepines, an essential property to reduce chances of postoperative complications by enabling the dentist to monitor the child in the clinic till the sedative effect gets worn off. In addition to the above properties, Midazolam produces somnolence[36] with euphoria and muscle relaxation[36] without inducing anesthetic sleep. A high therapeutic margin of safety[37] is also present, which is essential especially when the agent is being used in very young children, as in the present study. Midazolam also produces amnesia,[38] which further helps in reducing postoperative psychological trauma.

But, postoperative recovery is significantly delayed with this agent as compared to other agents like propofol,[39] ketamine[40] or sevoflurane[41] (inhalation route), where faster postoperative recovery allows for greater patient safety and is advantageous for day care procedures. Also, the levels of sedation achieved with midazolam are low, compared to ketamine, or propofol by intravenous route and sevoflurane. This level of sedation may not be sufficient for extensive clinical procedures in children like endodontics and sometimes, successful completion of procedure may not be possible,[35] where deeper level of sedation using the same agent with alternate routes or use of more potent agents like propofol may be warranted. Kapur et al[35] in a randomized double-blind placebo controlled trial, reported 10% rate of incomplete procedures (simplified restorative procedure) owing to failure of sedation with oral midazolam.

OPIOIDS

Morphine is an uncommonly used sedative drug these days and use of meperidine is also declining in present era. The drug has been used with reservation as it is a potent respiratory depressant which may place the patient at great risk after

completion of the procedure when the physical stimulation to keep them awake is the least.[18] Fentanyl is preferred pharmacologically to other opioids, because of its faster onset, shorter recovery, and lack of histamine release.[10] Its common use is to add rescue analgesia to midazolam or propofol in case the sedation by latter two is deemed insufficient. However, the sedative efficacy of fentanyl is not very admirable and this being the reason for addition of midazolam. One of the commonly described adverse effect of fentanyl is chest wall rigidity which is actually rare in practice as the dose (>5 μg/kg as a bolus dose) needed to produce this effect is much higher than that needed for sedation.[42]

KETAMINE

Ketamine introduced in 1965 is a phencyclidine derivative which can be administered by a variety of routes; either intravenously, intramuscularly, rectally, or orally.[43,44] It produces dissociative anesthesia and provides adequate level of sedation with a rapid recovery and less prominent reactions. Its uniqueness lies in fact that it is only sedative which stimulates the cardiovascular system rather than depressing it. It is the only drug available which preserves the oropharyngeal reflexes, even at its greatest depth of action. Although completely anesthetized, the patient usually does not require chin support or tongue retraction to maintain integrity of airway. This unique characteristic is ideally suited for dentistry. Moreover, its sedative effect is known to safely subdue the most combative of unmanageable, irrational, uncooperative patient.

Although the postoperative nausea and vomiting and emergence phenomenon are the adverse effects of this drug that may be of concern to pediatric dentists, recent data give weak support to this argument. The emergence phenomena are more common in patients older than 16 years of age, in females, in shorter operative procedures, in those receiving larger doses, and with more rapid administration.[45] The reported frequency of hallucinations varies between 5 and 30%, being lowest in children. Although reports indicate that the incidence of nausea and vomiting may range from 0 to 43%, the incidence in pediatric patients is somewhat less than 10%.[45] When vomiting occurs, it is almost always late in the recovery phase when the patient is alert and the airway may be cleared without assistance.

Adverse events related to airway and respiratory system[46,47] are rare with ketamine and occur in only 1.4 to 6.6% of cases, including laryngospasm in approximately 0.4%. Transient apnea with ketamine has been reported only after rapid intravenous administration or exceptionally high doses.[46,48] Although Green et al[46] highlighted the safe use of ketamine sedation for dental surgery and tonsillectomy, they have subsequently reported an increased incidence of laryngospasm (9.5%, all occurring during esophagogastroscopy) in procedures entailing stimulation of the oropharynx or hypopharynx. This signifies that ketamine though one of the safest sedative agent may not be safe for dental procedure even in subdissociative doses as low as 0.25 mg/kg.[39]

PROPOFOL

Propofol (2,6-disiopropylphenol) is a single intravenous agent that combines the safety and efficacy of the inhalation agents with the rapid metabolism of intravenous agents which could be delivered in a metered fashion allowing for titration. Propofol has many desirable characteristics for procedural sedation and analgesia: extremely rapid onset,[49] substantial potency[50,51] that reliably produces effective conditions for procedural sedation and analgesia, extremely short recovery (5 to 15 min),[39] and high satisfaction to patients as a result of its antiemetic and euphoric properties. Large emergency department,[52,53] gastroenterology,[54,55] and critical care series[56,57] show that propofol can be given to children in these settings with good efficacy, apparent safety, and rapid recovery. The depth of sedation achieved is not well described in these reports, but usually seems to be at or beyond levels consistent with deep sedation. Few reports[39,58] on its usage in pediatric dental sedation have established its safety and efficacy.

NITROUS OXIDE

Nitrous oxide-oxygen analgesia and sedation has been widely used in dentistry,[59,60] especially in children. It is one of the safest techniques with no recorded serious morbidities or mortalities associated with the technique when used for moderate sedation at recommended concentrations. It relieves pain and anxiety by altering the attitude of the patients so that dental procedures are no longer psychologically threatening. It also raises the pain threshold and reduces reaction to painful stimuli. Pain, however, is not completely eliminated and use of local anesthesia is still indicated. It can be thought of as a viable option for sedating children and adolescents with moderate anxiety but its success is doubtful for those with severe anxiety where deeper levels of sedation may be warranted. Further, another associated limitation of nitrous oxide sedation is the requirement of a certain degree of cooperation, thus restricting its use in potentially uncooperative children and in children <6 years of age.

SEVOFLURANE

Sevoflurane, another inhalation agent, is a well established and safe anesthetic agent with unique properties of rapid

uptake and rapid elimination. The combination of a fixed ratio of nitrous oxide and oxygen with a variable but subanesthetic concentration of sevoflurane, titrated clinically to allow dental treatment,[41,60] seems a natural way to improve the success of sedation. This technique seems to be a viable alternative to general anesthesia; but, use of this technique in nontheater settings is not feasible and this is an obvious limitation.

EVOLUTION OF GUIDELINES FOR SEDATION IN DENTISTRY

A decade after publication of the Poswillo report,[61] in 2000, the Department of Health published a document entitled A conscious decision[62] which discussed the poor monitoring and resuscitation standards in administration of general anesthesia in chair solely under supervision of dentists. The major impetus to this document came from reports of eight deaths in dentistry from 1966 to 1999. As an effect to this document, the practice of general anesthesia in chair ceased in UK, where currently general anesthesia for dental treatment is administered only in hospital setup in presence of an anesthetist. Since then, the practice of sedation in dentistry is being closely scrutinized.

Seeing the need to establish the guidelines to help dentists administer safe sedation, the first set of UK dental sedation guidelines were published in 2002.[63] The same year witnessed the Scottish Intercollegiate Guidelines Network guidelines[64] for pediatric sedation. These set of guidelines had a separate section on dental sedation and the practitioners had at their dispense the first evidence based explanations. The first UK guidelines were established by British Society of Paediatric Dentistry, but an year later, a dedicated task force Standing Dental Advisory Committee (SDAC) came into being which published a new set of guidelines.[65] Few more guidelines were produced later, such as General Dentist Council guidelines in 2005[66] and National Dental Advisory Committee report in 2006.[67] Still, the prime guideline regulating sedation practice standards in UK is SDAC report.

Similar to UK, the first sedation guidelines[68] in USA were result of sedation accidents, majority of which happened to take place in dental setup. The difference, however, was that in latter country the guidelines were laid much earlier (in 1985) and the fact that pediatricians AAP and pediatric dentists American Academy of Pediatric Dentistry (AAPD) worked in close association.[68,69] With the recognition of fact that apart from dentistry procedural sedation is being administered by a variety of medical professionals in multiple settings, these guidelines were revised in 1992[70] and further updated in 2002.[71] Following this the AAPD published their own set of independent practice guidelines.[72] Anyhow, the current guidelines were produced by joint committee AAP-AAPD in 2006[73] as an attempt to gain uniformity in sedation guidelines across various specialities.[74] These guidelines lay an emphasis on risk assessment, monitoring and proper armamentarium. Further, these guidelines are less detailed than UK guidelines.

CURRENT INTERNATIONAL STATUS OF PEDIATRIC DENTAL SEDATION PRACTICE

Globally, diverse specialities of practitioners administer sedation in different parts of world. Multiple specialities in addition to anesthesia administer sedation in countries like USA, Canada, Australia and New Zealand. On the other hand, no other specialist apart from anesthetists are licensed to administer procedural sedation and analgesia either in operating room or day care units in most of European, African and Asian countries. In countries like UK, Singapore and Hong Kong, only a handful of specialists after successful completion of a minimum training can administer sedation.

Another difference is in terminologies being followed, medications and routes being employed as well as in levels of sedation. In USA, AAP, American Society of Anesthesiologists (ASA) and the Joint Commission of Accreditation of Healthcare Organizations all agreed to abandon the use of oxymoron term 'Conscious sedation' and replace it with more appropriate term 'moderate sedation'.[75] On the other hand, this contradictory term is still being used in most of the Europe. Further, as per the updated American set of guidelines children aged <6 years usually require levels of anesthesia consistent with deep sedation to successfully complete most procedures in an emotionally comforting way not only for child and caretakers but for providers as well.[75] On the other hand Europeans believe that 'deep sedation' is consistent with levels of complete anesthesia and thus this state of sedation is rarely intentionally achieved. 'Conscious sedation', as they call, is the desired state on sedation continuum to be maintained for any dental intervention.[76] Unfortunately, evidence to establish the safe sedation techniques are nonexistent despite vast data in pediatric dental sedation research.[77] One practice that is majorly uniform cross-countries is monitoring practice which comprises of pulse oximetry, cardiac monitoring and dedicated sedation staff. The only way to have universally accepted uniform set of standard practice guidelines is to simulate research in deficient areas.

FUTURE PERSPECTIVE

The recently updated Cochrane review highlighted the need for quality research to collect evidence for efficacy of sedative agents used in pediatric dentistry. Out of plethora of vast majority of research papers, only a few could be pooled to collect weak evidence in favor of efficacy of oral midazolam.

Fortunately, there is sufficient evidence to ensure safety of midazolam and nitrous oxide sedation and analgesia.[78]

There is a definite need to improve pediatric dental sedation research to collect evidence on which a new set of standard practice guidelines can be formed. In addition to build evidence on efficacy and safety of sedative agents, there is a need to simulate research in deficient areas, such as:

- Development of assessment tool for indication for treatment under sedation
- Role of fasting in sedation
- Effect of restraint on sedation
- Feasibility of target controlled anesthesia with propofol in pediatric population
- Development of best tool to judge sedation depth appropriately, such as sedation scale or bispectral index.[79]

CONCLUSION

With the progression of time, as the newer agents and techniques will be introduced, pediatric dental sedation practice will keep on acquiring new faces. Newer agents, such as dexmedetomidine and newer techniques of administration of older agents, such as target controlled anesthesia with propofol might claim an upward rank in pharmacopoeia for pediatric dental sedation. An ardent vigilance and surge of newer dedicated quality research to build evidence for establishment of updated uniform policy statements will let our children sleep peacefully for their dental rehabilitation.

REFERENCES

1. Sheller B. Challenges of managing child behavior in the 21st century dental setting. Pediatr Dent 2004;26(2):111-113.
2. Bross DC. Managing pediatric dental patients: issues raised by the law and changing views of proper child care. Pediatr Dent 2004;26(2):125-130.
3. Pinkham JR. Fear of dentistry: a discussion of its usefulness to certain dental patients. ASDC J Dent Child 1983;50(2):111-113.
4. Wilson S. Pharmacological management of the pediatric dental patient. Pediatr Dent 2004;26(2):131-136.
5. Curson I, Coplan MP. The need for sedation in conservative dentistry. An investigation in the inner London area. Br Dent J 1970;128(1):19-22.
6. Folayan MO, Faponle A, Lamikanra A. A review of the pharmacological approach to the management of dental anxiety in children. Int J Paediatr Dent 2002;12(5):347-354.
7. Ustun Y, Gunduz M, Erdogan O, Benlidayi ME. Dexmedetomidine versus midazolam in outpatient third molar surgery. J Oral Maxillofac Surg 2006;64(9):1353-1358.
8. Mittal NP, Goyal M. Dexmedtedomidine: a potential agent for use in procedural dental sedation. Ind J Dent 2014;5:21-27.
9. Al Taher WMA, Mansour EE, El Shafei MN. Comparative study between novel sedative drug (dexmedetomidine) versus midazolam-propofol for conscious sedation in pediatric patients undergoing oro-dental procedures. Egypt J Anaesthesia 2010;26(4):299-304.
10. Krauss B, Green SM. Procedural sedation and analgesia in children. Lancet 2006;367(9512):766-780.
11. Kapur A, Chawla SH, Goyal A, Gauba K, Bhardwaj N. Efficacy and acceptabilty of oral-transmucosal midazolam as conscious sedation agent in pre-school children. J Indian Soc Pedod Prev Dent 2004;22(3):109-113.
12. Johnson E, Briskie D, Majewski R, Edwards S, Reynolds P. The physiologic and behavioral effects of oral and intranasal midazolam in pediatric dental patients. Pediatr Dent 2010;32(3): 229-238.
13. Bryson MH , Fulton RB, Faulds D. Propofol an update of its use in anesthesia and conscious sedation. Drugs 1995;50(3):513-559.
14. Da Costa LR, da Costa PS, Lima AR. A randomized double-blinded trial of chloral hydrate with or without hydroxyzine versus placebo for pediatric dental sedation. Braz Dent J 2007; 18(4):334-340.
15. Kantovitz KR, Puppin-Rontani RM, Gaviao MB. Sedative effect of oral diazepam and chloral hydrate in the dental treatment of children. J Indian Soc Pedod Prev Dent 2007;25(2):69-75.
16. Reeves ST, Wiedenfeld KR, Wrobleski J, Hardin CL, Pinosky ML. A randomized double-blind trial of chloral hydrate/hydroxyzine versus midazolam/acetaminophen in the sedation of pediatric dental outpatients. ASDC J Dent Child 1996;63(2):95-100.
17. Nathan JE. Management of the refractory young child with chloral hydrate: dosage selection. ASDC J Dent Child 1987; 54(2):93-100.
18. Coté CJ. Sedation for pediatric dental patients: a review. Pediatr Clin North Am 1994;41(1):31-35.
19. Olson DM, Sheehan MG, Thompson W, Hall PT, Hahn J. Sedation of children for electroencephalograms. Pediatrics 2001; 108(1):163-165.
20. Greenberg SB, Faerber EN, Aspinall CL, Adams RC. High-dose chloral hydrate sedation for children undergoing MR imaging: safety and efficacy in relation to age. AJR Am J Roentgenol 1993; 161(3):639-641.
21. Jastak JC, Pallasch T. Death after chloral hydrate sedation: report of a case. J Am Dent Assoc 1988;116(3):345-348.
22. Malviya S, Voepel-Lewis T, Tait AR. Adverse events and risk factors associated with the sedation of children by non-anesthesiologists. Anesth Analg 1997;85(6):1207-1213.
23. Cote CJ, Karl HW, Notterman DA, Weinberg JA, McCloskey C. Adverse sedation events in pediatrics: analysis of medications used for sedation. Pediatrics 2000;106(4):633-644.
24. American Academy of Pediatrics Committee on Drugs. Use of chloral hydrate for sedation in children. Pediatrics 1993;92(3): 471-473.
25. Malamed SF. Sedation: a guide to patient management. 5th ed. Missouri: Mosby Elsevier; 2010.p.624.
26. Shapira J, Holan G, Botzer E, Kupietzky A, Tal E, Fuks AB. The effectiveness of midazolam and hydroxyzine as sedative agents for young pediatric dental patients. ASDC J Dent Child 1996; 63(6):421-425.
27. Braham RL, Bogetz MS, Kimura M. Pharmacological patient management in pediatric dentistry: An Update. ASDC J Dent Child 1993;60(4-5):270-280.
28. Cathers JW, Wilson CF, Webb MD, Alvarez ME, Schiffman T, Taylor S. A comparison of two meperidine/hydroxyzine sedation regimens for the uncooperative pediatric dental patient. Pediatr Dent 2005;27(5):395-400.
29. Singh N, Pandey RK, Saksena AK, Jaiswal JN. A comparative evaluation of oral Midazolam with other sedatives as premedication in pediatric dentistry. J Clin Ped Dent 2002;26(2):161-164.
30. Lindsay SJ, Roberts GJ. Methods for behaviour research on dentally anxious children. The example of relative analgesia. Br Dent J 1980;149(6):175-179.

31. Gallardo F, Cornejo G, Auil B. Premedication with flunitrazepam, diazepam and placebo in the apprehensive child. ASDC J Dent Child 1984;51(3):208-210.
32. Tsinidou KG, Curzon ME, Sapsford DJ. A study to compare the effectiveness of temazepam and a chloral hydrate/hydroxyzine combination in sedating paediatric dental patients. Int J Paediatr Dent 1992;2(3):163-169.
33. Quarnstrom FC, Milgrom P, Moore PA. Experience with triazolam in preschool children. Anesth Pain Control Dent 1992;1(3):157-159.
34. Wood M. The safety and efficacy of using a concentrated intranasal midazolam formulation for paediatric dental sedation. SAAD Dig 2011;27:16-23.
35. Kapur A, Chawla SH, Goyal A, Gauba K, Bhardwaj N. Efficacy and acceptabilty of oral-transmucosal midazolam as a conscious sedation agent in pre-school children. J Indian Soc Pedod Prev Dent 2004;22(3):109-113.
36. Richter JJ. Current theories about the mechanism of benzodiazepine and neuroleptic drugs. Anesthesiology 1981;54(1):66-72.
37. Costa LR, Costa PS, Brasileiro SV, Bendo CB, Viegas CM, Paiva SM. Post-discharge adverse events following pediatric sedation with high doses of oral medication. J Pediatr 2012;160(5): 807-813.
38. Wilson KE, Girdler NM, Welbury RR. Comparison of oral midazolam and nitrous oxide sedation for dental extractions in children. Anaesthesia 2006;61(12):1138-1144.
39. Mittal N, Goyal A, Gauba K, Kapur A, Jain K. A double blind randomized trial of Ketofol versus Propofol in anxious pediatric patients. J Clin Pediatr Dent 37(4):415-420.
40. Bahetwar SK, Pandey RK, Saksena AK, Chandra G. A comparative evaluation of intranasal midazolam, ketamine and their combination for sedation of young uncooperative pediatric dental patients: a triple blind randomized crossover trial. J Clin Pediatr Dent 2011;35(4):415-420.
41. Hand D, Averley P, Lyne J, Girdler N. Advanced paediatric conscious sedation: an alternative to dental general anaesthetic in the UK. SAAD Dig 2011;27:24-29.
42. Billmire DA, Neale HW, Gregory RO. Use of IV fentanyl in the outpatient treatment of pediatric facial trauma. J Trauma 1985;25(11):1079-1080.
43. Aroni F, Iacovidou N, Dontas I, Pourzitaki C, Xanthos T. Pharmacological aspects and potential new clinical applications of ketamine: reevaluation of an old drug. J Clin Pharmacol 2009; 49(8):957-963.
44. Giovannitti AJ. Dental anesthesia and pediatric dentistry. Anesth Prog 1995;42:95-99.
45. Green SM, Roback MG, Krauss B, Brown L, McGlone RG, Agrawal D, McKee M, Weiss M, Pitetti DR, Hostetler AM, et al. Predictors of emesis and recovery agitation with emergency department ketamine sedation: an individual-patient data meta-analysis of 8,282 children. Ann Emerg Med 2009;54(2):171-180.
46. Green MS, Roback GM, Krauss B, Brown L, McGlone GR, Agrawal D, McKee M, Weiss M, Pitetti DR, Hostetler AM, et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. Ann Emerg Med 2009;54(2):158-168.
47. Green SM, Roback MG, Krauss B. Emergency department ketamine meta-analysis study group. Laryngospasm during emergency department ketamine sedation a case-control study. Pediatr Emerg Care 2010;26(11):798-802.
48. Smith JA, Santer LJ. Respiratory arrest following intramuscular ketamine injection in a 4-year-old child. Ann Emerg Med 1993; 22(3):613-615.
49. Van Hamelrijck J, Muller P, Van Aken H, White PF. Relative potency of eltanolone, propofol and thiopental for induction of anesthesia. Anesthesiology 1994;80(1):36-40.
50. Leslie K, Crankshaw DP. Potency of propofol for loss of consciousness after a single bolus dose. Br J Anesth 1990;64: 743-746.
51. Naguib M, Sari-Kouzel A, Seraj M, El-Gammal M, Gomma M. Induction dose-responses studies with propofol and thiopentone. Br J Anesth 1992;68(3):308-310.
52. Havel CJ, Strait RT, Hennes H. A clinical trial of propofol vs midazolam for procedural sedation in a pediatric emergency department. Acad Emerg Med 1999;6(10):989-997.
53. Vespasino M, Finkelstein M, Kurachek M. Propofol sedation: intensivists' experience with 7304 cases in a children's hospital. Pediatrics 2007;120(6):e1411-e1417.
54. Disma N, Astuto M, Rizzo G, Rosano G, Naso P, Aprile G, Bonanno G, Russo A. Propofol sedation with fentanyl or midazolam during oesophagogastroduodenoscopy in children. Eur J Anaesthesiol 2005;22(11):848-852.
55. Paspatis GA, Charoniti I, Manolaraki M, Vardas E, Papanikolaou N, Anastasiadou A, Gritzali A. Synergistic sedation with oral midazolam as a premedication and intravenous propofol versus intravenous propofol alone in upper gastrointestinal endoscopies in children: a prospective, randomized study. J Pediatr Gastroenterol Nutr 2006;43(2):195-199.
56. Sakata RK. Analgesia and sedation in intensive care unit. Rev Bras Anestesiol 2010;60(6):648-658.
57. Hall RW, Shbarou RM. Drugs of choice for sedation and analgesia in the neonatal ICU. Clin Perinatol 2009;36(2):215-226.
58. Hosey TM, Makin A, Jones MR, Gilchrist F, Carruthers M. Propofol intravenous conscious sedation for anxious children in a specialist paediatric dentistry unit. Int J Paediatr Dent 2004; 14(1):2-8.
59. Hallonsten AL. Nitrous oxide oxygen sedation in dentistry. Swed Dent J Suppl 1982;14:s9-10.
60. Soldani F, Manton S, Stirrups DR, Cumming C, Foley J. A comparison of inhalation sedation agents in the management of children receiving dental treatment: a randomized, controlled, cross-over pilot trial. Int J Paediatr Dent 2010;201:65-75.
61. Standing dental advisory committee. General anaesthesia, sedation and resuscitation in dentistry. Report of an expert working party. London: Department of Health, 1990.
62. Department of Health. A conscious decision: A review of the use of general anaesthesia and conscious sedation in primary dental care. Report of a group chaired by the chief medical and chief dental officer. 2000. Available at: http://www.dh.gov.uk/Publications and Statistics/Publications. Accessed on 20 February 2013.
63. Hosey MT. UK National Clinical Guidelines in Paediatric Dentistry. Managing anxious children: the use of conscious sedation in paediatric dentistry. Int J Paediat Dent 2002;12(5):359-372.
64. Scottish intercollegiate guidelines network. Safe sedation of children undergoing diagnostic and therapeutic procedures 2002; Revised on 2004. Available at: http://www.sign.ac.uk/guidelines/fulltext/58/index.html. Accessed on 20 February 2013.
65. Standing dental advisory committee, department of health. conscious sedation in the provision of dental care. Report of an expert group on sedation for dentistry. 2003. Available at: http://www.dh.gov.uk/PublicationsAndStatistics?Publications. Accessed on 20 February 2013.
66. General dental council. Standards for dental professionals, 2005. Available at: http://www.gdcuk.org/News+publications+and+events/Publications/Guidance+documents. Accessed on 20 February 2013.

67. Scottish dental clinical effectiveness programme, national dental advisory committee. Conscious sedation in dentistry, dental clinical guidance, 2006. Available at: http://www.scottishdental.org/cep. Accessed on 20 February 2013.
68. Committee on drugs, section on anesthesiology, American academy of pediatrics. Guidelines for the elective use of conscious sedation, deep sedation, and general anesthesia in pediatric patients. Pediatrics 1985;76:317-321.
69. American academy of pediatric dentistry. Guidelines for the elective use of conscious sedation, deep sedation, and general anesthesia in pediatric patients. ASDC J Dent Child 1986;53:21-22.
70. American academy of pediatrics committee on drugs: guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures. Pediatrics 1992;89:1110-1115.
71. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004-1017.
72. Guidelines for the elective use of conscious sedation, deep sedation, and general anesthesia in pediatric dental patients. Reference Manual 1999-2000. American Academy of Pediatric Dentistry, 1998:68-73.
73. Cote´ CJ, Wilson S. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. Pediatrics 2006;118:2587-2602.
74. Cote´ CJ. Sedation protocols-why so many variations? Pediatrics 1994;94:281-283.
75. Cote´ CJ. Round and round we go: sedation-what is it, who does it, and have we made things safer for children? Pediatr Anesth 2008;18:3-8.
76. Holroyd I. Conscious sedation in pediatric dentistry. A short review of the current UK guidelines and the technique of inhalational sedation with nitrous oxide. Pediatric Anesthesia 2008; 18(1):13-17.
77. Lourenço-Matharu L, Ashley PF, Furness S. Sedation of children undergoing dental treatment. Cochrane Database Syst Rev 2012; 14:CD003877.
78. Papineni A, Lourenço-Matharu L, Ashley PF. Safety of oral midazolam sedation use in paediatric dentistry: a review. Int J Paediatr Dent 2014;24(1):2-13.
79. Goyal A, Mittal N, Mittal P, Gauba K. Bispectral Index: Validity and utility in pediatric dental sedation. J Clin Pediatr Dent 2014; 38(4):290-295.