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Original Article

Safety of deep intravenous propofol sedation in the dental treatment of children in the outpatient department

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KEYWORDS
Deep intravenous sedation;
Propofol;
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Complication

Abstract *Background/purpose:* Intravenous sedation with propofol in the dental treatment offers an alternative to inhalation sedation or general anesthesia. The aim of this study was to evaluate the safety and identify risk factors for intraoperative complications.

Materials and methods: Uncooperative children who could not complete dental treatment under non-pharmacological behavior management or mild-to-moderate sedation in the outpatient pediatric department were selected. Details and time of dental treatment; intraoperative vital signs data, including blood pressure, heart rate, respiratory rate, pulse oxygen saturation (SpO_2), end-tidal carbon dioxide, and electrocardiogram; and incidence of intraoperative and postoperative complications were recorded.

Results: Overall, 344 children were selected, with 342 completing dental treatment. The dental treatment time was 20–155 (median, 85; interquartile range, 70–100) min. The number of treated teeth was at least 1 and at most 13 (median, 6; interquartile range, 5–8). Among 342 children, 35 (10.2%) had their treatment interrupted temporarily due to choking cough. No serious complications occurred; the incidence rate of minor complications was 47/342 (13.7%). Tachycardia was observed in 5/342 (1.5%) cases, oxygen desaturation ($SpO_2 < 95\%$) in 18, and hypoxemia ($SpO2 \leq 90\%$) in 25. The treatment duration was significant longer in cases with than without complications ($P < 0.05$), and children coughing during treatment

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were more likely to have complications ($P < 0.05$). Postoperative restlessness occurred in six children, but there was no vomiting, aspiration, or respiratory obstruction.
Conclusion: Decreased oxygen saturation is the most common complications. Cough during treatment and longer treatment duration were risk factors for complications.

Introduction

Oral drug sedation, nitrous oxide inhalation sedation, intravenous sedation, and general anesthesia are commonly used pharmacological behavior management methods for dental treatment of uncooperative children in outpatient departments.

Some studies suggest that intravenous sedation by propofol target-controlled infusion (TCI) is effective for managing dentally anxious adults and adolescents as a safe alternative to general anesthesia.[1–3] However, the depth of sedation in previous reports is mostly moderate and conscious. Furthermore, some children still cannot complete dental treatment under moderate sedation, and deeper sedation levels, including deep sedation, may be required.

Deep sedation is a drug-induced depression of consciousness during which patients cannot be easily aroused but may respond purposefully following repeated verbal or painful stimulation. The ability to maintain independent ventilatory function may be impaired. Patients may require assistance in maintaining patent airway regardless of the procedure and practitioner manipulation, and spontaneous ventilation may be inadequate. However, cardiovascular function is usually unaffected. Reflex withdrawal from a painful stimulus may occur, although it is not considered a high-functioning and purposeful response and may be accompanied by partial or complete loss of protective airway reflexes.[4]

The incidence of adverse events in pediatric intravenous sedation may be higher than that in adults; the most common adverse events are vomiting, agitation, hypoxia, and apnea.[5] The disadvantages of using propofol include hypotension, apnea, and airway obstruction.[6] The American Academy of Pediatrics (AAP) proposed that children younger than 6 years (particularly younger than 6 months) may have greater risks of adverse events because they are particularly vulnerable to the effects of sedative medications on respiratory drive, airway patency, and protective airway reflexes.[7]

During oral treatment, water mist and tooth debris produced by cutting and the pressure on the jaw lead to cough and affect airway patency; opening the airway by head tilt and jaw lift poses a dilemma as it also increases the potential for aspiration of pooled fluid in the upper airway and increase in susceptibility to coughing spells, possibly leading to decreased blood oxygen saturation.[3,8] During office-based propofol sedation for dental care, the most stringent attention should be paid to preventing aspiration of fluids retained in the pharynx, airway obstruction owing to therapeutic maneuvers, and respiratory inhibition inherent to sedation because the airway is patent during sedation.[3,9]

Therefore, we investigated the safety of deep intravenous propofol sedation in outpatient dental treatment of uncooperative children and identified factors for complications during treatment.

Materials and methods

This study was performed at the department of Pediatric Dentistry and Anesthesiology, Peking University School and Hospital of Stomatology, and was approved by the ethics committee of the hospital (ref no. PKUSSIRB-201626005). The guardians of all patients signed informed consent. Uncooperative children in the outpatient pediatric department were selected for dental treatment under deep intravenous sedation during January 2016—December 2020.

The following children were included:

1. Children aged >2.5 years.
2. Children with treatment failure who underwent non-pharmacologic behavior management.
3. Children who could not be sedated with nitrous oxide or oral drugs owing to age or other reasons.

The following patients were excluded[4,10]:

1. Patients with American Society of Anesthesiologists (ASA) grade III or above.
2. Patients with diseases affecting airway patency, including severe adenoid or tonsillar hypertrophy; sleep apnea; small mandible, congenital malformation, and other difficult airway; morbid obesity (aged under 5 years, defined as a Body Mass Index (BMI) z-score >3 SD than the reference median, and over 5 years, defined as a BMI z-score >2 SD than the reference median)[11,12]; and recent upper respiratory tract infection.
3. Patients with a history of narcotic drug allergies.
4. Patients with other general conditions not suitable for drug sedation.

Intravenous sedation and treatment process

All anesthesia procedures were conducted by an anesthetist. Thirty minutes before venepuncture, 2 μg/kg of dexmedetomidine (Jiangsu Hengrui Medicine Co., Ltd., Lianyungang, China) was administered intranasally or 0.5 mg/kg of midazolam (Jiangsu Nhwa Pharmaceutical

Co., Ltd., Xuzhou, China) was administered orally, according to the degree of cooperation of the children to achieve basic sedation.

Once the child was calm or asleep, venepuncture was performed. If the child was unable to cooperate with the venepuncture or refused to accept the oral or intranasal sedation before the operation, mask inhalation of sevoflurane (SEV) was used to induce sleep before reattempting venepuncture. Propofol was injected using TCI (CP660TCI, Beijing slgo Medical Technology Co., Ltd., Beijing, China) during the operation; the concentration of the effect-site was 2–3 μg/ml. The TCI was set according to body weight, length, age, and sex; and the concentration was titrated based on the sedation depth which was monitored using the Bispectral index (BIS) (Covidienprivate Ltd., Singapore) and patient response. The targeted BIS value was 50–70.

A rubber dam was used to isolate most of the exogenous water and debris and avoid the accumulation thereof in the oropharynx. If the rubber dam could not be inserted, measures such as strengthening suction and gauze isolation were instituted to prevent aspiration. Local anesthesia was administered before painful stimulation. During deep sedation, airway monitoring was continuously performed using end-tidal carbon dioxide (ETCO2) (Vamos, Drägerwerk AG & Co. KGaA, Lübeck, Germany). If necessary, temporary airway assistance was provided, such as head tilt and chin lift procedures.[4] Protective stabilization was applied throughout the treatment to prevent involuntary movements.[10] If transient respiratory depression occurred, treatment was suspended and sedation depth lightened. Face mask oxygen ventilation was used when necessary. During treatment, patients maintained spontaneous breathing and 100% oxygen was continuously inhaled through nasal cannulae. Vital signs including blood pressure (BP), heart rate (HR), respiratory rate, electrocardiogram, and pulse oximetry saturation (SpO2) were monitored continuously (BSM-6501C; Nihon Kohden Corporation, Tokorozawa city, Japan). If respiratory suppression continued or airway obstruction was unresolved, general anesthesia (GA) using a laryngeal mask airway (LMA) or endotracheal (ET) intubation was used. After the operation, the children were transferred to the recovery room, and their vital signs were monitored. Oxygen was continuously inhaled by the patients until they were fully awake.

Adverse events

Persistent laryngeal spasm, cardiac arrest, and a need for emergency ET intubation during treatment were classified as serious adverse events. Minor cardiovascular complications included tachycardia (HR $>$ 120 beats/minute) and bradycardia (HR $<$ 60 beats/minute). Oxygen desaturation was defined as SpO_2 90–95%, while hypoxemia was defined as $SpO_2 \leq 90\%$ for at least 10 s.

Data recording and analysis

We observed and recorded whether the treatment was completed successfully and the number, type, and duration of tooth treatment. Data regarding the following were recorded: BP, HR, SpO_2, $ETCO_2$, BIS, cough, body movements, airway obstruction during the operation, postoperative restlessness, vomiting, aspiration, and other complications. Postoperative restlessness was scored according to the Riker sedation-agitation scale.

All statistical analyses were performed using SPSS 26.0 (IBM, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to test data normality. Differences in characteristics between patients with and without complications were analyzed using the chi-square test (for categorical variables) and Mann–Whitney U test (for continuous variables). Statistical significance was set at *P*-values <0.05.

Results

Overall, 344 children, including 235 males and 109 females with ages ranging from 2.8 to 16.1 years (median, 4.9; interquartile range [IQR], 4.3–5.9), were selected. Two of the selected patients underwent GA using a LMA because of obvious snoring after sedation (before the dental treatment) and difficult airway maintenance. Hence, 342 children (234 males and 108 females), aged between 2.8 and 16.1 years (median, 4.9; IQR, 4.3–5.9), completed the dental treatment under deep intravenous sedation, among whom 37 (10.8%) had neurological disorders, including 30 with autism spectrum disorder, six with intellectual disability, two with Angelman syndrome, and one with Tourette syndrome. After basic sedation, 230 (67.3%) children accepted the venepuncture, while 112 (32.7%) could not, and after inhalation of SEV, venepuncture was performed.

The duration of dental treatment was 20–155 min (median, 85; IQR, 70–100). The number of treated teeth was at least 1 and at most 13 (median, 6; IQR, 5–8). Overall, 2155 teeth were treated in this study. The treatment protocols used are shown in Fig. 1.

Among 342 children, treatment was temporarily interrupted due to choking or cough in 35 children (10.2%), which stopped after treatment was suspended and oral suctioning was performed. Among the 35 children, sputum was found in 4 patients during suctioning, while 1 patient experienced gingival bleeding and overflow into the pharyngeal cavity.

No serious complications occurred in any patients who completed treatment. The incidence of complications is

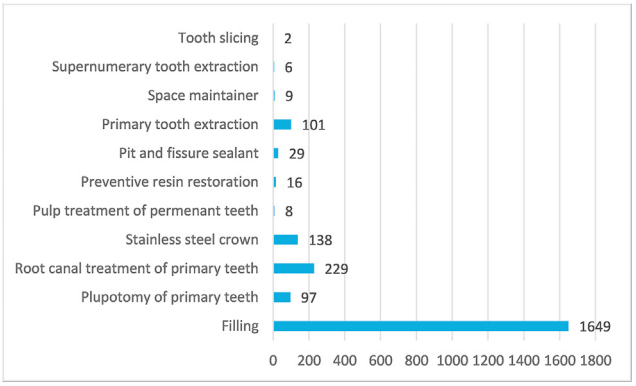

Figure 1 Frequency of the different types of dental treatment.

summarized in Table 1. The lowest recorded reading of SpO_2 was 52% in one case. However, all patients with complications recovered within 30 s after the operation was suspended. Among them, 7 cases received face mask oxygen, while others were treated by suctioning of the pharyngeal cavity combined with the head-tilt-chin-lift maneuver.

The Mann–Whitney U test showed that the treatment duration was significantly longer in cases which developed complications ($P < 0.05$). There was no statistically significant difference in the age and number of treated teeth between patients with and without complications (Table 2).

The chi-square tests found that children who cough during treatment were more likely to have complications ($P < 0.05$) (Table 3). In addition, postoperative restlessness occurred in six children, but vomiting, aspiration, or respiratory obstruction was not observed.

Discussion

Dental treatment of uncooperative children has always been a challenge for clinicians in pediatric dentistry. For such patients, forceful treatment methods with protective stabilization[13–15] or dental treatment under sedation or GA are used.[16–19] Oral sedation with benzodiazepines and inhalational conscious sedation with nitrous oxide-oxygen are the most commonly used methods in uncooperative patients. However, the use of this sedation is not possible in all children, especially in children with intellectual disabilities or young children. Intravenous sedation can be an alternative to allow dental treatment to be conducted in totally uncooperative patients or in patients with special medical conditions.[20] Compared with oral sedation and nitrous oxide-oxygen inhalational sedation, intravenous sedation has the advantages of rapid onset, effective, controllable anesthesia time, easy titration, and anesthesia depth adjustment.

However, an important concern is the complications associated with dental treatment under deep intravenous sedation. Some scholars propose that the incidence of complications in children undergoing procedural sedation (especially deep sedation) may be higher than that in adults.[5,21,22]

Respiratory problems are the most reported side effects in children undergoing intravenous sedation (5.5–31.7%).[23] Herein, a decrease of blood oxygen saturation was observed in 12.6% (43/342) of cases; however, all recovered within 30 s. The lowest pulse oximetry readings of 7 children were below 70%, the lowest of which was 52% in one case who required face mask oxygen, while the others recovered after the operation was stopped and a jaw thrust performed. The AAP have suggested that the vast majority of sedation complications can be managed with simple methods, such as supplemental oxygen provision, airway opening, suctioning, oral or nasopharyngeal airway placement, and bag-mask-valve ventilation.

Cough during the operation was closely related to complications. Both swallowing and coughing reflexes are important airway protective mechanisms that clear the larynx and upper airways of excessive saliva and secretions and/or foreign matter.[24] In situations such as deep sedation, these reflexes are depressed, which may prevent patients from protecting their own airways, thus allowing secretions and foreign matter to enter the airways, resulting in decreased oxygenation. Despite this, patients may still cough during procedures.

An important cause for coughing maybe the water nebulized during the procedure. It has been pointed out that airway restriction may be related to events associated with the dental procedure, such as the presence of blood, increased secretions, and exogenous water.[25] Kohjitani et al. investigated the relationship between the frequency of coughing episodes and intraoral use of water, and water remaining in the oropharyngeal space under intravenous sedation. They found that the amount of oropharyngeal suctioning was significantly correlated with intraoral use of water, and the frequency of coughing episodes was significantly correlated with the amount of oropharyngeal suctioning per minute, suggesting that the accumulation of water in the oropharynx increased vulnerability to the cough reflex in dental treatments performed under intravenous sedation.[9] Sputum was found in 4 children during suctioning, and their SPO_2 decreased below 70%, suggesting that children should be screened for a history of recent or

Table 1 Complications during dental treatment.

Complications		Yes (n)			No (n)
Cardiovascular events	Tachycardia	5			337
	Bradycardia	0			342
Respiratory events	Oxygen desaturation ($SpO_2 < 95\%$)	18			299
	Hypoxemia ($SpO_2 \leq 90\%$)	≤90% 12	≤80% 6	≤70% 7	

SpO_2, pulse oximetry saturation.

Table 2 Univariate analysis of complications.

Complications	Age (years)[a]	Treatment teeth (n)	Treatment duration (min)
Yes	4.9 (4.2; 6.0)	7 (5; 8)	90.0 (75.0; 110.0)
No	4.9 (4.3; 5.9)	6 (5; 8)	85.0 (65.0; 95.0)
P	0.800	0.223	0.041

[a] Values are represented as median and interquartile ranges at 25% and 75%.

Table 3 Univariate analysis of complications.

Complication	Systemic disease		Cough during treatment		Inhalation of SEV	
	Yes	No	Yes	No	Yes	No
Yes	4	43	26	21	14	33
No	33	262	9	286	98	197
P	0.801		0.000		0.739	

SEV, sevoflurane.

current respiratory tract infection before treatment. Mallory et al. reported that upper respiratory tract infections are significant predictors of adverse events during procedural sedation in children.[22]

It is noted, however, that a rubber dam was not used in most studies reviewed as the authors believed that it may hinder emergency maneuvers if adverse events occur. In the event oxygen desaturation, the patient needs oxygen administration and removal of the rubber dam may delay this maneuver, and that the oropharynx could not be cleaned easily.[23,25] We used a rubber dam in most of the procedures, especially those which would produce a greater quantity of water mist, as the rubber dam isolates most of the exogenous water, avoiding the accumulation thereof in the oropharynx, and reduces the occurrence of cough. Furthermore, when breathing problems occurred, we found that removing the rubber dam did not impact the anesthetist's ability to institute emergency treatment.

This study also found that the treatment duration was longer in patients with complications than those without. The disadvantages of propofol include respiratory depression and airway obstruction, which can lead to hypoxemia.[6] During longer dental treatments, a higher dose of propofol is often required. This can lead to deeper sedation which could cause greater respiratory depression.[26] Additionally, the possibility of increased salivary secretion and accumulation in the oropharynx with greater duration of treatment can result in a greater incidence of adverse respiratory events.

Another adverse event found was tachycardia, which was observed in 5 (1.5%) cases. One was a 2.8-year-old child who developed a tachycardia of 121 beats/min. Since the HR of younger children is faster, the tachycardia of this child may be due to individual and age-related differences. One child developed tachycardia due to decreased oxygen saturation after coughing. In three children, tachycardia occurred when the pulp was exposed during endodontic treatment, which was likely caused by pain due to poor local anesthesia.

Other similar studies have suggested that age may be related to the risk for complications.[10,21,22] In this study, there was no significant difference in the incidence of complications among age groups; however, this may be impacted by the fact that there was only a small number of young children (<4 years old) in this study. Further exploration in follow-up research is needed to clarify this association.

Although no serious complications occurred in this study, propofol sedation remains associated with adverse effects including airway obstruction and respiratory and cardiovascular suppression.[6,25] In children with respiratory, cardiac or metabolic conditions; or with diseases that affect airway patency, there is a higher risk of airway obstruction and hypoxemia. Hence, they are unsuitable for dental treatment under deep sedation, highlighting the importance of patient selection, preoperative assessment, close patient monitoring, and presence of an anesthetist throughout the procedure.[7]

No cough, throat pain, vomiting, aspiration, or respiratory obstruction was observed in any of the children. Propofol has antiemetic properties which reduces the occurrence of vomiting and nausea.[6] Moreover, there is a lower frequency of agitation upon awakening with the use of propofol than sevoflurane.[27] Since no ET intubation is performed during intravenous sedation, irritability caused by throat pain secondary to intubation is avoided. Some studies have shown that nausea and lethargy may occur within 24 h after sedation. Unfortunately, participants were only observed for 2 h after sedation. Therefore, our findings should be interpreted in the context of these limitations.

In conclusion, deep intravenous sedation with propofol allows dental treatments to be effectively performed in uncooperative pediatric patients in the outpatient department. The most common complication is the decrease of oxygen saturation. Cough during treatments is closely related to complications during treatment, and the longer the treatment duration, the more likely respiratory depression will occur. The study findings may promote the use of this method in dental treatment.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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