JKDSA 2014 ; 14(3) : 167-172

Original Article

Effect Site Concentrations of Propofol for Dental Treatment under Deep Sedation in Intellectually Disabled Patients

Brian Seonghwa Lee, Teo Jeon Shin*, Hyun-Jeong Kim, Yoon Ji Choi, Soo Eon Lee, Juhea Chang†, Kwang-Suk Seo

Department of Dental Anesthesiology, School of Dentistry, Seoul National University, *Department of Pediatric Dentistry, School of Dentistry, Seoul National University, †Clinic for Persons with Disabilities, Seoul National University Dental Hospital, Seoul, Korea

Background: Propofol is the most commonly used anesthetic for sedation and target-controlled infusion (TCI) is useful for dental treatment. However, it is important to assess and maintain an adequate depth of sedation in patients with severe intellectual disabilities Therefore, in this study we aimed to evaluate the adequate propofol target concentration for dental treatment in severely intellectually disabled patients.
Methods: We undertook retrospective review of the sedation records of severely intellectually disabled patients who underwent dental treatment under TCI propofol sedation from September 2011 to April 2012. We evaluated the initial target concentration, stabilized concentration of propofol and monitored vital signs, including BIS score using sedation records.
Results: Total 20 patients (10 male and 10 female patients) were included in the study. Every participant was severely intellectually disabled. The mean sedation duration was 70 ± 16 (45-100) minutes. The initial propofol target concentration infusion amount was 2.7 ± 0.45 (2.0-3.0) mcg/ml. The propofol effect site concentration (Ce) was 2.6 ± 0.7 (1.0-4.0) mcg/ml. The average value of BIS was 52.6 ± 13 (28-81). During the treatment period, there were no severe complications.
Conclusions: The average propofol Ce for deep sedation without any complications in intellectually disabled patients was 2.6 mcg/ml.

Key Words: Deep sedation; Mentally disabled persons; Propofol

INTRODUCTION

The need of receiving routine dental treatment for people with disabilities is very crucial to keep their oral health intact. However, in reality it has been reported in U.S department of Health and Human Services Health Resources Services Administration in 2001 that patients with special needs exhibited poor oral hygiene, more severe periodontal disease, more decayed tooth surfaces, and greater treatment needs than peoples without disabilities [1]. There are several elements inhibiting them to provide appropriate dental treatment such as psychological barriers, economic barriers, and educational efforts. However, one of the most barriers to receive treatment in the dental field is their behavioral management difficulties [2]. Disabled Patients who have severe anxiety, communication disabilities, and involuntary movement disorders might be arduous to provide normal dental treatment. Therefore, deep sedation or general anesthesia is considered as the first aid of treatment plan in many cases. Deep sedation or general anesthesia can offer certain degree of quality dental care without patient cooperation in the status of reduced or subdued body movement [3]. Moreover, It is helpful to induce a positive attitude toward future routine dental care [4].

Received: 2014. 9. 30. • **Revised:** 2014. 10. 1. • **Accepted:** 2014. 10. 2.
Corresponding Author: Kwang-Suk Seo, Department of Dental Anesthesiology, Seoul National University School of Dentistry, 28 Yeongeon-dong Jongno-gu, Seoul 110-768, Republic of Korea
Tel: +82.2.2072.0622 Fax: +82.2.766.9427 email: stone90@snu.ac.kr

Among various sedation techniques, intravenous sedation has been widely used to provide deep sedation to disabled patients [5]. Especially, target-controlled infusion (TCI) first reported has been widely used to titrate the intended sedative level [6]. Advance in drug delivery techniques has permitted the development of TCI system, with drugs delivered to reach and sustain specific target drug concentrations at the effect site. With the assistance of TCI system, it is possible to adjust and maintain the effect site concentration (Ce) of drugs incorporated within TCI system. Among the sedatives, the pharmacokinetic and pharmacodynamic (PK-PD) properties of propofol has been extensively investigated. With its favorable properties such as fast recovery, antiemetic effect, and fast titration, the use of propofol is increasing in the field of dentistry.

However, it is hard to assess and maintain an adequate depth of sedation in patients with intellectually disabled patients because of the problems with airway maintenance during dental treatments and inappropriate pain control. This unique feature in the disabled patients makes it difficult to evaluate the adequate effect-site concentration of propofol for maintaining sedation. Moreover, little has been reported about the proper dosage of both initial concentration and Ce during procedure for the disabled patients.

Therefore, in this study we aimed to evaluate the adequate propofol Ce for dental treatment in intellectually disabled patients who were conducted at Seoul National University Dental Hospital. We undertook retrospective review of the sedation service records of severely intellectually disabled patients over the age of 15 to analyze the extent of propofol Ce to be maintained in the deep sedation status.

PATIENTS AND METHODS

This study was approved by the institutional review board of Seoul National University Dental Hospital before the research. We reviewed all the charts of disabled patients over the age of 15 receiving propofol by use of TCI for deep sedation from Seoul National University Dental Hospital from September 1, 2011 to April 30, 2012.

1. Propofol TCI sedation for disabled patients

As patients with disabilities admitted to outpatients, we scheduled for the patients the available date and time of deep sedation after the evaluation of the patient's cooperation and the extent and degree of treatment invasiveness. Along with preoperative evaluation, we have conducted appropriate examination laboratory test for each patient. Also, we educated and scheduled patients to be presented the day after fasting, if needed.

In our institute, the sedation protocol for the disabled was standardized. In brief, for all patients we used Orchestra TCI syringe pump (Base Primia,Fresinius Kabi, France) and set pharmacokinetic model of 2% propofol (Fresenius Kabi, France) into Schnider model. After intravenous cannulation, we adjusted the initial propofol Ce 2-3 μg/ml according to the degree of cooperability. To provide an adequate sedation state, we adjusted propofol Ce 0.5 μg/ml per every step according to the sedative level. We provided 3-5 liters/min of oxygen through the nasal cannula and monitored the patients with noninvasive arterial blood pressure, ECG, pulse oximetry, carbon dioxide capnography, and BIS (bispectral index) monitors. If the patients achieved loss of consciousness and those statuses were stabilized, we offered appropriate amount of 2% lidocaine local anesthetic injection near the site of the pain to be induced. If patients regained consciousness during the procedure of dental treatment, their cooperation might

be impossible to achieve through their mobilization. It is crucial to maintain the depth of deep sedation and be supported by additional important indicators such as respiratory rate, airway maintenance, and vital signs. If appropriate level of sedation have been reached, we sustained the selected propofol Ce without changing it. If necessary, airway intervention or administration of other types of sedatives would be given during dental sedation. If the medical condition were met, we discharged patients to their home.

2. Data collection

We reviewed all disabled patients receiving propofol by use of target-controlled infusion for deep sedation from Seoul National University Dental Hospital with disabilities from September 1, 2011 to April 30, 2012. We collected the data regarding the changes in propofol target concentration and vital signs, propofol infusion duration, total sedation duration, dental treatment duration, recovery duration, and complications and types of disabilities and dental treatments. The detailed data that we collected were as follows

a. Initial propofol Ce and the changes in propofol Ce during dental treatment (Fig. 1)
b. Adverse effects occurred during sedation
c. Basic demographic data: patient's gender, age, body weight, height, and duration of the procedure
d. Hemodynamic data during sedation (heart rate, respiratory rate, arterial blood pressure, and blood oxygen saturation)
e. The bispectral index (BIS) data during sedation
f. Additional administration of other sedation medications and emergency aid
g. Recovery profiles at post-anesthetic care unit
h. The types of side effects during and after sedation

3. Statistical analysis

Characteristics of selected patients and categorical data were presented by frequency analysis. The continuous variables of propofol effect site target concentration were expressed as means ± standard deviation (S.D.) and showed the range between minimum and maximum

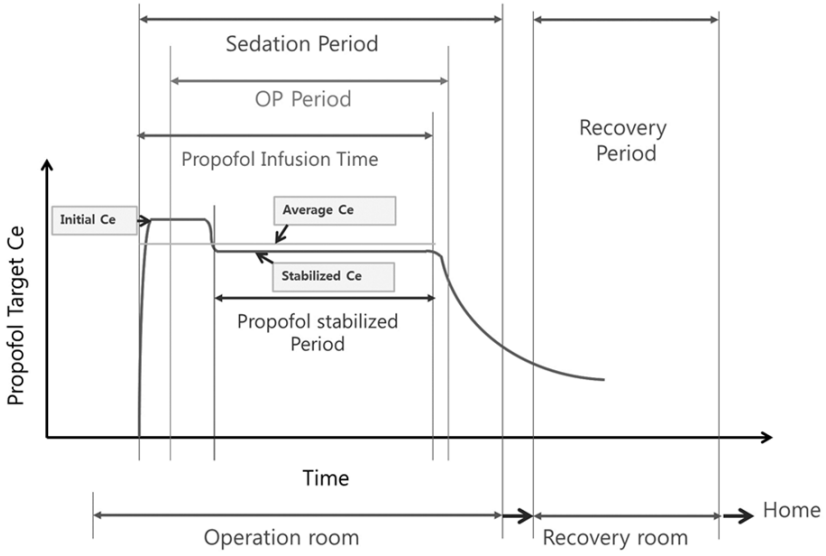

Fig. 1. Evaluation Indexes of propofol effect site concentration change and time variables (Note. Ce = effect-site concentration, initial Ce stands for an initial set target concentration in effect-site, stabilized Ce means an effect-site target concentration during dental treatment without patient mobilization nor side effect, and average Ce implies the mean concentration during total sedation period).

values. The ordinal data was presented as numbers (percentage).

RESULTS

Total 20 patients (10 male and 10 female patients) were included in the study. The ages of the patients were 36.6 ± 22 (15-80) years. Basic demographical data including weight, height, and ASA physical status classes were shown in Table 1. Every participant had severe intellectual disabilities who were 5 of mental retardation, 4 of autism, 5 of brain and cerebral palsy disorder, 2 of epilepsy, 2 of Down syndrome, and 2 of dementia patients. The kinds of dental treatment were cavity treatment, surgical tooth extraction, crown setting treatment, and scaling on Table 1. The initial propofol Ce was 2.7 ± 0.5 (2.0-3.0) μg/ml. The stabilized propofol Ce was 2.6 ± 0.7 (1.0-4.0) μg /ml. Sedation status and hemodynamic status during sedation were described in details on Table 2. The mean sedation duration was 70 ± 16 (45-100) minutes. All patients were hemodynamically stable during the treatment. The mean value of BIS was 52.6 ± 13 (28-81). During the treatment period, there were no sudden movement of the patients and severe airway obstruction. Every patient was discharged after a 1-hour period of recovery room stay without medical complications (Table 2).

Table 1. Characteristics of patients

Characteristics	Value
Male/Female	10/10
Age (yrs.)	36.6 ± 22 (15-80)
Weight (kg)	53.1 ± 13.0 (34-88)
Height (cm)	160 ± 11 (140 -178)
ASA Physical status I/II/III	4/13/2
Types of disabilities	
Autism	4
Mental retardation	5
Brain disorder, CP	5
Dementia	2
Down syndrome	2
Epilepsy	2
Types of dental treatment	
Surgical extraction	4
Scaling	3
Crown	8
Caries treatment	7

Values are mean ± SD, ASA PS stands for American society of Anesthesiologists patient status.

Table 2. Hemodynamic status and sedation duration

Characteristics	Value ± SD (Range)
Total Sedation Duration (min)	70 ± 16 (45-100)
Dental Treatment Duration (min)	42 ± 12 (25-70)
Recovery Room Stay (min)	44 ± 16 (25-90)
Systolic Blood Pressure (mmHg)	104 ± 15 (74-160)
Diastolic Blood Pressure (mmHg)	55 ± 14 (42-96)
Oxygen saturation (%)	98 ± 2 (95-100)
BIS	52.6 ± 13 (28-81)

Values are mean ± SD, BIS stands for the bispectral index.

DISCUSSION

In this study we suggest 3.0 mcg/ml as the initial propofol target concentration for target controlled infusion (TCI) in order to administer deep sedation during dental treatment for incooperative adult patient. Usually, the doctor who uses TCI infuser changes the target concentration according to state of sedation of patient during operation. But the initial target concentration of ordinary patient usually selected for the best concentration for fast induction and anesthesia stabilization. And, the initial target concentration could be adjusted according to the conditions of patients. At now, little has been reported about the proper dosage of initial target concentration for the disabled. Therefore, in this study the stabilized propofol effect-site concentration during dental treatment under deep sedation was 2.6 ± 0.7 (1.0-4.0) μg /ml, so initial propofol target concentration of 3.0 μg /ml even though there are indivisual variations among the cases. This target concentration would be meaningful for the doctors who want to administer propofol as anesthetics for deep sedation in special care dental clinic.

Sedation with TCI pump have been increasing recently. TCI of propofol for deep sedation has some

advantages such as fast induction, little intraoperative wakening and short recovery time for discharge when compared to manual infusion of the sedatives [7]. Averagely, when propofol infusion pump has been terminated patients recover less than 5 minutes in cases of short time sedation procedures [8]. It was because the continuous infusion pump controlled by pharmacokinetic parameters less fluctuated the peaks and valleys of drug concentrations in the plasma rather than the bolus technique [7]. Moreover, when we target the intended Ce with TCI, it is possible to titrate the effect depending on the sedation level that we target [8]. Theoretically, the concentration of the drug in the effect - site reflects the drug's effect. The Ce can be easily calculated just by linking the predicted plasma concentration to the effect-site compartment. There have been numerous literatures to investigate the PK-PD features of propofol [9]. TCI pump inversely calculates the infusion rate to reach the targeted Ce from the PK and PD parameters incorporated with the TCI pump. Titrating the sedative state of patient during operation can be easily achieved by changing effect-site concentration when using TCI pump for sedation. However, the PK and PD parameters of propofol incorporated into the TCI pump that we used in this study is estimated from ordinary patient, not disabled patient. At now, little has been reported about the proper dosage of Ce for the disabled to maintain deep sedation. In this study, propofol Ce was maintained within the range of 2.6 ± 0.7 (1.0-4.0) μg/ml for deep sedation during dental treatment, even though there are individual variations of propofol Ce among the cases.

Usually, TCI sedation with the mixture of propofol and remifentanil was widely used in the medical field and dentistry in order to control pain during procedure. In fact, opioids has side effect of respiration depression, so in case of conscious sedation the effect of respiratory suppression is minimal, on the level of deep sedation opioid could be dangerous. So effective local anesthesia was critical to achieve optimal sedation conditions.

In this study, the median propofol Ce was higher than that reported in previous studies. In a study of patient-maintained propofol TCI sedation for oral surgery, the median propofol Ce was 2 μg/ml (0.9-2.8 μg/ml) at the end of procedure [10]. In case of achieving conscious sedation, not deep sedation with propofol TCI during dental treatment, the median propofol Ce was 1.6 μg/ml in anxious group and 1.4 μg/ml in non-anxious group respectively [11].

We titrated propofol Ce to maintain deep sedation, not conscious sedation in this cases. In case of those who have behavioral disabilities, most disabled patients were possible to finish the treatment plan under deep sedation, not conscious sedation. It is highly likely that mentally disabled require higher sedative dose due to their lack of the ability to cooperate and higher level of anxiety.

In this study, the BIS value had very wide range (28-81) during sedation, because during deep sedation the target concentration was adjusted according to the sedation conditions such as treatment compliance, patient movement and side effect such as airway obstruction instead of BIS value. Also, BIS values was not fairly correlated with patient movement, and side effect such as airway obstruction. BIS value is not helpful as an indicator for maintaining deep sedation. In one study of deep sedation, BIS values showed a marked variability among individuals during deep sedation (5th-95th percentiles: 25-81) in agreement with our findings [12]. It is unclear why BIS had a wide variations while maintaining deep sedation. The algorithm of BIS is derived from the processed EEG of mentally intact, not disabled persons. Therefore, there is a possibility of falsely high or low BIS obtained from the disabled person. There have been literatures to report false BIS values in the disabled [13]. Therefore, BIS monitoring may be not suitable for indi-

cating an exact endpoint corresponding to deep sedation although further study is required to clarify this issue [12].

We have some limitations in our study. First, the study was retrospective in nature. The severity of mental disability and types of dental procedures were not controlled, making the interpretation of the results difficult. Second, there may be some bias to evaluate sedation depth for mentally disabled patients, especially severe mental disability. Moreover, BIS, widely used to monitor anesthetic depth, was not useful as an sedation depth indicator in our study. Therefore, a further prospective controlled study should be needed to investigate the range of propofol Ce for sedation depending on the severity of mental disability and dental procedures.

In conclusion, The average propofol Ce for deep sedation without any complications in intellectually disabled patients was 2.6 mcg/ml, and it was higher than those for dental treatment under conscious sedation without intellectual disability. However, using titration of target concentration, propofol TCI was a useful and safe method in their management during dental treatment.

참고문헌

1. Bonito AJ: Executive summary: dental care considerations for vulnerable populations. Spec Care Dentist 2002; 22(3 Suppl): 5S-10S.
2. Romer M: Consent, restraint, and people with special needs: a review. Spec Care Dentist 2009; 29(1): 58-66.
3. American Academy of Pediatric Dentistry. Clinical Affairs Committee-Sedation and General Anesthesia Subcommittee: Guideline on use of anesthesia personnel in the administration of office-based deep sedation/general anesthesia to the pediatric dental patient. Pediatr Dent 2012; 34(5): 170-2.
4. Caputo AC: Providing deep sedation and general anesthesia for patients with special needs in the dental office-based setting. Spec Care Dentist 2009; 29(1): 26-30.
5. Manley MC, Skelly AM, Hamilton AG: Dental treatment for people with challenging behaviour: general anaesthesia or sedation? Br Dent J 2000; 188(7): 358-60.
6. Schwilden H and Schuttler J: Target controlled anaesthetic drug dosing. Handb Exp Pharmacol 2008; (182): 425-50.
7. Casagrande AM: Propofol for office oral and maxillofacial anesthesia: the case against low-dose ketamine. J Oral Maxillofac Surg 2006; 64(4): 693-5.
8. Candelaria LM and Smith RK: Propofol infusion technique for outpatient general anesthesia. J Oral Maxillofac Surg 1995;53(2): 124-8; discussion 9-30.
9. Shafer A, Doze VA, Shafer SL, White PF: Pharmacokinetics and pharmacodynamics of propofol infusions during general anesthesia. Anesthesiology 1988; 69(3): 348-56.
10. Leitch JA, Sutcliffe N and Kenny GN: Patient-maintained sedation for oral surgery using a target-controlled infusion of propofol - a pilot study. Br Dent J 2003; 194(1): 43-5.
11. Oei-Lim VL, White M, Kalkman CJ, Engbers FH, Makkes PC and Ooms WG: Pharmacokinetics of propofol during conscious sedation using target-controlled infusion in anxious patients undergoing dental treatment. Br J Anaesth 1998; 80(3): 324-31.
12. Keyl C, Trenk D, Laule S, Schuppe C, Staier K, Wiesenack C, et al: Predicted and measured plasma propofol concentration and bispectral index during deep sedation in patients with impaired left ventricular function. J Cardiothorac Vasc Anesth 2009; 23(2): 182-7.
13. Duarte LT and Saraiva RA: When the bispectral index (bis) can give false results. Rev Bras Anestesiol 2009; 59(1): 99-109.