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치의학석사 학위논문

Effects site concentrations of propofol using target controlled infusion (TCI) in dental treatment under deep sedation between intellectual disability types

장애 종류에 따른 깊은진정 하 치과치료 시
프로포폴을 목표농도조절법으로 정주 시 효과치
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2019 년 08 월

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Effects site concentrations of propofol
using target controlled infusion (TCI) in
dental treatment under deep sedation
between intellectual disability types

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2019 년 월

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Abstract

Effects site concentrations of propofol using target controlled infusion (TCI) in dental treatment under deep sedation between intellectual disability types

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Objective: This research will provide specific data regarding the dose needed to achieve propofol effect site concentration using target-controlled infusion between intellectual disabled patients. As well as detail the efficacy method for reach a safe level of consciousness using target control infusion without hemodynamic changes that occur along sedation procedure, in addition to detail any other adverse effect that occurs during procedure. This information will provide clinically useful data on patient with different kinds of intellectual disability treated by deep sedation using propofol in the dental environment.

Methods: We proceeded to perform a study retrospective review of the sedation service records of intellectually disabled patients from age over 15 years and weight over 30kg. We reviewed all charts of patients receiving propofol by use of target-controlled infusion for deep sedation from Seoul National University Dental Hospital in the Special care dental clinic from May 2008 to September

2018. The initial Propofol effect site target concentration was selected according to each patient's medical condition. These patients were under constantly monitoring, and to provide an adequate deep sedation state, we adjusted the target concentration of propofol according to the state of unconsciousness through BIS, patient stimulus response and vital signs monitoring according to condition of dental treatment. We compare Propofol infusion dosage between each impairment group.

Results: The study was enrolled 138 patients, classified according to the type of mental disability they suffered: 51 of Mental Retardation, 36 of Autism, 30 of Brain lesion, 12 Genetic diseases, 9 of Dementia. These patients underwent different types of dental treatments according their diagnosis were: 112 restoratives (caries treatment), 13 minor surgeries (tooth extraction), 7 prosthodontics, 5 periodontics treatment 1 implant. The duration of dental treatments was 43 ± 18 minutes, the total sedation time between all the groups was 73 ± 23 minutes, total values of BIS in all the groups was 57 ± 12 . In the case of propofol maintenance Ce dosage, the values of each group were: mental retardation 3 ± 0.5 (2-4) $\mu\text{g/ml}$, autism 3.1 ± 0.7 (2-5) $\mu\text{g/ml}$, brain lesion 2.8 ± 0.7 (1.5-5) $\mu\text{g/ml}$, genetic disease 2.9 ± 0.9 (1-4) $\mu\text{g/ml}$, dementia 2.3 ± 0.7 (1-3.4) $\mu\text{g/ml}$, being statistically significant the group of dementia requiring lower dose than the other groups.

Conclusions: The dosage to reach safe effective propofol effect-site concentration (Ce) was lower in the group of dementia in compared with the

other intellectual disability types. Since there were no complications of any kind we can say that deep sedation is a great alternative to general anesthesia in patients with intellectual disabilities for dental treatments taking into account the time factor.

Keywords: Deep sedation, dental treatment, intellectual disability, target control infusion, propofol, effect-site, bispectral index.

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1. Introduction

What is disability? Many of them describe as a condition that can develop at a given moment in the life of the human being and could be physic or mentally, temporarily or permanently that limits the person in their daily activities and their interaction with the world [1]. It is estimated that more than one billion people live with some type of disability; that is, around 15% of the world population (according to WHO in the estimates of the world population in 2010) [2]. Intellectual disability affects about one percent of the population and within 85 percent have mild intellectual disability. This condition involves problems in the development of mental abilities in two areas, intellectual functioning (reasoning, learning, judgment) and adaptive functioning (activities of daily), besides suffering from other conditions that affect in the neurodevelopmental, medical and physical in the case of cerebral palsy, epilepsy, ADHD, autism spectrum disorder and depression and anxiety disorders [3].

Patients with disabilities have historically been excluded from society, in a certain way, at present this situation has been changing in all countries of the world with the application of new laws, adaptations of many spaces for people with disabilities, inclusion in centers of jobs, schools, etc., however, despite these changes, still faces many barriers in today's society, especially in those developing countries. In our area of dentistry, these patients frequently face many obstacles due to a cultural barrier by part of dentists due to the lack of training in cultural competence and in

the management of patients with disabilities during dental treatment, in which is added fear, because these patients mostly have other systemic complications, however this should not be an impediment to deny dental consultation, since with the help of an interdisciplinary medical-dental management and a good training in the management of such patients would eradicate these obstacles and improve in this area the quality of life of disabled patients [4]

In another aspect, the lack of oral health in disabled patients is one of the biggest problems in the dental area, the prevalence and severity of oral diseases are higher than other groups of people in general, since there are many factors that influence this deficit of oral care like: low physical skills or reasoning to understand the importance of oral health and the type of pharmacological treatment that is being administered, this must be added that most oral care depends on their caregivers (Altun et al., 2010) [5]. All these characteristics increase the time and lack quality of dental treatment because individuals cannot attend to their oral health, also these individuals frequently refuse dental treatment and cooperate, because the anxiety or fear (Sakaguchi, Higuchi, Maeda, & Miyawaki, 2011) [6]. Thereby, one of the main purposes of providing anesthesia for patients with intellectually impairment is to establish and maintain a state of cooperation and to reduce the risk of some complication as well as to provide a treatment without pain, which would reduce the fear and the anxiety to the dental treatment (Caputo, 2009) [7].

Today, many associations such as the ADA (American Dental Association), ADSA (American Dental Society of Anesthesiology), KDSA (The Korean Dental Society of Anesthesiology), among others, have proposed a series of guidelines for safety procedure of sedation according to the degree of depth and also for anesthesia, these guidelines, the advancement of technology, the amount of information and continuing education for dentists has helped to improve the conditions of private clinics that has allowed the use of outpatient general anesthesia and sedation by highly qualified dentist and fulfilling the requirements according to the guidelines of your country of residence (Corcuera-Flores, Delgado-Munoz, Ruiz-Villandiego, Maura-Solivellas, & Machuca-Portillo, 2014) [8]. It has been shown that deep sedation is recommended for disabled patients who are difficult to treat and allows a better management of the patient, since the patient is in a state of reduced body movement and responding only to painful or repeated stimuli, which make the dental treatment comfortable for the dentist as the patient (Chi, Kim, Seo, Yang, & Chang, 2016) [9].

Among the drugs used for sedation, propofol is one of the most popular intravenous anesthetic agents in modern medicine, both for general anesthesia and sedation (Asahi, Kubota, & Omichi, 2009) [10]. Propofol has an onset of action: 30-45 seconds and a duration of between 3 and 10 minutes (the dissipation is a function of redistribution of the CNS drug); Metabolized by hepatic conjugation to inactive compound and excreted for the most part in urine has a half-life of 40 minutes. Due

to these characteristics, propofol has many advantages over other anesthetics such as: providing a faster anesthetic induction, a recovery of less time, therefore, this allows an earlier discharge of the patient and a faster recovery of the neurological functions and social, less postoperative nausea and vomiting (PONV) and emergency delirium (Chidambaran, Costandi, & D'Mello, 2015) [11]. These characteristics can improve thanks to the advance in the intravenous anesthetic techniques that has conceived the development of the target controlled infusion (TCI) that have demonstrated efficacy and safety in the anesthetic maintenance through different pharmacological models that permit to achieve the peak effect of the drug, helped with the bispectral index (BIS) that, while we are titrating an specific anesthetic agents, this allows the anesthetist to adjust the amount of anesthetic agent needed, resulting in a more rapid awaking from anesthesia, also, help to avoid a state of over sedation or any cardiopulmonary complication.

However, it is difficult to evaluate and maintain an adequate depth of sedation in patients with severe intellectual disability due to the different communication difficulties and sometimes may have other medical disease, for this reason these patients may be more sensitive to sedative such propofol. Therefore, because of this, the sedative dose needed for an adequate depth of sedation cannot be estimated in patients with intellectual disability, this makes sedation sometimes higher than expected, which sometimes delays the recovery, also there are

probabilities of a respiratory tract obstruction and an overdose of propofol (이승화, 2013) [12].

Therefore, there are advantages of propofol as a sedative agent and its titration through TCI with the help of BIS during the sedation process, which allows monitoring of changes in the level of consciousness and allows maintenance of stable doses and attainment of the effect-site concentration; thus, help to preventing any complications while performing the dental treatment. Given this, there is a need for further investigation of deep sedation with propofol in intellectually disabled patients to improve the quality of dental care for these patients.

This research will provide specific data regarding the dose needed to achieve Propofol effect site concentration using target-controlled infusion between these patients. As well as detail the efficacy method for reach a safe level of consciousness without hemodynamic changes that occur along this, in addition to detail any adverse effect that occurs. This information will provide clinically useful data on patient with different kind of intellectual impairment treated with deep sedation in the dental environment. Also, this study tested the null hypothesis that there are no differences in the dose necessary to achieve the site effect between the different mental illness groups.

2. Material and Methods

This study was approved by the IRB No. S-D20190002 of Seoul National University School of Dentistry. We performed a retrospective review of sedation service records of intellectually disabled patients aged above 15 years and weighing over 30 kg. We reviewed all the charts of patients receiving propofol via TCI for deep sedation in the special care dental clinic of Seoul National University Dental Hospital from May 2008 to September 2018.

2.1 Patients

The databases were examined to identify all patients who underwent in deep sedation, we included all the records of patients with intellectual disability over the age of 15 years and receiving propofol using TCI for dental treatment in the Special care clinic for patients with Intellectual impairment, resulting 138 patients attended at Seoul National University Dental Hospital, from May 1, 2008 to September 30, 2018 (Fig. 1).

Inclusion criteria were:

- Age \geq 15 years
- ASA physical status \leq III
- Weight \geq 30kg

- Any intellectual impairment patient receiving dental treatment (restorative, endodontic, periodontics, minor surgery, dental extraction, and prosthodontics)

- Any intellectual disability and not cooperating fully with dental treatment. Also, some of these patients had seizures history and receiving anticonvulsant medication.

Exclusion criteria were:

- All the patients undergoing in conscious sedation.
- Patients ASA status over IV and uncontrolled or severe medical condition (uncontrolled epilepsy, uncontrolled heart disease and any other uncontrolled chronic disease).

- Incomplete medical records.

2.2 Propofol administration using Target Control Infusion

Once disabled patient is admitted to outpatients, anesthetic pre-treatment evaluation is realized by the anesthetist and dentist surgeon. The day of appointment, the anesthetist informed to the patient's guardian all the recommendation about indication after procedure, also received explanation about de deep sedation procedure (possible risk and post anesthetic time care).

Depending on the degree of the patient cooperation, we properly inserted intravenous catheter of the patients, if the patients is uncooperating, the anesthesiologist administrate any other sedative drugs or use sevoflurane induction. The propofol was infused using the Orchestra TCI apparatus (Base Primia, Fresenius Kabi, France) with Schnider pharmacokinetic model. The initial Propofol effect site target concentration was selected according to each patient's medical condition.

All the patient was monitored with noninvasive arterial blood pressure, ECG, pulse oximetry, carbon dioxide capnography, respiratory monitoring unit, and BIS (Bispectral index) monitors. To provide an adequate deep sedation state, the anesthetist titrated the effect target concentration of propofol according to the state of unconsciousness through BIS, patient stimulus response and vital signs monitoring according to condition of dental treatment. For maintain the patency of airway and avoid respiratory distress we provided 3-5 liters/min of oxygen through the nasal cannula. If necessary, airway intervention was applied.

When dental treatment had finalized, propofol infusion is stopped and we move the patient to the Post Anesthetic Care Unit (PACU), here the patient is kept under observation to take care of any adverse post anesthetic effect, also the patient is given oxygen therapy through a mask with reservoir of 5-6 liters of oxygen for 10 to 15 minutes to prevent hypoxic state while the patient regains consciousness to be discharged from the clinic.

2.3 Bispectral Index Scale Monitor setting

To performing deep sedation and monitoring patient's consciousness, all patients were monitored for BIS scores using the BIS VISTA Monitoring System (Covidien, Mansfield, MA, USA) and a specific BIS Quatro Sensor (Aspect Medical Systems, Newton, Massachusetts, USA), the front sensor is located according to the product guidelines on each patient's forehead and connected to a BIS Vista monitor. During the procedure, BIS scores were monitored continuously and recorded every 10 minutes for prevent complications associated with overdose and maintain proper sedation depth which displays the patient's arousal state as a score of 0-100 points. We adjusted the propofol dose increasing or decreasing according to value of the BIS scale (Fig. 2).

2.4 Data Analysis.

We analyzed medical records of all the enrolled patients, and obtained details on: types of mental impairment, propofol titration (changes in target concentration, duration of each change, and total infusion duration), vital signs, total sedation duration, dental treatment type, duration of dental treatment, complications during sedation, and other induction drugs administrated. Based on these records, we grouped the patients according to the type of intellectual disability (autism, mental

retardation, dementia, genetic disease, and brain lesion). We also obtained basic patient demographic information, e.g., gender, age, weight, height, and any other organ complication.

- The patients were match up into different kind of intellectual disability groups (autism, mental retardation, dementia, genetic disease, brain lesion) according to the medical history clinic record.

- Basic demographic evaluation was described like patient's gender, age, weight, height, and any other organ complication.

- About the Propofol record review, we evaluated:

1. Initial propofol target concentration.

2. Changes in effect-site concentration of propofol during dental treatment period by reviewing the chart of each patient (Fig. 3).

3. Duration of stabilize dose of propofol.

The initial C_e allows to quickly reach a therapeutic concentration, and maintenance C_e is the ones that keep the pharmacological effect of propofol that allows a dental treatment without interruption, less painful and more comfortable for the patient and without effects secondary.

4. Total propofol infusion time and total dosage evaluation

5. Adverse effects occurred during sedation.
6. Type and duration of dental treatment
7. Hemodynamic information during intraoperative period.
8. Depth of sedation according to Bispectral Index (BIS) information.
9. Administration of additional sedation drugs and emergency aid.

2.5 Statistical analysis

The study included descriptive and analytical data. All the data were analyzed with SPSS version 25 for Windows (SPSS Inc., USA) software and expressed as means \pm SD, with $P < 0.05$ considered statistically significant. We used measures analysis of variance (ANOVA) to compare Propofol infusion dosage between each impairment group (group and propofol TCI factors), and we used LSD multiple comparison post hoc test to compare PPF steady/mean and values between the groups.

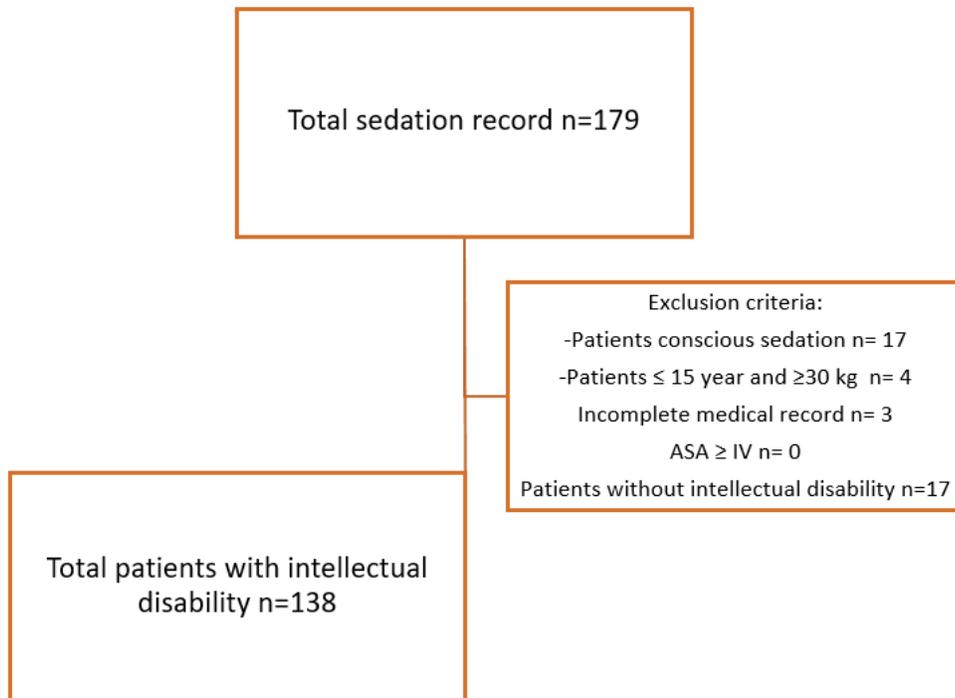


Fig. 1 Patient selection flow chart applying inclusion and exclusion criteria.

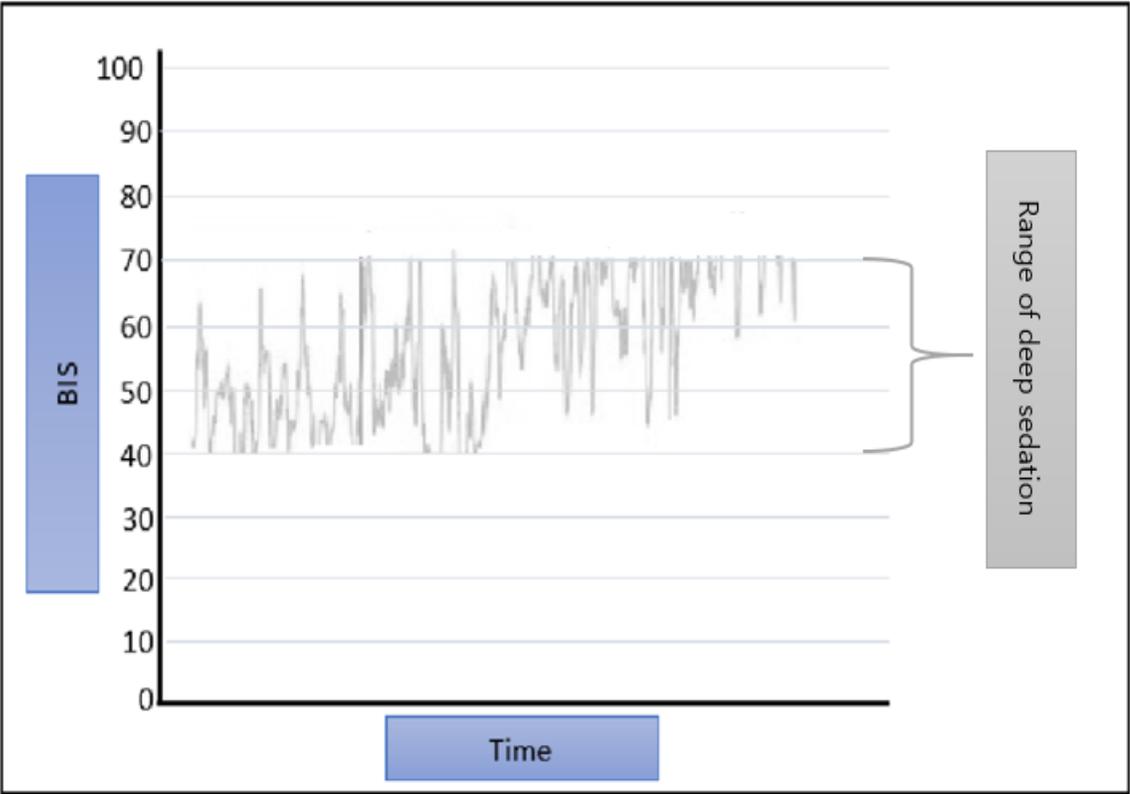


Fig. 2 Bispectral index (BIS) scale. The scale values are from 0 to 100; 0 means complete cortical EEG suppression or cortical silence and 100 means the patient is awake (Johansen, 2006). According to our data we classified deep sedation in the range 70-40 into BIS scale.

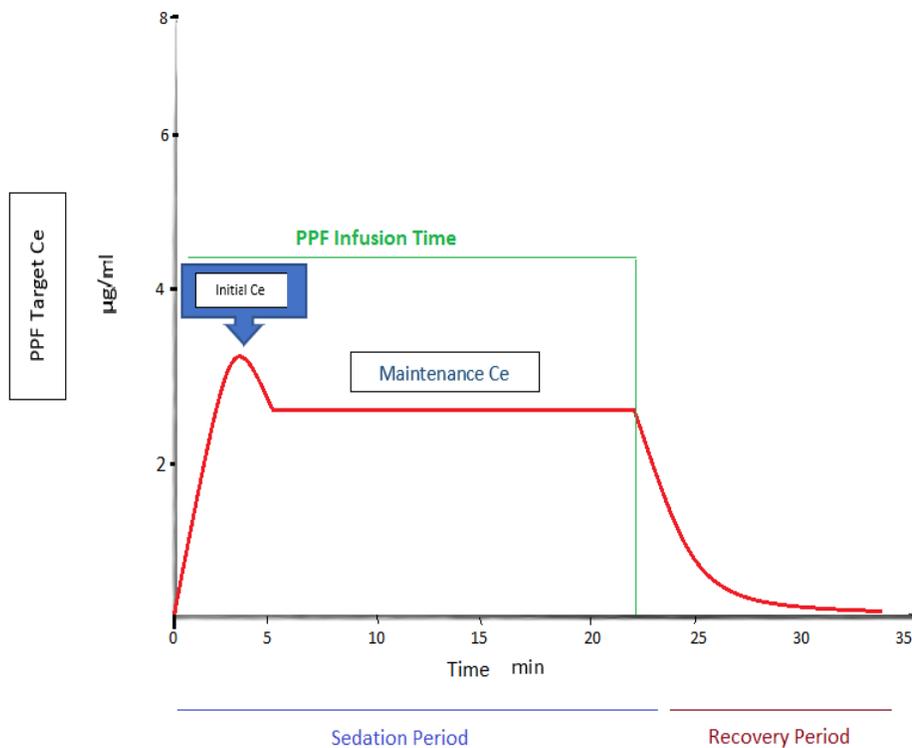


Fig 3. Propofol effect site concentration evaluation of change according time variables (Effect-site concentration (Ce)), initial Ce stands for an initial set target concentration in effect-site, Maintenance Ce means effect-site target concentration during dental treatment procedure with the patient in a state of immobilization with no side effect.

3. Results

These patients were classified according to the type of mental disability they suffered where 51 of Mental Retardation 36 of Autism, 30 of Brain lesion, 12 Genetic diseases (Down's Syndrome), 9 of Dementia (Fig. 4). Basic demographical data (gender, weight, height, and ASA classes) according each group were showed on table 1, where we found significant difference between the ages of patients, $p < 0.05$ being dementia the group with older patients. Also, weight and height show significant differences $p < 0.05$ being autism with higher values than the other groups. According to the clinical history of the selected patients in organ complications were found some patients with problems in the lungs, kidneys, allergies, heart and seizures resulting in less than 10 percent of the total population studied (see on the table 2), despite of these results, were not representing a high-risk factor for not doing sedation procedure. These patients underwent different types of dental treatments according their diagnosis were: 112 restoratives (caries treatment), 13 minor surgeries (tooth extraction), 7 prosthodontics, 5 periodontics treatment 1 implant; the duration of the different dental treatments was 43 ± 18 minutes (table 3). According to the data collected about the sedation process, the total sedation time between all the groups was 73 ± 23 minutes, total values of BIS in all the groups was 57 ± 12 ; other parameters are showing in table 4 grouped according to the type of intellectual disability like: systolic blood pressure (SBP), diastolic blood pressure

(DBP), heart rate, pulse oximetry < 90, other sedatives drugs, sevoflurane induction and discontinuation of procedure, in which according to these results we did not find abnormal hemodynamic values that meant any complication during the procedure, 15 patients received sevoflurane induction and other 13 patients received another sedative drug in the procedure, with all this we affirm that sedation procedure was successfully and allowed to complete their dental treatments.

Respecting propofol infusion data using target control infusion, initial propofol dose in each group were: mental retardation 2.9 ± 0.4 (2-4) $\mu\text{g/ml}$, autism 3.1 ± 0.7 (2-5) $\mu\text{g/ml}$, brain lesion 2.6 ± 0.7 (1-4.5) $\mu\text{g/ml}$, genetic disease 2.9 ± 0.5 (2-4) $\mu\text{g/ml}$, dementia 2.6 ± 0.7 (2-4); by ANOVA we found significant differences $p < 0.05$ in dose of propofol effect site concentration, where the autism group need higher doses than the brain lesion and dementia groups through the analysis by post hoc LSD; In the case of propofol maintenance dosage, the values of each group were: mental retardation 3 ± 0.5 (2-4) $\mu\text{g/ml}$, autism 3.1 ± 0.7 (2-5) $\mu\text{g/ml}$, brain lesion 2.8 ± 0.7 (1.5-5) $\mu\text{g/ml}$, genetic disease 2.9 ± 0.9 (1-4) $\mu\text{g/ml}$, dementia 2.3 ± 0.7 (1-3.4) $\mu\text{g/ml}$, being statistically significant the group of dementia requiring lower dose than the other groups. In the Fig. 5 show the maintenance C_e propofol between each group using mean and 95% confidence intervals of mean; table 5 show us other propofol infusion data by group with P value.

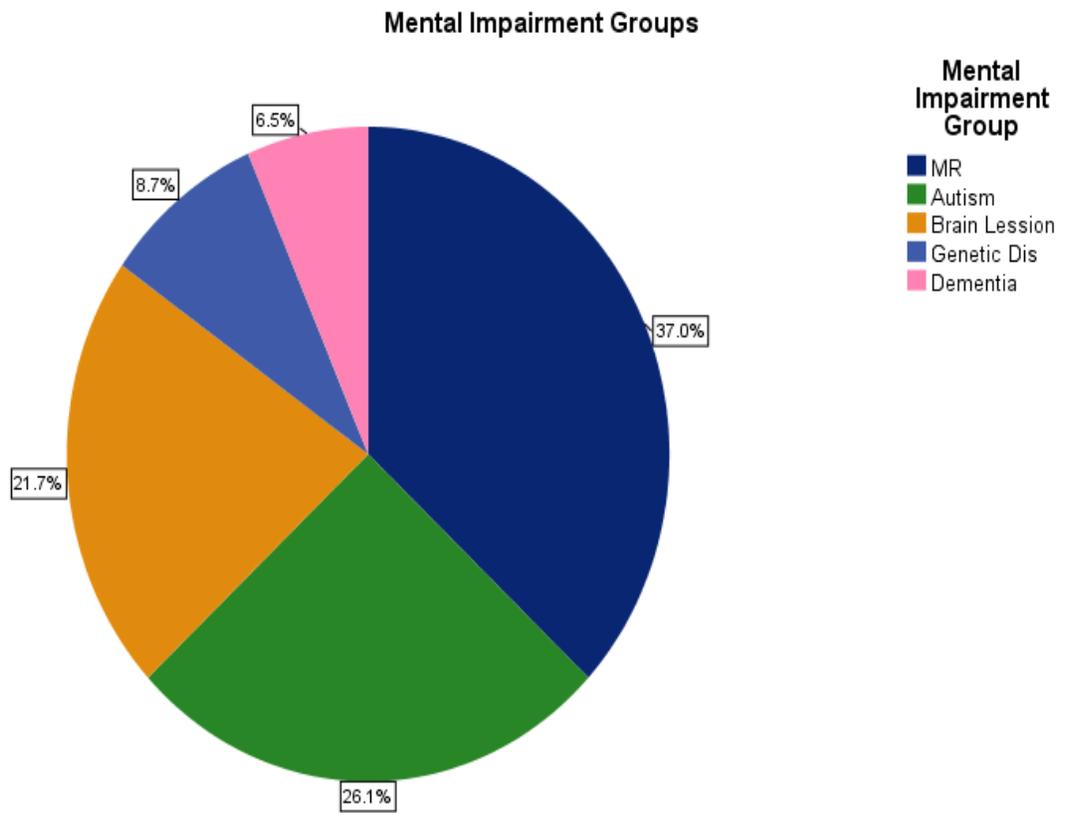


Fig. 4. Classification of 138 patients according to their diagnosis into 5 groups of intellectual disability groups.

Table 1. Patients' demographic characteristics-data

<i>Characteristic</i>	<i>MR</i>	<i>Autism</i>	<i>Brain lesion</i>	<i>Genetic disease</i>	<i>Dementia</i>	<i>P values</i>
<i>Age</i>	25 ± 7 (15-46)	24. ± 7 (15-38)	40 ± 21 (17-81)	26 ± 8 (19-46)	73 ± 9* (51-81)	P = 0.001
<i>Weight (Kg)</i>	59 ± 16 (34-93)	67 ± 12* (40-96)	52 ± 12 (30-73)	55 ± 15 (34-78)	52 ± 17 (32-77)	P = 0.001
<i>Height (cm)</i>	160 ± 10 (145-180)	170 ± 7* (138-182)	160 ± 9 (144-175)	153 ± 7* (145-164)	159 ± 7 (155-175)	P = 0.001
<i>Gender M: F</i>	26:25 (51)	29:7 (36)	17:13 (30)	9:3 (12)	1:8 (9)*	P = 0.01
<i>ASA I: II: III</i>	8:43:0	9:27:0	0:19:11*	0:12:0	0:4:5*	P = 0.001

Note: Values are mean ± SD. P < 0.05 consider like statistically significance. * Mean statistically significance than the other groups.

Table 2. Organ Complications

	Mental Retardation	Autism	Brain Lesion	Genetic disease	Dementia	Total (%)
<i>Heart</i>	1	1	4	5	2	13 (9.4%)
<i>Lung</i>	0	0	0	0	2	2 (1.4%)
<i>Kidney</i>	0	0	0	0	1	1 (0.7%)
<i>Liver</i>	1	0	1	0	0	2 (1.4%)
<i>Allergy</i>	0	0	2	0	2	4 (2.8%)
<i>Seizures</i>	19	7	8	0	0	34 (24.6%)

Other complications that patients present according to each group. Values are mean \pm SD.

Table 3. Dental Treatments according to clinical Diagnostic

<i>Dental treatments</i>	<i>Number of cases</i>	<i>Total treatment time (min)</i>
<i>Restaurative</i>	112	45 ± 18
<i>Surgical extraction</i>	13	27 ± 11*
<i>Prosthodontic TX.</i>	7	38 ± 15
<i>Periodontic treatment</i>	5	49 ± 23
<i>Implant</i>	1	55
<i>Total</i>	138	43 ± 18

P = 0.012

Tx. = Treatment, and the data values are Means ± SD and P < 0.05 consider like statistically significance. * Mean statistically significance than the other groups.

Table 4. Sedation Values

	<i>Mental retardation</i>	<i>Autism</i>	<i>Brain lesion</i>	<i>Genetic Disease</i>	<i>Dementia</i>	<i>Total</i>	<i>P value</i>
<i>Total Sedation time (min)</i>	72 ± 25	74 ± 22	74 ± 23	74 ± 22	71 ± 16	73 ± 23	P= 0.98
<i>SBP</i>	104 ± 14	106±16	107±20	101±13	102 ± 17	105±16	P= 0.70
<i>DBP</i>	58 ± 11	57 ± 13	60 ± 10	59 ± 10	58 ± 11	58 ± 11	P= 0.91
<i>Heart rate</i>	76 ± 12	77 ± 13	79 ± 16	78 ± 11	68 ± 7**	77 ± 13	P= 0.36
<i>SpO₂ < 90</i>	0	0	0	0	0	0	-
<i>Sevoflurane Induction</i>	6	7	2	0	0	15	-
<i>Other sedative drugs</i>	3	2	5	3	0	13	-
<i>BIS</i>	54 ± 12	55 ± 10	58 ± 11	58 ± 10	74 ± 5*	57 ± 12	P=0.004
<i>Discontinuation of procedure</i>	0	0	0	0	0	0	-

Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Pulse oximetry (SPO₂). We established that pulse oximetry values of less than 90 represent a hypoxic condition of the patient, which is why they were taken as complications within the time of sedation. BIS (Bispectral index score). Values are Means ± SD and P < 0.05 consider like statistically significance. * Mean statistically significance than the other groups. ** Dementia < Brain lesion post hoc test (LSD p<0.045)

Table 5. Propofol Target Infusion Status

<i>Impairment groups</i>	<i>Mental retardation</i>	<i>Autism</i>	<i>Brain lesion</i>	<i>Genetic Disease</i>	<i>Dementia</i>	<i>Total</i>	<i>P value</i>
<i>Characteristics</i>							
<i>Initial propofol concentration (Ce) µg/ml</i>	2.9 ± 0.4 (2-4)	3.1 ± 0.7 (2-5)**	2.6 ± 0.7 (1-4.5)**	2.9 ± 0.5 (2-4)	2.6 ± 0.7 (2-4)**	2.9 ± 0.6 (1-5)	P= 0.021
<i>Average propofol concentration (Ce) µg/ml</i>	3 ± 0.4 (2-4)	3.1 ± 0.7 (1.66-4.75)	2.7 ± 0.7 (1.5-4.24)	2.8 ± 0.7 (1.70 - 4)	2.4 ± 0.5* (1.5-4.75)	2.9 ± 0.7 (1.5-4.75)	P= 0.009
<i>Maintenance propofol concentration (Ce) µg/ml</i>	3 ± 0.5 (2-4)	3.1 ± 0.7 (2-5)	2.8 ± 0.7 (1.5-5)	2.9 ± 0.9 (1-4)	2.3 ± 0.7* (1-3.4)	2.9 ± 0.7 (1- 5)	P= 0.016
<i>Highest propofol concentration (Ce) µg/ml</i>	3.3 ± 0.7 (2-7)	3.5 ± 0.9 (2.5-6)	3 ± 0.7 (1.50-5)	3.2 ± 0.6 (2-4)	2.8 ± 0.6* (2-4)	3.3 ± 0.8 (1.5-7)	P= 0.046
<i>Lowest propofol concentration (Ce) µg/ml</i>	2.7 ± 0.5 (1.50-4)	2.7 ± 0.7 (1-4)	2.3 ± 0.7 (1-4)	2.4 ± 0.9 (1-4)	2 ± 0.6* (1-3.4)	2.6 ± 0.7 (1-4)	P= 0.005
<i>Counts of propofol Concentration (Ce) Changes</i>	2 ± 1 (1-6)	3 ± 2 (1-6)	3 ± 1 (1-6)	3 ± 2 (1-6)	2 ± 1.1 (1-5)	2 ± 1 (1-6)	P= 0.73

Note: Values are Means ± SD and ANOVA test P < 0.05 consider like statistically significance. ** Induction dose autism > brain lesion and dementia with post hoc test (LSD p<0.05). * Mean statistically significance than the other groups.

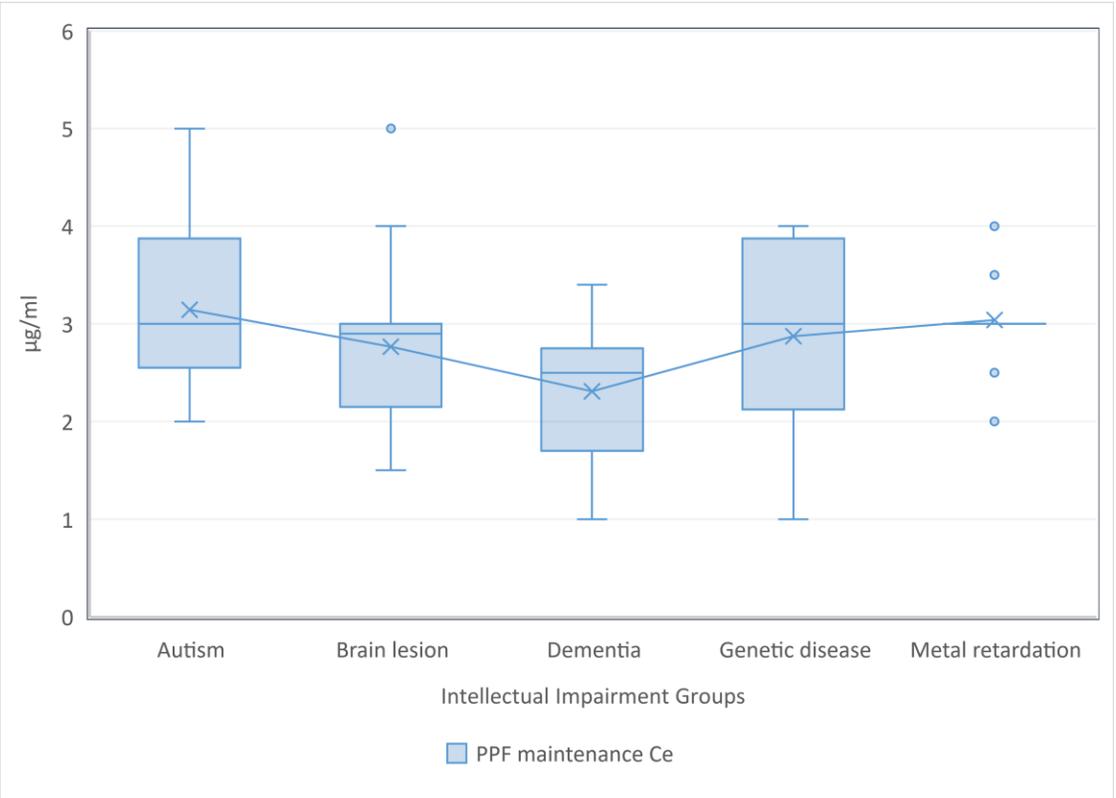


Fig. 5. Dosage of the propofol effect-site concentration.

4. Discussion

Patients with a disability arrived at the dental clinic with deplorable oral health due to either lack of self-reasoning capacity, motor coordination, or medications that mitigate problems related to the increase of oral affections; therefore, good clinical management of these patients is required for successful dental treatment completion. Since these patients are more sensitive to high-stress situations, the use of appropriate anesthesia techniques is recommended

The implementation of anesthesia provides optimal conditions for dental treatment for disabled patients, so additional care must be taken based on their physical and mental conditions. It is necessary to execute an individualized anesthetic plan and a good teamwork between the dentist and the dental anesthesiologist to get a procedure without any kind of altercations and conclude satisfactorily. Sedation can be classified according to the depth required by the treatment as mild, moderate and deep with respect to their levels of consciousness and the ability to maintain ventilation and cardiovascular functions; then have general anesthesia that is the complete loss of consciousness with incapacity to maintain ventilation and cardiovascular functions (Wang, Lin, Huang, & Fan, 2012) [13].

Conscious sedation was the goal of a level of sedation, since the patient can respond to any verbal or tactile stimulus; However, in the case of patients with disabilities who have low levels of cooperation and high levels of anxiety, this type

of conscious sedation has a lower success rate (Shin, Yoo, Kim, Kim, & Kim, 2016) [14]; therefore, the use of deep sedation or general anesthesia in these patients is more suitable for performing dental procedures, therefore, for the selection of which kind anesthetic technic perform we should be taken the risk-benefit factor (Messieha, 2009) [15].

The objectives of the deep sedation in patients with intellectual disability are: reduce the patient's anxiety and fear of treatment, decrease the pain sensation making the treatment more comfortable for the patient and in turn produce amnesia during the procedure, also increase the patient's tolerance in those long-term procedures, avoid the risks associated with general anesthesia and achieve a rapid recovery, in addition compared to general anesthesia, minor postoperative complications (Morimoto et al., 2017) [16], also deep sedation is perform for reduce movement in the patient due to lack of cooperation in those case that dental treatment cannot be carry out with minimal sedation.

Deep sedation can be easily and safely achieved intravenously by the ease of handling the doses as we can titrate to achieve the desired effect, among the most commonly used sedative drugs like benzodiazepines between this one, we have midazolam which is considered the drug most commonly used to induce sedation in dental procedures (Yoshikawa et al., 2013) [17] and despite this drug has sedative, hypnotic, anxiolytic, amnesic and muscle relaxant effects, but, it has been

demonstrated that produces delayed that in the recovery of patients with disabilities after finished the treatment, that's why propofol, thanks to its peculiar pharmacological characteristics, makes it more suitable for deep sedation because sedation can be performed safely and effectively in dental office setting to patients with disabilities (Vaessen, Schouten, van der Hoeve, & Knape, 2017) [18].

The advance in drug delivery techniques by intravenous has permitted the development of target-controlled infusions (TCI) system, whereby drugs delivered to reach and sustain specific target drug concentrations at the effect site. With the assistance of TCI system is possible to adjust and maintain the effect site concentration (C_e) of drugs incorporated in the system. Studies such as J Mu, et al (2018) concludes and demonstrates that the use of TCI allows high doses of propofol to be achieved without causing a prolonged recovery and that it makes the titration method of propofol easier in anesthesia or sedation (Mu, Jiang, Xu, Yuen, & Irwin, 2018) [19]. As this result, target-controlled infusions have begun to be used widely to administer propofol for sedation and in a variety of settings, including endoscopy, bronchoscopy, and dental procedures (Sheahan & Mathews, 2014) [20]. However, this does not avoid the fact that sometimes complications may arise during or after treatment such as: obstruction of the respiratory tract, cardiovascular and respiratory depression, nausea, vomiting, fainting, among others that may appear as a side effect of the drug used.

However, in the titration of propofol, we have found studies that show how useful the Bispectral Index (BIS) is as a coadjutant for the appropriate doses that allow us to maintain the depth of anesthesia ("AMBULATORY ANAESTHESIA," 2012) [21]. There are also studies that show us the effectiveness of both TCI and BIS together to achieve adequate sedation of the patient in an effective and safe way without complications of overdose during the dental procedure [6].

In our study the dentists were able to complete successfully the different kind of dental treatments without any intraoperative complication (hemodynamic changes, hypoxia, interruption of procedure, etc.). The total time of the different treatments was around one hour, which made possible the implementation of deep sedation in these patients because the treatment time was not too long and also, with the help of the local anesthesia technique, make the dental treatments less uncomfortable for the patient, as well as most of the patients were in ASA classification II, which makes them suitable for this procedure.

In the case of the sedation process in our study, we rejected our null hypothesis because we found significant differences in the dose from the effect site concentrations in one of the groups of intellectual disability, which was in the dementia group. Also, with regard to induction dosage, dementia and brain lesion group were needed slightly low propofol concentration compared with autism group this is because the groups of brain lesion and dementia are more sensitive to propofol. Also, in our study found that propofol maintenance Ce dosage for dementia

group was lower than the other intellectual impairment group. There are some reports about the dose needed for the effect site concentrations under deep sedation with propofol in patients with intellectual impairment in the dental environment that had reported lower doses (1.0 - 5.0 mcg/ml) for the effect site than those without intellectual disability using titration of target concentration [12], another study has reported that noncommunicative/ nonverbal children with cerebral palsy (CP) require less propofol (3.29 mg/kg) than otherwise healthy children (Saricaoglu, Celebi, Celik, & Aypar, 2005) [22]; however, none of these studies compared the required dose between patients with different types of intellectual impairment. However, a study has reported that the propofol dose required for an anesthesia procedure is not affected by the type of intellectual disability but rather by the antiepileptic used and consumption time, since this has been shown to cause patients to become more sensitive to sedative drugs (Ouchi & Sugiyama, 2015) [23].

There are different types of dementia but most of these patients suffer from Alzheimer's diseases (most common) that usually this patients present symptoms like depression, and delirium that over time are getting worse, adding the advanced age of these patients (So et al., 2017) [24]. These patients with dementia who usually take antidepressants or low-dose antipsychotics producing a higher sensitivity to sedatives, also can receive antiepileptic drugs treatment for their neurological disorders, making them more susceptible, because it has been demonstrated that antiepileptic drugs diminish the hepatic metabolism (Patsalos,

Froscher, Pisani, & van Rijn, 2002) [25]; in addition, we must add the multiple comorbidities that this group presents, therefore, the doses of sedatives such as propofol will be low. For these reasons, during sedation procedure we have to be more cautious through continuously vital sign monitoring (Johansen, 2006) [26] and perform a good preoperative evaluation to achieve the best possible expected outcome postoperatively (Funder, Steinmetz, & Rasmussen, 2009) [27]. These patients, due to their condition, could develop a postoperative delirium due to the sedative agents used, but according to S. Alcorn et al, 2017, for prevent this we have to avoid benzodiazepines and anticholinergic drugs, careful titration both volatile and IV anesthetic agents, and ensuring effective multimodal postoperative analgesia (Alcorn & Foo, 2017)[28].

With all this there is no doubt that deep sedation can be successfully implemented in patients with intellectual disabilities as an alternative to general anesthesia, always taking into account the patient's medical conditions, the safety guidelines for the sedation procedure, interdisciplinary work between the dentist and the anesthetist that which is an important point to consider in order to successfully carry out any procedure, the communication between both professionals must be the key, Moreover, for successful implementation, an individualized plan for each patient, based on their specific conditions, must be developed [8].

5. Conclusion

The dosage to reach safe effective propofol effect-site concentration (C_e) was lower in the group of dementia in compared with the other intellectual disability types. Since there were no complications of any kind we can say that deep sedation is a great alternative to general anesthesia in patients with intellectual disabilities for dental treatments taking into account the time factor.

6. Acknowledge

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장애 종류에 따른 깊은진정 하 치과치료 시 프로포폴을 목표농도조절법으로 정주 시 효과치 농도 비교

목 표: 이 연구는 협조장애를 가진 환자의 깊은진정 하 치과치료 시 propofol을 이용하여 목표농도조절주입(TCI)을 할 때 효과치 농도 설정에 대한 정보를 제공하고자 합니다. 장애의 종류에 따라 진정 수준의 유지 및 혈액학적 변화나 부작용의 발생없이 안전한 수준을 유지하는 데 필요한 propofol의 농도는 차이가 있습니다. 이 연구를 통하여 장애 종류 별 깊은진정 하 치과치료에서 적절한 propofol의 효과치 농도에 대한 임상적으로 유용한 데이터를 제공하고자 합니다.

방 법: 서울대학교치의학대학원 윤리위원회 승인(IRB 번호 S-D20190002)을 획득한 후, 2008년 5 월부터 2018년 9월까지 서울대학교치과병원에서 propofol TCI를 이용한 깊은진정법을 시행하여 치과치료를 받은 15세 이상, 몸무게 30kg 이상의 협조장애 환자의 진정 기록을 후향적으로 분석하였다. 초기

Propofol 효과 부위 표적 농도는 각 환자의 건강 상태에 따라 선택되었습니다. 이 환자들이 지속적 모니터링을 받았고 적절한 깊은 진정 상태를 제공하기 위해 BIS를 통한 무의식 상태, 환자 자극 반응 및 치과 치료 상태에 따른 생체 신호 모니터링을 통해 propofol의 목표 농도를 조정했다. 각 장애 집단 사이의 propofol을 주입한 효과처 농도를 비교 분석하였다.

결 과: 이 연구의 대상자는 협조장애 유형에 따라 분류된 138명의 환자, 즉 정신지체 51명, 자폐증 36명, 뇌손상 30명, 유전질환 12명, 치매 9명이었다. 이 환자들은 보존치료 112명, 발치 13명, 보철 치료 7명, 치주 치료 5명, 임플란트 시술 1명을 받았다. 치과치료 시간은 43 ± 18 분이었고 모든 대상자의 총진정시간은 73 ± 23 분이었다, 마지막으로 모든 군에서 BIS의 값은 57 ± 12 이었다. 모든 환자에서 치과치료 중 부작용 발생은 없었다. 각 그룹에서 치과치료 시행 중 propofol 효과처 농도는 정신지체 3 ± 0.5 (2-4) $\mu\text{g/ml}$, 자폐증 3.1 ± 0.7 (2-5) $\mu\text{g/ml}$, 뇌손상 2.8 ± 0.7 (1.5-5) $\mu\text{g/ml}$, 유전질환 2.9 ± 0.9 (1-4) $\mu\text{g/ml}$, 치매 2.3 ± 0.7 (1-3.4) $\mu\text{g/ml}$ 이었다. 치매환자에서 치과치료 시 propofol 효과처 농도에 유의 한 차이가 있음을 발견했다($p < 0.05$).

결론 : 안전한 효과적인 프로포폴 효과 현장 농도(C_e)에 도달하기 위한 용량은 다른 지적 장애 유형에 비해 치매 그룹에서 더 낮았다. 어떤 종류의 부작용도 없었기 때문에 깊은 진정이 치과 치료가 필요한 지적 장애를 가진 환자들에게 일반적인 마취의 좋은 대안이라고 볼 수 있다.

주요어: 깊은 진정, 치과 치료, 협조 장애, target control infusion, 프로포폴, 효과처 농도, 이중분광지수.

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