Correlation Between Body Movements and Salivary Secretion During Sedation

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During dental sedation, control of the cough reflex is crucial for a safe and smooth procedure. Accumulated saliva is one of the predisposing factors for coughing. Body movements during dental sedation appear to enhance salivation. Therefore, the aim of this study was to investigate the difference in salivary secretion between the with-movements state and the without-movements state during sedation. Salivary weight for 1 min was measured 3 times in 27 patients with intellectual disability during dental treatment under deep sedation with midazolam and propofol. The observed variables were body movements, bispectral index (BIS), and predicted propofol effect-site concentration. A total of 81 measurements were classified into the with-movements state ($n = 39$; ie, measurements during which body movements were observed) or the without-movements state ($n = 42$; ie, measurements during which no body movements were observed). The median salivary weight was significantly smaller in the without-movements state compared with the with-movements state (0.03 vs 0.11 g, $P < .0001$). The BIS was significantly lower in the without-movements state. There was no significant difference in the predicted propofol effect-site concentration between the 2 states. Significant correlation was observed between salivary weight and BIS in the with-movements state ($r = 0.44$, $P = .004$). The findings indicate that salivary secretion decreased according to deep sedation. Furthermore, immobility also reduced salivary secretion. We concluded that one reason that immobility is beneficial is because of the resulting decreased salivary secretion during dental treatment under deep sedation.

Key Words: Deep sedation; Intellectual disability; Dental treatment; Salivary secretion; Cough reflex; Body movements; Midazolam; Propofol; Bispectral index.

Sedation for dentistry is indicated for many patients, such as disabled, medically compromised, phobic, and emetic patients. Sedation is commonly of 2 types: one is moderate (conscious) sedation and the other is deep sedation with unconsciousness. Unconscious (here-

after, deep) sedation is often indicated for patients with intellectual disability owing to difficulty with gaining their cooperation or their refusal to cooperate when conscious sedation is adopted.

However, in dental treatment under deep sedation, which is basically performed in the supine position, there is often difficulty controlling upper airway patency and protective airway reflexes such as swallowing and coughing. The upper airway patency markedly decreases after transition from the conscious to the unconscious state.¹ Furthermore, the mandatory mouth opening for

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dental treatment also impairs upper airway patency.² Commonly, head tilt, neck extension, and mandibular advancement are performed to improve airway patency.^{3–6} Simultaneously, these positions markedly compromise the swallowing action.⁷ Typically, water and saliva accumulating in the oropharyngeal space are transported to the hypopharynx and then to the esophageal space by swallowing. However, these fluids can impinge on laryngeal structures, which may induce the cough reflex. Although coughing is one of the important protective airway reflexes that prevent aspiration, vigorous coughing interrupts a dental procedure and may predispose a patient to laryngospasm, oxygen desaturation, and other adverse events. Therefore, sedation management that limits oral fluids that may travel to the hypopharynx is important for a safe and smooth dental procedure.

Kohjitani et al⁸ reported that coughing during dental sedation depends on the amount of accumulated oropharyngeal fluids and does not depend on the intraoral use of water. Their findings indicate that saliva is as important as accumulated oropharyngeal water from the dental procedure, and this can induce the cough reflex. Hence, the control of salivary secretion should decrease coughing during dental treatment under deep sedation.

Salivary secretion is controlled by higher brain centers, which include the cerebral cortex and limbic system, the reflex center, and various peripheral sensory inputs. Generally, the volume of resting saliva is approximately 0.3–0.4 mL min⁻¹, but daily variation is observed. The volume of saliva stimulated by taste or mastication is more than 2 mL min⁻¹. Unstimulated saliva is secreted spontaneously or evoked by low-grade mechanical stimulation such as movements of the jaw and tongue. There have been many reports that salivary secretion markedly decreases during sleep,^{9,10} but chewing-like movements during sleep are considered to increase salivary secretion.¹¹ On the basis of this finding, it is speculated that body movements, particularly tongue movements, during deep sedation also increase salivary secretion, which may induce the cough reflex.

Several studies have been conducted to determine the effects of anesthetic agents on salivary secretion.^{12–16} However, there have been no studies in which salivary secretion during dental treatment under deep sedation was investigated. Moreover, the correlation between salivary secretion and body movements during dental treatment under deep sedation has not been verified experimentally. We developed a suction system, Coolex (APT Inc, Osaka, Japan) (see Appendix), for the accurate measurement of the volume of saliva secreted during dental treatment with supply of water. In our preliminary study, we verified that the collection rate of this suction

system was 96.8% (total of 32 trials, ie, 4 trials in each of 8 healthy volunteers).¹⁷ The aim of this current study was to compare salivary volume in the presence of body movements with that in the absence of body movements. To this end, we measured salivary weight during a dental procedure with deep sedation and observed body movements simultaneously.

METHODS

Subjects

This study was approved by the ethics committees of Tokyo Medical and Dental University and Saitama Prefectural General Rehabilitation Center. Written informed consent was obtained from either the parents or the legal guardians of participants.

Twenty-seven dental patients with intellectual disabilities were recruited in this study. They consisted of those with only intellectual disability (22 patients) and those with intellectual disability associated with autism (5 patients). The exclusion criteria were as follows: aged less than 16 or more than 50 years, obesity (body mass index > 30), upper airway or pulmonary infection, chronic respiratory diseases (asthma, chronic obstructive pulmonary disease, bronchiectasis), and uncontrolled or severe medical conditions except epilepsy.

Sedation

The experimental protocol is shown in Figure 1. All the patients fasted more than 4 hours for solids and 2 hours for liquids (the usual 6-hour restriction was amended to 4 hours for some patients where the 6-hour restriction would have resulted in behavioral problems).^{18,19} Sedation was induced intravenously using 0.06 mg kg⁻¹ midazolam (Dormicum; Astellas, Tokyo, Japan) and a bolus administration of propofol (1% Diprivan injection kit; Astra Zeneca, Osaka, Japan) using a syringe pump (TCI pump TE-371; TERUMO Corporation, Tokyo, Japan) until glazing of the eyes or marked ptosis was observed. Thereafter, propofol was continuously infused at a rate of 4.0 mg kg⁻¹ h⁻¹ (66.66 mcg kg⁻¹ min⁻¹). Lack of eye opening or movements after prodding or shaking was defined as loss of consciousness. During the 5 minutes after reaching unconsciousness, a mouth-opening apparatus and a multipurpose vacuum instrument, Coolex, were fitted in the oral cavity. The infusion rate of propofol was increased when body movements occurred before the experimental procedure, such as placing the Coolex or mouth opening. The infusion rate

Figure 1. Experimental protocol.

was not changed during the experimental procedure but could be adjusted after the experimental protocol was completed until the end of the procedure.

During the procedure, electrocardiographic traces, blood pressure, heart rate, respiratory rate, and arterial oxygen saturation were continuously monitored using an automated vital sign monitor (BMS6000; Nihon Kohden Co, Tokyo, Japan). Electroencephalographic signals were processed by the BIS monitor (Vista A-3000; Covidien Japan, Inc, Tokyo, Japan). The anesthesiologist was blinded to the BIS of the patients.

The patients were spontaneously breathing with oxygen (2 L min^{-1}) supplemented via a nasal catheter. When necessary, the airway patency was secured by head tilt and mandibular advancement, which were performed by the surgical dentist, who was well trained in airway management and cardiopulmonary resuscitation procedure.

Measurement of Salivary Secretion

Salivary weight was measured 3 times in each patient during dental treatment, which was scaling of the right upper dentition. Two pieces of gauze (12-ply, $5 \times 5 \text{ cm}$; Hakujiji, Tokyo, Japan) were placed in the oral cavity for 1 min; one piece of gauze was placed in the sublingual region to collect saliva derived from the submandibular and sublingual glands and the other piece was placed in the oral vestibule of the left upper molar dentition to collect saliva derived from the left parotid gland. Both pieces of gauze were weighed using an electronic balance with an accuracy of $1 \times 10^{-2} \text{ g}$ immediately after removal.

Dental scaling was performed using an ultrasonic scaler with water continuously supplied. The multipur-

pose vacuum instrument Coolex was placed on the right upper dentition and connected to the other universal dental vacuum circuit. The universal dental vacuum and Coolex enabled the measurement of salivary weight accurately even during the dental procedure with supplied water. The universal dental vacuum was handled by a skilled dental hygienist. As stated earlier, in the preliminary experiment, we verified that the collection rate of this suction system was 96.8%.

Observed Variables

The observed variables during each measurement of saliva were the patient's body movements, BIS, and predicted propofol effect-site concentration. The body movements were assessed by the anesthesiologist: a measurement during which the patient showed any movements of the hands and/or legs, head, or tongue was classified into the with-movements state and one during which the patient showed no movements was classified into the without-movements state.

BIS was recorded every 5 s on the computer, and the median per minute was calculated. The propofol effect-site concentration was predicted on the basis of a 3-compartment pharmacokinetic simulation model²⁰ using the simulation software in the automated anesthesia recording system.

Data Analyses

All statistical analyses were carried out using open-access R statistical software.²¹ $P < .05$ was considered statistically significant.

Table 1. Profiles of Patients*

Male	17
Female	10
Age (y)	37.2 (5.9)
Height (cm)	160.1 (10.2)
Weight (kg)	54.6 (10.1)
BMI	21.3 (3.9)

* Values are means with SD in parentheses. BMI indicates body mass index.

Differences in salivary weight, BIS, and predicted propofol effect-site concentration between the with-movements state and the without-movements state were analyzed using the exact Wilcoxon Mann-Whitney rank-sum test with the “coin” package.²² Spearman correlation coefficient by rank was used to examine correlations between salivary weight and median BIS.

RESULTS

Deep sedation was indicated for all the patients because of their noncooperation for the dental procedure. The profiles of the patients are shown in Table 1, and a summary of their disabilities is shown in Table 2. Upper airway obstruction was observed in all the patients, which was improved by head tilt and mandibular advancement. The infusion rate of propofol was adjusted when body movements were observed after the experimental procedure. The dental procedure was successfully completed in all of the patients without any interruption by the cough reflex or the need for further airway management. Salivary weight for 1 min was measured 3 times in each of the 27 patients undergoing dental scaling under deep sedation. The median salivary weight (interquartile range [range]) was 0.06 (0.03–0.13 [0.01–1.34]) g, the median BIS was 59.2 (47.0–68.0 [24.2–83.2]), and the median predicted propofol effect-site concentration was 1.45 (1.11–1.76 [0.48–4.79]) $\mu\text{g mL}^{-1}$. Body movements were observed in 39 measure-

Table 3. Movement and Their Breakdown

	No. of Cases
Without movements	42
With movements	39
Head	6
Arms and/or legs	28
Tongue	25

ments, and none in 42 measurements. Table 3 shows a summary of the body movements. No body movements interrupted the dental procedure and no restraint was required.

Figure 2 shows the salivary weights in the without-movements and with-movements states. The salivary weight was significantly lower in the without-movements state than in the with-movements state, 0.03 (0.02–0.06 [0.01–0.92]) versus 0.11 (0.05–0.25 [0.01–1.34]) g, $P < .0001$. The BIS was also significantly lower in the without-movements state, 53.0 (36.9–62.4 [24.2–82.1]) versus 64.2 (57.5–73.6 [41.5–83.2]), $P < .0001$. There were no significant differences in the predicted propofol effect-site concentration between the 2 states, 1.67 (1.16–1.78 [0.48–4.79]) versus 1.34 (1.03–1.57 [0.75–2.09]) $\mu\text{g mL}^{-1}$, $P = .12$.

Figure 3 shows the scatter plots of BIS versus salivary weight in the without-movements and with-movements states. No significant correlation was seen in the without-movements state ($r = 0.11$). A moderate but significant correlation was seen in the with-movements state ($r = 0.44$, $P = .004$).

DISCUSSION

During dental treatment under deep sedation for patients with intellectual disability, control of the cough reflex is important for a smooth procedure. One of the factors that can trigger the cough reflex is accumulated saliva migrating to the hypopharynx. Therefore, we investigat-

Table 2. Summary of Disabilities*

	No.	Severity of Intellectual Disability			
		Mild†	Moderate	Severe	Markedly Severe
Intellectual disability	22			3	19
With epilepsy	13			1	12
Without epilepsy	9			2	7
Autism with intellectual disability	5		1	3	1
With epilepsy	2			2	
Without epilepsy	3		1	1	1
Total	27	0	1	6	20

* Values are expressed as number of patients.

† There were no patients in this category.

Figure 2. Box plots of salivary weight in without-movements and with-movements states. Boxes indicate the median and 25% (bottom box; Q1) and 75% (top box; Q3), upper whiskers indicate $Q3 + 1.5$ interquartile range (IQR); lower whiskers indicate $Q1 - 1.5$ IQR. * indicates significant differences ($P < .0001$).

ed the difference in salivary secretion according to body movements during a dental procedure under deep sedation. As a result, we found that body movements during deep sedation affect salivary secretion. In this study, coughing did not occur, but this may have been because of capture of salivary flow by gauze used during the experimental procedure.

The observed median salivary weight for 1 min in this study was 0.06 (0.03–0.13 [0.01–1.34]) g. Because the specific gravity of saliva is 1.000–1.008, its weight (g) in this study could be estimated as salivary volume (mL). Compared with the volume of resting saliva, which is commonly reported to be in the range of 0.3–0.4 mL min^{-1} , this result indicates reduction in salivary volume during deep sedation. Although salivary secretion is controlled by higher brain centers, reflex centers, and peripheral sensory inputs, the effect of the higher brain centers could be reasonably eliminated because this study was performed in the unconscious state. It is speculated that suppression of brain stem regions in which salivary centers are located reduces salivary volume.

A significantly smaller volume of saliva was observed in the without-movements state than in the with-movements state (0.03 vs 0.11 g). Furthermore, a significant correlation was observed between BIS and salivary weight in the with-movements state. On the other hand, salivary secretion did not increase depending on the depth of sedation in the without-movements state. Accordingly, our study indicated that deep sedation

Figure 3. Scatter plots of bispectral index (BIS) versus salivary weight in (A) without-movements (closed circles) and (B) with-movements (open circles) states.

inhibits salivary secretion and that immobility further reduces salivary volume. The body movements we evaluated included hand and/or leg, head, and tongue movements. Among them, we speculate that tongue movements would be the main factor that explains the decrease in salivary secretion.

Commonly, subjective assessments such as Observer's assessment of alertness/sedation (OAA/S) scale or the use of the Ramsay sedation scale are carried out to determine sedation depth. However, these methods are not effective for patients with intellectual disabilities for whom communication is difficult. Accordingly, objective assessment variables such as BIS, predicted

effect-site concentration, or vital signs are utilized to determine the dosages of anesthetic agents. In this study, we also adopted BIS and predicted propofol effect-site concentration as the objective indicators of sedation depth. However, there was a marked variation in BIS in both the with-movements state and the without-movements state even after the loss of consciousness.

Our results imply that at dosages of applied anesthetic agents determined from BIS, body movements may still occur, which can increase salivary secretion. Therefore, we suggest that lack of reactivity to dental stimulation should be a guide for the adequate depth of sedation. This may not correlate with BIS or effect-site concentration, leading to increased salivary flow. Minimizing salivary flow would be expected to decrease the likelihood of coughing or laryngospasm.

This study has experimental limitations. We had to measure salivary weight during dental treatment. Therefore, we selected dental scaling because it is a common procedure, the intensity of stimulation of the ultrasonic scaler is reasonably consistent, and it is easy to recruit subjects. However, dental scaling is accompanied by water supply. We therefore needed to use the Coolex to prevent the collected saliva from mixing with irrigated water. Consequently, the salivary weights in this study were obtained from the submandibular and sublingual glands, and from 1 parotid gland. Although the Coolex captured almost all of the treatment-based water, some may have escaped confounding results. Because the amount of water used was the same for all participants, we felt the salivary volume was considered reliable.

Although it has been shown that increased salivary secretion can lead to coughing under sedation unrelated to surgical water use, the volumes of saliva measured were small. The difference in saliva flow between the with-movements group and the without-movements group was an average of 0.08 g/min; assuming a specific gravity of 1.00, this yields 0.08 mL/min. Depending on the length of the procedure, the clinical significance of this volume cannot be accurately predicted.

CONCLUSIONS

In this study, we investigated the difference in salivary weight between the states of body movements and immobility during deep sedation in dental patients with intellectual disabilities. We found significantly higher salivary secretion in the presence of body movements.

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APPENDIX

Coolex is a multipurpose vacuum instrument. The silicone tube is connected to the vacuum device and the aluminum wire inside the tube confers flexibility to the silicone tube. The silicone tube retracts gently and securely against soft parts such as the cheeks, lips, or tongue. The distal end of the silicone tube, which is placed around the dentition, has 22 or 26 small holes for suctioning saliva and irrigating with liquid in the oral cavity (Appendix Figure).

Appendix Figure. (A) Picture of Coolex. (B) Picture of Coolex placed on the right upper dentition.