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Comparison of vital sign stability and cost effectiveness between midazolam and dexmedetomidine during third molar extraction under intravenous sedation

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Abstract (J Korean Assoc Oral Maxillofac Surg 2022;48:348-355)

Objectives: To compare the vital sign stability and cost of two commonly used sedatives, midazolam (MDZ) and dexmedetomidine (DEX).

Patients and Methods: This retrospective study targeted patients who underwent mandibular third molar extractions under intravenous sedation using MDZ or DEX. The predictor variable was the type of sedative used. The primary outcome variables were vital signs (heart rate and blood pressure), vital sign outliers, and cost of the sedatives. A vital sign outlier was defined as a 30% or more change in vital signs during sedation; the fewer changes, the higher the vital sign stability. The secondary outcome variables included the observer's assessment of alertness/sedation scale, level of amnesia, patient satisfaction, and bispectral index score. Covariates were sex, age, body mass index, sleeping time, dental anxiety score, and Pederson scale. Descriptive statistics were computed including propensity score matching (PSM). The *P*-value was set at 0.05.

Results: The study enrolled 185 patients, 103 in the MDZ group and 82 in the DEX group. Based on the data after PSM, the two samples had similar baseline covariates. The sedative effect of both agents was satisfactory. Heart rate outliers were more common with MDZ than with DEX (49.3% vs 22.7%, *P*=0.001). Heart rate was higher with MDZ (*P*=0.000). The cost was higher for DEX than for MDZ (29.27±0.00 USD vs 0.37±0.04 USD, *P*=0.000).

Conclusion: DEX showed more vital sign stability, while MDZ was more economical. These results could be used as a reference to guide clinicians during sedative selection.

Key words: Conscious sedation, Third molar, Tooth extraction, Midazolam, Dexmedetomidine

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I. Introduction

Surgical extraction of the third molar is a common procedure performed in oral and maxillofacial surgery; however, it can cause extreme stress in patients who experience fear and anxiety about dental treatment. Sedation is useful, as it can reduce the fear of tooth extraction and increase satisfaction with dental treatment[1].

Of various sedative agents, midazolam (MDZ) and dexmedetomidine (DEX) are used frequently[2,3]. MDZ is a derivative of benzodiazepine with sedative, anti-anxiety, muscle relaxant, and anticonvulsant properties. It promotes cardiopulmonary stability, has multiple routes of administration and a short half-life, induces antecedent memory loss, and results in good patient satisfaction[1,4]. DEX exhibits effective sedative, analgesic, and anxiolytic effects with minimal respiratory system suppression[4]. In addition, it has a sympatholytic effect that can relieve tachycardia and hypertension[5].

Studies comparing the efficacy of MDZ and DEX in the field of oral and maxillofacial surgery have been actively conducted; however, numerous biases are present, and studies comparing the aspect of cost are rare[6]. Therefore, the purpose of this study was to investigate differences in the sedative effects of MDZ and DEX in patients undergoing surgical extraction of the mandibular third molar. The investigators hypothesized that DEX would be advantageous compared

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to MDZ in terms of vital sign stability despite the relatively high price. The specific aim of the study was to compare the efficacy of the two agents with consideration of vital sign stability and cost.

II. Patients and Methods

1. Study design/sample

This was a retrospective cohort study with two groups of patients to whom either MDZ or DEX was administered as an intravenous sedative. The study population was comprised of all patients who presented to our hospital voluntarily for evaluation and management of impacted lower third molars between 2013 and 2021. To be included in the study sample, patients had to have undergone surgical extraction of the lower third molar bilaterally under MDZ or DEX moderate sedation. The exclusion criteria were American Society of Anesthesiology (ASA) physical status III-V; metabolic disorders due to kidney or liver disease; use of drugs that affect the cytochrome P450 enzymes or gamma-aminobutyric acid receptors; use of sedatives within the last month; other surgical procedures such as cyst removal, fistula closure, implant placement, or pericoronitis; or surgical cases with a total time of more than 1 hour. The study was approved by the Institutional Review Board of SMG-SNU Boramae Medical Center (No. 10-2020-201) and conducted following the tenets of the 1964 Declaration of Helsinki and its later amendments.

2. Sedation protocol

The patients were kept nil by mouth starting 6 hours before surgery. Aiming for moderate sedation with a verbal response[7], the peripheral oxygen saturation (SpO_2), bispectral index score (BIS), heart rate (HR), systolic noninvasive blood pressure (SBP), and diastolic noninvasive blood pressure (DBP) were continuously monitored. The BIS was measured by attaching an electroencephalographic sensor (BIS Quatro Sensor; Covidien, Mansfield, MA, USA), which was connected to an electroencephalographic monitoring system (BIS Vista Monitoring System; Aspect Medical Systems, Norwood, MA, USA), to the patient's forehead. An 18-gauge peripheral line was secured, and crystalloid (Hartmann Soln; Daihan Pharm, Seoul, Korea) was administered at a rate of 100 mL/hr. The absence of allergic reaction to antibiotics was confirmed through a skin test, and prophylactic antibiotics (Yamatetan Injection; Jeil Pharmaceutical, Seoul, Korea) were administered. Each sedative administration was performed in the manner described below. After the surgical procedure, analgesics (Denogan inj; YUNGJIN Pharm, Seoul, Korea) and methylprednisolone (Salron inj; Han Lim Pharm, Seoul, Korea) were administered. In the recovery room, SpO_2, HR, and noninvasive blood pressure were continuously monitored until discharge. After recovering in the recovery room and confirming that the discharge criteria were met, the patients were permitted to go home.

1) MDZ

An opioid analgesic (30 mg, Pethidine HCl Injection; Bio & Chemical R&D, Seoul, Korea) at a concentration of 5 mg/mL was administered over 1 minute. Thereafter, MDZ (midazolam injection; Bukwang Pharmaceutical, Seoul, Korea) at a concentration of 0.2 mg/mL was injected at a rate of 0.06 mg/kg/2 minutes. Surgical aseptic draping was performed while observing changes in the vital signs. Local anesthesia was administered 5 minutes after MDZ administration, and the surgery was initiated 5 minutes after local anesthesia. As a maintenance dose after local anesthesia during the tooth extraction, an additional 1 mg of MDZ was injected over 1 minute when the patient exhibited anxious or agitated behavior. If the SpO_2 dropped below 94 and the patient did not respond to a mild stimulus, over-sedation was considered, the operation was temporarily stopped, and a trapezius squeeze was performed. If the patient failed to respond, 0.2 mg of flumazenil (flunil injection; Bukwang Pharmaceutical) was injected for 15 seconds. If consciousness was not restored within 1 minute, an additional 0.1 mg of flumazenil was administered.

2) DEX

As the initial dose, DEX (Precedex; Pfizer Pharmaceutical Korea, Seoul, Korea) was injected at 1 μg/kg/10 minutes. Surgical aseptic draping was performed while observing changes in the vital signs. Local anesthesia was administered 5 minutes after the injection was finished, and the surgery was started 5 minutes after local anesthesia. A maintenance dose was injected at 0.5 μg/kg/hr, and in the case of hypo-sedation, the dose was increased to 1 μg/kg/hr. The infusion was stopped at the beginning of the primary closure. In the case of bradycardia, a 1 mg bolus of atropine was administered intravenously and repeated every 3-5 minutes if necessary. Although MDZ has no analgesic effect, DEX does. Therefore, a small amount of opioid is used preoperatively in our hospital only when using MDZ, and no analgesics are used with DEX. Hence, the MDZ group received MDZ and

pethidine, while the DEX group received only DEX.

3. Impacted mandibular third molar extraction protocol

All extractions were performed by two oral and maxillofacial surgeons with more than 10 years of experience. The oral cavity of the patient was disinfected with chlorhexidine gluconate (Hexamedine Garg 0.12% 100 mL; Bukwang Pharmaceutical), and surgical aseptic draping was performed. After inducing local anesthesia with lidocaine (lidocaine HCl 2% injection 1:100,000 epinephrine; Huons, Seoul, Korea), an oblique incision and sulcus incision posterior to the second molar were made to form an envelope flap. The alveolar bone around the impacted tooth was partially removed, and tooth sectioning was performed under sufficient irrigation. The sectioned crown and remaining root were removed using an elevator. After removing the granulation tissue via curettage, sufficient normal saline irrigation of the extraction socket was performed. The flap was repositioned, and sutures were placed with a non-absorbable suture (4-0 dafilon; B. Braun Korea, Seoul, Korea) after confirming that no residual tooth or root fragments were present[8].

4. Variables

The predictor variable was the type of sedative. The two sedative agents were randomly assigned to each patient. For all patients who met the inclusion criteria, the two agents were used alternately, and among them, the patients who met the exclusion criteria were excluded from the study. Hence, the allocation ratio of the final study sample could not be 1:1, and the two groups were slightly heterogeneous. The primary outcome variables were vital signs, vital sign outliers, and cost of the sedatives. The vital signs recorded in this study were HR, SBP, and DBP. The vital sign outlier was defined as cases showing a difference of 30% or more at least once compared to that just before sedation. The investigators determined that the lower the proportion of these outliers, the higher the vital sign stability of the sedative. The cost incurred when using the two agents was also investigated. Since the sedation protocol of the two groups was the same except for the type of sedative, the total sedation cost difference between the two groups was the same as the price difference between the two sedatives. Therefore, in this study, each sedative price, corresponding to the amount of the drug used in each patient, was defined as the cost. Since opioid analgesics were additionally used in the MDZ group, their cost was also included. The secondary outcome variables were the observer's assessment of alertness/sedation scale (OAAS), level of amnesia about the extraction, patient satisfaction, and BIS. The OAAS was evaluated by the main surgeon on a scale of 1-5. A score of 5 indicated an immediate response to calling the patient's name in a soft voice, whereas a score of 1 indicated no response even if the trapezius squeeze was performed[9]. The level of amnesia was calculated by asking the patient whether they remembered the local anesthesia procedure, the overall surgical procedure, and the suturing procedure the day after the surgery. The whole process was scored out of 3 points, 1 point for each step the patient remembered and 0 if the patient did not remember. Patient satisfaction was rated on a scale of 1-5; the score was 5 points if the patient was very satisfied with sufficient sedation during the surgery and 1 point if the patient was very dissatisfied because of continuous discomfort during the surgery due to insufficient sedation. The SpO_2, BIS, HR, SBP, and DBP were recorded right before sedation, 5 minutes after sedative administration, during local anesthesia, 20 minutes after local anesthesia, and at the start of the primary closure. The covariates included were sex, age, body mass index, sleeping time ratio, dental anxiety scale (DAS), and Pederson scale. The sleeping time ratio was calculated as the ratio of sleep time the day before the surgery to normal sleep time. The DAS is a measure of the stress level associated with dental treatments. It was measured using a questionnaire, and 20 points were measured through four questions[10]. The Pederson scale was measured via panoramic radiographs to evaluate the difficulty of the extraction, and the average of the left and right scores was used as the final score[11].

5. Data collection/analysis

This study investigated the medical records of all the study participants. Two surgeons with at least 3 years of clinical experience evaluated the clinical parameters. After data collection was complete, all parameters were gathered, and we checked for missing data. Since the two groups were heterogeneous due to the nature of the retrospective study, propensity score matching (PSM) was used to control for bias due to covariates. Pearson's chi-square test or Fisher's exact test was used to analyze nominal variables, and Student's *t*-test, paired *t*-test, or Pearson's correlation analysis was used to analyze continuous variables. All statistical analyses were performed using IBM SPSS Statistics (ver. 26.0; IBM, Armonk, NY, USA). Statistical significance was set at $P<0.05$.

III. Results

Among the 185 patients, 103 received MDZ and 82 received DEX. The mean age was 27.34±9.15 years (range, 13-60 years). Most patients were healthy without any systemic diseases. There were 9 cases of diabetes mellitus or hyperten-

Table 1. Comparison of the covariates involved in third molar extraction under intravenous moderate sedation in cases stratified according to the sedative used

	Before PSM (n=185)				After PSM (n=150)		
	Total (n=185)	MDZ (n=103)	DEX (n=82)	*P*-value	MDZ (n=75)	DEX (n=75)	*P*-value
Sex, male	108 (58.4)	54 (52.4)	54 (65.9)	0.066[1]	40 (53.3)	48 (64.0)	0.185[1]
Age (yr)	27.34±9.15	25.62±7.89	29.49±10.16	0.005[2,*]	26.75±8.71	27.84±8.71	0.443[2]
BMI (kg/m^2)	22.25±3.22	22.03±3.03	22.53±3.44	0.297[2]	22.00±3.19	22.33±3.50	0.554[2]
Sleeping time ratio	0.91±0.26	0.90±0.25	0.92±0.27	0.665[2]	0.92±0.25	0.90±0.27	0.623[2]
DAS	10.98±3.15	11.23±2.85	10.67±3.48	0.239[2]	11.12±3.00	10.77±3.48	0.514[2]
Pederson scale	5.72±1.35	5.44±1.33	6.08±1.29	0.001[2,*]	5.71±1.39	5.98±1.29	0.223[2]

(PSM: propensity score matching, MDZ: midazolam, DEX: dexmedetomidine, BMI: body mass index, DAS: dental anxiety score)
[1]Pearson's chi-square test. [2]Student's *t*-test.
*P<0.05.
Values are presented as number (%) or mean±standard deviation.
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Table 2. Comparison of factors involved in third molar extraction under intravenous moderate sedation in cases stratified according to the sedative used

	Before PSM (n=185)				After PSM (n=150)		
	Total (n=185)	MDZ (n=103)	DEX (n=82)	*P*-value	MDZ (n=75)	DEX (n=75)	*P*-value
Vital sign outlier (n)							
Heart rate	66 (35.7)	48 (46.6)	18 (22.0)	0.001[1,*]	37 (49.3)	17 (22.7)	0.001[1,*]
SBP	11 (5.9)	8 (7.8)	3 (3.7)	0.351[3]	6 (8.0)	3 (4.0)	0.494[3]
DBP	28 (15.1)	16 (15.5)	12 (14.6)	0.865[1]	12 (16.0)	12 (16.0)	>0.999[1]
Heart rate (BPM)							
T0	74.22±16.37	76.78±16.17	71.01±16.16	0.017[2,*]	74.75±14.37	71.19±16.23	0.157[2]
T1	72.04±19.43	79.41±19.63	62.78±14.70	0.000[2,*]	78.65±18.50	62.76±14.67	0.000[2,*]
T2	80.13±18.98	86.21±19.53	72.49±15.22	0.000[2,*]	85.07±17.32	72.75±15.49	0.000[2,*]
T3	86.82±18.71	95.89±17.71	75.41±12.81	0.000[2,*]	93.88±14.96	75.89±12.91	0.000[2,*]
T4	84.51±19.08	94.63±17.07	71.79±12.90	0.000[2,*]	92.89±15.87	72.05±13.12	0.000[2,*]
SBP (mmHg)							
T0	134.05±20.34	134.37±19.92	133.66±20.30	0.812[2]	133.35±18.44	134.08±19.24	0.812[2]
T1	133.71±20.59	133.83±19.96	133.57±21.48	0.935[2]	134.15±19.28	133.89±20.54	0.938[2]
T2	136.01±23.99	138.61±24.18	132.73±23.48	0.097[2]	139.43±23.87	133.32±22.50	0.109[2]
T3	135.42±20.90	140.72±19.70	128.76±20.58	0.000[2,*]	139.83±19.09	129.68±19.46	0.002[2,*]
T4	133.97±22.73	140.12±20.77	126.24±22.85	0.000[2,*]	138.99±19.84	126.24±21.74	0.000[2,*]
DBP (mmHg)							
T0	77.03±12.25	75.46±12.33	79.00±11.92	0.049[2,*]	76.33±11.92	78.92±11.32	0.175[2]
T1	74.76±12.64	72.30±12.10	77.84±12.69	0.003[2,*]	73.40±11.49	77.59±11.79	0.029[2,*]
T2	72.50±13.01	71.38±13.58	73.90±12.18	0.185[2]	72.65±13.79	73.47±11.26	0.693[2]
T3	68.83±12.69	69.72±12.75	67.71±12.60	0.285[2]	70.72±12.83	67.67±12.50	0.138[2]
T4	70.95±13.56	72.71±14.55	68.74±11.92	0.043[2,*]	74.15±15.09	68.51±11.11	0.010[2,*]
Cost (USD)[4]	13.18±14.39	0.37±0.04	29.27±0.00	0.000[2,*]	0.37±0.04	29.27±0.00	0.000[2,*]
OAAS	4.43±0.68	4.47±0.73	4.38±0.62	0.384[2]	4.53±0.68	4.37±0.63	0.139[2]
Amnesia	1.21±1.17	1.26±1.18	1.15±1.16	0.504[2]	1.16±1.21	1.17±1.16	0.945[2]
Satisfaction	4.14±1.14	4.20±1.14	4.06±1.15	0.400[2]	4.16±1.20	4.01±1.17	0.449[2]
BIS							
T0	92.46±4.75	92.10±4.85	92.91±4.61	0.244[2]	91.71±4.59	92.65±4.66	0.102[2]
T1	82.76±6.36	80.46±5.10	85.66±6.61	0.000[2,*]	80.63±5.30	85.41±6.55	0.000[2,*]
T2	85.41±6.52	82.47±5.33	89.11±6.00	0.000[2,*]	82.23±5.56	89.47±5.69	0.000[2,*]
T3	84.84±6.00	84.09±4.85	85.79±7.11	0.066[2]	84.53±4.87	85.77±6.69	0.197[2]
T4	86.07±5.98	86.17±5.61	85.94±6.43	0.794[2]	86.27±5.90	85.71±6.45	0.580[2]

(PSM: propensity score matching, MDZ: midazolam, DEX: dexmedetomidine, SBP: systolic noninvasive blood pressure, DBP: diastolic noninvasive blood pressure, BPM: beats per minute, T0: the moment right before sedative administration, T1: 5 minutes after sedative administration, T2: the time of injection of the local anesthetic agent, T3: 20 minutes after local anesthesia, T4: the time of the start of the primary closure, USD: US dollar, OAAS: Observer's Assessment of Alertness/Sedation Scale, BIS: bispectral index score)
[1]Pearson's chi-square test. [2]Student's *t*-test. [3]Fisher's exact test.
[4]Including the cost of opioid analgesics.
*P<0.05.
Values are presented as number (%) or mean±standard deviation.
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sion, 1 case of stable angina, 1 case of epilepsy, and 1 case of chronic myeloid leukemia. All of these were well-controlled. The SpO_2 was maintained above 95 in all patients, and there were no cases of respiratory failure or bradycardia. No reversal agent was administered due to over-sedation when using MDZ, and no atropine was used for DEX. Table 1 summarizes the comparison of the covariates in the two groups before and after PSM. Before PSM, there was a statistically significant difference in age and Pederson scale between the two groups; however, this was corrected through PSM. Supplementary Table 1 summarizes the correlation between the covariates and vital signs. All covariates except for the sleeping time ratio affected vital signs. Therefore, to study vital signs only by sedative difference, the covariates of the two groups had to be corrected, and for this purpose, PSM was used. Table 2 summarizes the comparison of outcome variables according to sedative differences. Post-PSM data showed that the frequency of vital sign outliers changed by more than 30% compared to the initial value, which was 49.3% in the MDZ group and 22.6% in the DEX group for HR. However, no patients required cardiac care due to this change. HR showed a higher value in the MDZ group during all periods of sedative administration.(Fig. 1. A) SBP was higher in the MDZ group 20 minutes after local anesthesia and at the beginning of the primary closure.(Fig. 1. B) DBP was higher in the DEX group 5 minutes after sedative administration and in the MDZ group at the beginning of the primary closure.(Fig. 1. C) As for the average cost of sedatives per patient, the

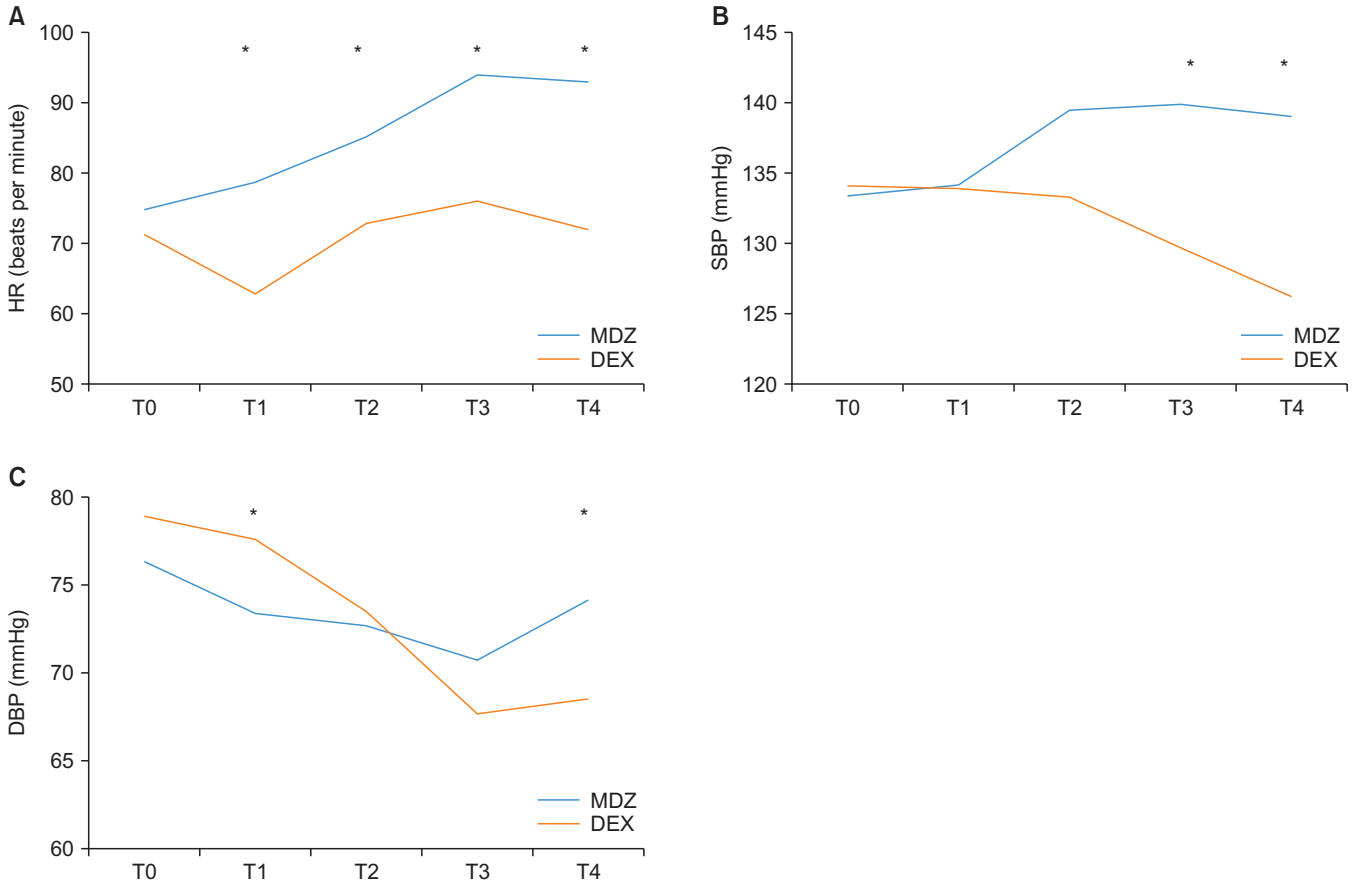

Fig. 1. Comparison of vital signs between the two treatment groups during the course of surgery in each period. A. Comparison of heart rate (HR): After sedative administration, HR increased in both groups, but it showed a higher value in the midazolam (MDZ) group than the dexmedetomidine (DEX) group in all periods. B. Comparison of systolic noninvasive blood pressure (SBP): After sedative administration, SBP increased in the MDZ group and decreased in the DEX group, showing a higher value in the MDZ group 20 minutes after local anesthesia and thereafter. C. Comparison of diastolic noninvasive blood pressure (DBP): After sedative administration, DBP decreased in both groups, showing a higher value in the DEX group 5 minutes after sedative administration and in the MDZ group at the beginning of the primary closure. *P<0.05 by Student's t-test. (T0: the moment right before sedative administration, T1: 5 minutes after sedative administration, T2: the time of injection of the local anesthetic agent, T3: 20 minutes after local anesthesia, T4: the time of the start of the primary closure)

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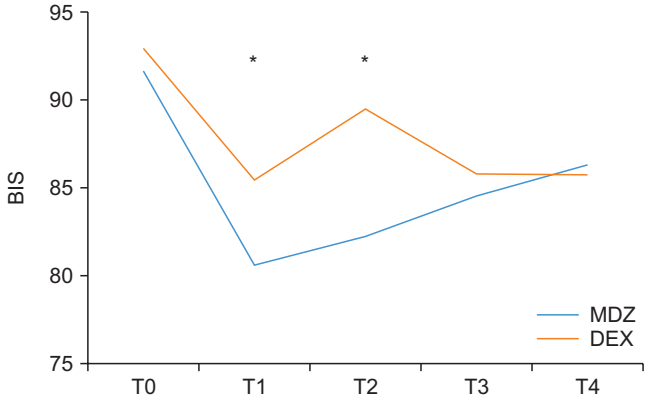

Fig. 2. Comparison of the bispectral index score (BIS) between the two treatment groups during the course of surgery in each period. *P<0.05 by Student's t-test. (T0: the moment right before sedative administration, T1: 5 minutes after sedative administration, T2: the time of injection of the local anesthetic agent, T3: 20 minutes after local anesthesia, T4: the time of the start of the primary closure, MDZ: midazolam, DEX: dexmedetomidine)
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MDZ group had a much lower cost. There was no significant difference in the OAAS, level of amnesia, or patient satisfaction between the two groups. The BIS showed a lower value in the MDZ group 5 minutes after sedative administration and at the time of local anesthesia.(Fig. 2) Supplementary Tables 2 and 3 summarize the comparison of values according to each time interval in each group.

IV. Discussion

Since MDZ and DEX are the most commonly used sedatives, it is of clinical value to compare the sedative effect, vital sign stability, and cost of the two agents. The purpose of this study was to compare the differences between the two drugs, focusing on these points. In this study, the sedative effect assessed by the surgeon and the patient was similar between the two groups. DEX was advantageous over MDZ in vital sign stability; however, this difference did not have clinical significance in relatively healthy patients within ASA II. In terms of cost, MDZ was advantageous compared with DEX.

Demographic differences among patients can affect differences in the degree of dental anxiety. Acharya et al.[12] and Udoye et al.[13] have reported significant differences in dental phobia according to sex and age, using the DAS questionnaire. Similar results were also reported in a study by Appukuttan et al.[14], which used the Tamil version of the modified DAS questionnaire. In addition, since dental anxiety can affect the hemodynamic vital signs[15], differences in dental anxiety may cause errors in the analysis of vital sign-related effects of sedative agents. However, in this study, no difference in dental anxiety was found between the two groups. This study was retrospective in nature; however, we aimed to reduce study bias as much as possible by correcting for dental anxiety and covariates, such as sex and age, through the PSM method. Therefore, differences in the hemodynamic signs observed in this study were mainly due to differences between the two drugs themselves.

Representative reactions of DEX on the cardiovascular system are bradycardia and lowering of blood pressure. Since these reactions can be controlled by using an appropriate infusion rate, DEX can be used as a sedative agent in patients with ischemic heart disease[16]. In addition, this characteristic of DEX acts as an advantage in reducing blood loss during surgery and securing a field of view in the surgical field[17]. In this study, HR and SBP decreased more, and the amount of change was smaller for DEX compared with MDZ. Thus, it was possible to confirm the clinical stability of DEX from a hemodynamic point of view. In many previous studies, the clinical hemodynamic stability of DEX compared with that of MDZ has been supported. In a study conducted by Yu et al.[18] comparing the SpO_2 and hemodynamic effects of the MDZ/fentanyl combination and DEX/fentanyl combination during sedation for surgical extraction, the HR was lower in the DEX/fentanyl group. Barends et al.[19] reported that MDZ could cause unwanted hypertension during surgery. In addition, in a randomized double-blinded study comparing the sedation effects of DEX and the MDZ/fentanyl combination, the mean arterial pressure and HR were lower in the DEX group[20]. However, unlike these study results, in a study comparing the sedation effect of MDZ and DEX in elderly patients undergoing spinal anesthesia, the mean arterial pressure during the intraoperative 120 minutes was higher with DEX than with MDZ[21]. Therefore, medical staff performing sedation must be prepared for such exceptional cases.

In this study, the cost of the two agents were significantly different, with MDZ costing much less. In a study comparing the cost-effectiveness of MDZ and DEX in patients undergoing mechanical ventilation in an intensive care unit environment, Lachaine and Beauchemin[22] also reported that MDZ was cheaper than DEX in terms of price itself. However, they concluded that DEX was more economical when considering the cost of managing mechanical ventilation and delirium[22]. In addition, in another study comparing the economic feasibility of MDZ, DEX, and propofol in an intensive care set-

ting, DEX was reported to be the least expensive[23].

Sedation agents have been compared for their vital sign stability and cost as well as various other variables, and each study has shown slightly different results. In this study, there was no statistically significant difference in the OAAS or satisfaction in the two groups. However, Wang et al.[24] reported that the OAAS value was higher in the MDZ group than in the DEX group. In addition, in a systematic review comparing the efficacy and safety of MDZ and DEX, the DEX group had higher satisfaction for patients and clinicians than the MDZ group[19]. In this study, the BIS value was lower 5 minutes after sedative administration and during local anesthesia in the MDZ group than in the DEX group. However, Fan et al.[2] reported that there was no statistically significant difference in the BIS between the two groups.

The demographic data, such as the patient's sex and age, and various factors that can affect the sedative effect, such as BMI, sleep time, fear of dental treatment, and type and difficulty of the surgery, were controlled for in this study. Thus, this study has the strength of objectively evaluating the effects of the sedatives themselves and the stability of the vital signs with relatively little bias. In addition, the efficacy of the drugs was compared in consideration of the cost, which has not been addressed well in previous studies. To the best of our knowledge, this study is the first paper to compare the cost-effectiveness of sedation agents during the extraction of third molars under intravenous sedation. However, this study has several limitations. First, it has an inherent limitation as a retrospective nonrandomized concurrent cohort study, despite the effort to correct bias through PSM. Second, the dosing of MDZ and DEX is different for each study, and this might act as a study bias. Third, unlike DEX, MDZ does not have an analgesic effect by itself; hence, pethidine was used in combination with MDZ to reflect the characteristics of these drugs, which could act as a confounder. Fourth, the respiratory rate and capnography were not monitored. Fifth, this was an analysis of the state during sedation, and the recovery after sedation was not analyzed. It is necessary to evaluate the respiratory rate and capnography during sedation and the degree of recovery after sedation through prospective studies in the future.

V. Conclusion

The sedative effects of MDZ and DEX were similar in this study, and the surgeons and patients were relatively satisfied. Given the difference in vital sign stability and cost, the indications for the use of MDZ or DEX during extraction of third molars under intravenous moderate sedation can be summarized as follows. First, the use of MDZ is recommended for patients who are generally relatively healthy, considering the cost. Second, in patients with systemic diseases with cardiac and hemodynamic instability, such as uncontrolled hypertension or myocardial infarction, the use of DEX, which has more favorable vital sign stability, is recommended, despite the high cost.

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Authors' Contributions

J.Y.K. performed analysis and interpretation of data collected, and wrote the manuscript. H.L. participated in conception and design of study, edited and drafted the manuscript. S.Y.P. acquired data and searched clinical literatures. Y.S.H. revised the manuscript critically. All authors approved the final version of manuscript.

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Ethics Approval and Consent to Participate

The study was approved by the Institutional Review Board of SMG-SNU Boramae Medical Center (No. 10-2020-201). Patient consent was waived due to the retrospective nature of the study.

Supplementary Materials

Supplementary data is available at http://www.jkaoms.org.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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