Clinical Report

Survey on Choice of Intravenous Sedative Agent at Department of Dental Anesthesiology, Tokyo Dental College Chiba Hospital between 2010 and 2011

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Abstract

Use of intravenous sedation is increasing in the management of dental patients in consideration of accompanying diseases and patient demand for comfort and safety. We surveyed choice of sedative agent and dosage on the basis of accompanying diseases or conditions in patients receiving treatment at the Department of Dental Anesthesiology, Tokyo Dental College Chiba Hospital between 2010 and 2011. A total of 5,256 patients were reviewed and divided into the following categories: 1) medically compromised patients (MC); 2) minor oral surgery (OS); 3) cerebral palsy (CP); 4) mental retardation (MR); 5) mental disorder (MD); and 6) dental phobia with/without gag reflex. The investigated variables were sex, age, weight, duration of sedation, and dosage of agent. Dosage of midazolam (M), M plus propofol (MP), and P alone was investigated. A total of 2,336 patients were managed by intravenous sedation during the study period. The combination of MP was used in approximately 63–79% of patients in all categories, except MC. Midazolam was used in approximately 47% in the MC group. Propofol was used in approximately 32% of patients in the MR group. Other agents (minor tranquilizers, analgesics, and so on) were used in approximately 12% in the OS group. The dose of M was approximately 0.05–0.06 mg/kg. When MP was administered, the dose of M showed no difference among groups. The dose of P, however, tended to be lower in the MC and CP groups than in the other groups. These results suggest that MP is chosen for intravenous sedation in most types of dental treatment.

Key words: Intravenous sedation — Midazolam — Propofol — Dosage

Introduction

Intravenous sedation is widely used to ensure that dental treatment is safe and comfortable. The Japanese Dental Society of Anesthesiology published guidelines on

intravenous sedation for dental treatment in March 2010²⁾. These guidelines were then later posted on the Medical Information Network Distribution Service website in February 2011¹⁾. They give a comprehensive description of the appropriate method of use and dosage

for each agent. No detailed description is given, however, regarding choice of agent or dosage in consideration of accompanying diseases or conditions. In earlier studies published in 2002 and 2003, before these guidelines became available, we described the criteria used at our own hospital for choosing an agent for intravenous sedation. However, we did not investigate the dosage actually administered^{5,6)}.

In this study, therefore, we surveyed the choice of sedative agent in patients receiving intravenous sedation at our hospital between 2010 and 2011 and compared it with that in our previous reports. In addition, we also investigated and compared the dosage of each agent administered depending on accompanying diseases or conditions.

Methods

The participants comprised outpatients receiving intravenous sedation at the Department of Dental Anesthesiology of Tokyo Dental College Chiba Hospital between January 2010 and December 2011. This study was approved by the Ethics Committee of Tokyo Dental College (approval no.502).

1. Patient categories

The patients were grouped into the following categories: (1) those with medical conditions such as hypertension, bronchial asthma, or diabetes mellitus (MC group); (2) those undergoing oral surgery such as extraction of impacted tooth or implant surgery (OS group); (3) those with cerebral palsy without mental retardation (CP group); (4) those with conditions such as mental retardation or autism (MR group); (5) those with mental disorders such as schizophrenia or panic disorder (MD group); and (6) those with dental phobia, with or without an abnormal gag reflex (DP group).

2. Sedative agents

Sedative agents included (1) midazolam (M), (2) midazolam plus propofol (MP), (3)

propofol alone (P), or (4) other. The “other” category included benzodiazepines other than M, sodium thiopental, ketamine hydrochloride, fentanyl citrate, or pentazocine. Although choice of sedative agent was fundamentally based on our previous reports^{5,6)}, the final decision was made by the dental anesthesiologist based on the patient’s condition and treatment plan. The investigated variables were sex, age, weight, duration of sedation, and dosage of agent. Dosage of M, MP, and P was investigated.

3. Statistical analysis

Data are expressed as the mean $\pm$ standard deviation. Statistical comparisons between groups were performed by using an χ^2 test and a one-way analysis of variance (ANOVA). The Student-Newman-Keuls test was used for multiple comparisons. A value of $p < 0.05$ was regarded as significant.

Results

The number of patients managed by intravenous sedation during the study period was 2,336 out of a total of 5,256 cases. Table 1 shows sex, patient age, and duration of sedation. Age was classed as the age at initial treatment during the study period. There were more women in all groups, except those including people with disabilities (the CP and MR groups). A significant difference was observed in the distribution of the sex ratio. The largest number of patients was observed in the MC group, followed by the DP group. The DP group contained the largest total number of cases, followed by the MR group. The mean age in the MC group was 62.4 years, which tended to be higher than that in the other groups ($p = 0.06$). The mean duration of anesthesia in the OS group was 71.1 min, which tended to be longer than that in the other groups ($p = 0.06$).

Figure 1 shows the agents used. The most commonly administered was MP, while M was administered as a single or repetitive bolus injection. While P was administered by

Table 1 Patients characteristics

	Male/Female	Age (years)	Time (min)
MC	550/703 (380/444)	62.4 ± 15.2	52.1 ± 24.6
OS	137/226 (128/207)	42.2 ± 16.9	71.1 ± 20.9
CP	40/22 (7/5)	43.7 ± 13.3	46.5 ± 10.0
MR	948/406 (203/130)	32.2 ± 11.0	40.8 ± 12.8
MD	199/393 (51/111)	44.0 ± 18.8	42.3 ± 13.1
DP	690/942 (242/428)	39.8 ± 14.1	40.0 ± 21.1

Cases were divided into the following categories, 1: Medically compromised patients (MC); 2: Minor oral surgery (OS); 3: Cerebral palsy (CP); 4: Mental retardation (MR); 5: Mental disorder (MD); 6: Dental phobia with/without gag reflex (DP).

Male/Female, Upper row: Number of cases; Lower row: Number of patients.

Fig. 1 Kind of agents

M: Midazolam, MP: Midazolam + propofol, P: Propofol, Other: Other minor tranquilizer, analgesics.

infusion in most cases, it was also given as a repetitive bolus injection in a small number of cases. In the case of MP, bolus injection of M was followed by infusion or repetitive bolus injection of P.

Figure 2 shows the relationship between patient category and administered agent. In the MC group, the number of cases receiving M was almost the same as that receiving MP. In the OS, CP, MR, MD, and DP groups, however, MP was chosen in the largest

Fig. 2 Kind of agents used for each category

Patients categories, MC: Medically compromised patients; OS: Minor oral surgery; CP: Cerebral palsy; MR: Mental retardation; MD: Mental disorder; DP: Dental phobia with/without gag reflex.

Agents, M: Midazolam; MP: Midazolam + propofol; P: Propofol; Other: Other minor tranquilizer, analgesics.

number of cases. In the MD and DP groups, in particular, almost all patients received MP.

Total dose per unit weight of agent in each group is given in Table 2. The dose of M was approximately 0.05–0.06 mg/kg, with no significant difference except for in the CP group ($p=0.005$). Where MP was administered, although the dose of M showed no variation

Table 2 Total doses per unit weight of the agents in each group

	M	MP		P
		M	P	
MC	0.05 ± 0.02	0.05 ± 0.02	1.34 ± 1.14	1.18 ± 0.72
OS	0.06 ± 0.03	0.07 ± 0.03	2.37 ± 1.58	
CP	0.1 ± 0.01*	0.06 ± 0.02	0.75 ± 0.33	
MR	0.06 ± 0.03	0.05 ± 0.02	2.69 ± 1.60	3.56 ± 1.37
MD	0.05 ± 0.01	0.05 ± 0.02	2.20 ± 1.04	4.17 ± 1.82
DP	0.06 ± 0.02	0.05 ± 0.03	2.13 ± 1.12	3.21 ± 0.97

*: p=0.005 higher than the other groups (mg/kg: mean ± SD)

The administered agents were classified into the following 3 groups: Midazolam alone (M); Propofol alone (P); Midazolam + propofol (MP).

Table 3 Doses per unit weight per hour of the agents in each group

	M	MP		P
		M	P	
MC	0.07 ± 0.04	0.06 ± 0.02	1.46 ± 1.08	2.66 ± 1.85
OS	0.09 ± 0.07	0.04 ± 0.01	1.51 ± 1.28	
CP	0.21 ± 0.02*	0.14 ± 0.02**	2.14 ± 1.05	
MR	0.09 ± 0.05	0.08 ± 0.05	3.80 ± 1.96	5.33 ± 1.64
MD	0.05 ± 0.01	0.05 ± 0.01	2.39 ± 0.76	4.69 ± 1.30
DP	0.09 ± 0.03	0.07 ± 0.03	2.66 ± 1.25	4.73 ± 1.52

*: p=0.015 higher than the other groups (mg/kg: mean ± SD)

**: p=0.004 higher than the other groups

The administered agents were classified into the following 3 groups: Midazolam alone (M); Propofol alone (P); Midazolam + propofol (MP).

between groups, the dose of P tended to be lower in the MC and CP groups than in the other groups (p=0.09). When P alone was used, the dose tended to be lower in the MC group than in the other groups (p=0.06). The weights of some patients in the OS and CP groups were not recorded, so these groups were excluded from the analysis.

Doses per unit weight per hour are given in Table 3. The dose of M was significantly higher in the CP group than in the other groups (p=0.015). When MP was administered, no significant difference was observed in the dose of M, except in the CP group (p=0.004). The dose of P in this combination, however, tended to be lower in the OS and

MC groups than in the other groups (p=0.06). When P was used alone, no significant difference was observed in dose between any of the groups, although it tended to be lower in the MC group (p=0.06). The weights of some patients in the OS and CP groups receiving P alone were not recorded, so these groups were excluded from the analysis.

Discussion

The number of cases in which intravenous sedation is being used for patient management during dental treatment at our department is increasing year by year. In

the past five years, in particular, 2,500–3,000 patients a year have been managed under intravenous sedation⁷⁾.

In terms of patient background, the proportion of men was greater among patients with cerebral palsy and mental retardation. This may be because male patients are strong, and are therefore more likely to require behavioral control by means of intravenous sedation. Patients in the MC group were older than in the other groups, as might be expected in cases of conditions such as hypertension and diabetes. The duration of anesthesia was longer in the OS group than in the other groups. This may have been due to the comparatively longer times required for procedures such as extraction of an impacted tooth or implant insertion. Although patient classification in this study was not the same as that in previous studies^{5,6)}, similar results were observed.

Guidelines on intravenous sedation in dental treatment were published by the Japanese Dental Society of Anesthesiology in March 2010. They include the statement that agents used in intravenous sedation should ideally exert sedative, hypnotic, anxiolytic, amnesic, and other central depressant effects, with rapid awakening, antiemetic action, and few side effects. Benzodiazepines, particularly M, have been anticipated to exert sedative, hypnotic, anxiolytic, and amnesic effects, with faster awakening than with other agents. Although the anxiolytic effect of P is mild, its effect appears rapidly and awakening is also fast; therefore, P is also listed as an appropriate drug for use in intravenous sedation.

In a previous study⁶⁾, M was used in 54% of the total number of cases, followed by P (25%) and MP (16%) between 2002 and 2003. We reported that M was more frequently used to relieve mental stress and anxiety in dental-phobic patients and patients with other medical conditions, whereas P alone was more commonly used in patients with an abnormal gag reflex or disabilities as it allows better control of the depth of sedation.

The present results showed that M, P, and MP were used in almost the same circumstances

as those between 2003 and 2007⁵⁾. An increase was observed in use of MP, however, especially in the DP group, while use of P showed an increase in the other groups. Deep sedation is frequently required in MR patients. The level of sedation can be easily adjusted with administration of P, which may explain why it was frequently chosen in this group.

In the present study, we found that MP was chosen for most patients, excluding those suffering from other medical conditions. This is presumably because M has strong amnesic effects and P compensates for difficulties in controlling depth of sedation after administration of M. Repetitive administration of M carries the risk of causing respiratory and circulatory depression. In addition, deep sedation may be required in anxious patients, as P has only a weak amnesic effect⁴⁾. In the MC group, M was used in almost the same type of case as MP. This is because many patients in the MC group required light sedation with short duration for simple dental treatments under anxiolytic conditions.

The dose of M when administered either alone or as MP was almost the same in all groups, except OS and CP. According to Dental Anesthesiology, 7th ed.⁴⁾, the recommended dose of M for intravenous sedation is 0.05–0.07 mg/kg, and the dose of P should be 4 mg/kg/h on average. In this study, we found almost the same results, with the exception of in the CP group. The doses used for patients in the CP group were larger because a greater amount of M was required to inhibit increased muscle tension through excitation. Except for in the MR group, the dose of P in combination with M was 1.5–2.5 mg/kg/h, which was lower than that when P was used alone. The dose of P tended to be lower in the MC group than in the other groups. Many of the patients with other conditions were elderly. These patients may have required a smaller dose to reach the target level of sedation.

Although sedation levels were not addressed in the present study, conscious sedation was more commonly used in the MC group with the aim of relieving mental stress, whereas

deep sedation was more frequently used in the other groups. Events including intraoperative respiratory depression and reduction in SpO₂ were observed in patients who underwent deep sedation. However, these events were improved by elevation of the lower jaw or oxygen administration, and no patient required more high-level treatment.

According to Kaneko³⁾, elderly patients require a lower dose of drugs than healthy younger adults. In this study, we also found that the dose of P tended to be lower in patients in the MC group, although this difference was not significant, suggesting that age must also be taken into account when determining the dose of intravenous sedative to be administered. We intend to undertake future studies that also cover the sedation level and perioperative complications.

Conclusion

The present results revealed that MP was the most commonly administered drug in all groups except the MC group. When MP was administered, although there was no significant difference in the dose of M except in the CP group, the dose of P tended to be lower in the OS and MC groups than in the other groups. Various factors are involved in the choice of agents for intravenous sedation. Therefore, it is important both to consider the patient's safety and comfort and to ensure that dental treatment can be managed safely.

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