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Original Article

Meta-analysis for Efficacy and Safety of Propofol during Dental Sedation

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Background: Dental sedation reduces fear and phobia during dental treatment and helps patients get quality treatment by inducing adequate consciousness control. Propofol has recently grabbed the spotlight, but no meta-analysis for efficacy and safety of propofol in dentistry has yet been performed. Thus, the purpose of this study was to perform meta-analysis to verify the efficacy and safety of propofol for use in dental sedation.

Methods: Articles published between 1980 and 2010 were searched in the web sites, journals and medical database including The Cochrane Library, MEDLINE and EMBASE. And a total of 22 studies were selected among the randomized controlled trials (RCTs) that compared the use of propofol with other sedatives (control group). The data was collected from these studies and meta-analysis for efficacy and safety was performed using Comprehensive Meta-Analysis 5.0 (CMA 5.0).

Results: The patient recovered significantly faster and discharged significantly earlier in the propofol group (SMD = −1.442, $P < 0.001$). The satisfaction of patient and that of operator was higher in the propofol group ($P < 0.05$). The incidence of arrhythmia and apnea/ hypoventilation was significantly lower in the propofol group (OR = 0.071, $P < 0.05$), and there was no significant difference in the other side effects. On the level of sedation, although the sedation score was significantly lower in the propofol group (SMD = −0.430, $P < 0.05$).

Conclusions: The present analysis showed that the use of propofol resulted in high satisfaction levels on the part of the patients and operators, a shorter recovery time, and faster hospital discharge. The incidence of complications, however, was lower in the propofol groups or not much different between the propofol and control groups. Thus, the adequate use of propofol in dentistry is believed to be helpful for the effective and safe sedation of the patients.

Key Words: Dental sedation; Efficacy; Meta-analysis; Propofol; Randomized controlled trial (RCT); Safety

INTRODUCTION

Fear and phobia during dental treatment cause psychological distress, sometimes difficulty in controlling behavior, and repulsion to treatment on the part of the patients, and result in inappropriate treatment outcomes. Dental sedation is part of the efforts to reduce fear of dental treatment. It can provide psychological stability to the patients and can help them obtain quality treatment. As such, it has become an essential part of the rapidly developing dental-care environment.

In particular, intravenous sedation can be useful for various purposes. Propofol (2, 6-diisopropylphenol), which has grabbed the spotlight of late, is an intravenous sedative [1]. Its rapid action onset, short recovery time, and adequate sedation effect have made it a great help to dental treatment [2].

Due to the characteristics of dental treatment, procedures involving the oral cavity and maxillofacial area should be performed with extra care. In particular, as an overdose of most sedatives leads to respiratory depression, dental sedation using sedatives should be approached with much caution. Local anesthetization, however, when performed during dental treatment, can be of great help for dental sedation due to its

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potent analgesic effect.

As is typical with most other sedatives, propofol has efficacy but may also cause complications. Thus, meta-analyses of the evidence-based medicine for the efficacy and safety of propofol were recently conducted[3]. No meta-analysis has yet been conducted, however, on the efficacy and safety of propofol for use in dental sedation.

As such, the purpose of this study was to examine randomized controlled trial (RCT) that compared the sedative effect of propofol alone or in combination with other sedatives with those of other sedatives, and to perform meta-analysis to verify the efficacy and safety of propofol for use in dental sedation.

METHODS

1. Search strategy

Articles published between 1980 and 2010 were searched in the medical database using the term 'propofol', 'sedation', 'dental' and 'oral' including The Cochrane Library, MEDLINE and EMBASE. Web sites and journals of relevant societies were also searched. The year 1980 was chosen as the starting year for the search because propofol was discovered in the 1970s and was introduced to clinical practice in the 1980s [4]. No restriction was applied to the search language. A total of 322 studies on the relevant theme were yielded by the search.

2. Study selection

The abstracts of the 322 studies were examined. Among the 322 studies, 83 RCTs that compared the use of propofol alone or in combination with other agents with that of other sedatives were selected. Then, among the 83 studies, a total of 22 studies that meet the purpose of the present study and that can be statistically analyzed were selected by two independent investigators, by mutual agreement, and were included in the final meta-analysis.

3. Quality assessment

To assess the quality of the 22 studies, 'Jadad scale' was used [5]. 'Jadad scale' is a process that assesses an RCT by assigning an RCT score based on whether randomization was mentioned or not in the RCT (0/1), on appropriate or wrong randomization (1/−1), on whether double-blinding was mentioned or not in the RCT (0/1), on appropriate or wrong double-blinding (1/−1), and on whether withdrawal or dropout was mentioned or not in the RCT (0/1), with the total score ranging from 0 to 5. The study quality was assessed as poor (0-2), good (3-4), or excellent (5). The assessment of the study quality was independently performed by two investigators, by mutual agreement. The rate of agreement between the investigators (Kappa coefficient) was 0.6. If an investigator did not agree to the other's assessment, they reached an agreement via discussion.

4. Data extraction

Items that can collect the data required for the characteristics of each study and for meta-analysis were devised and used (Table 1). The items for the major selected outcomes among the data required for this study are as follows:

1) Items for efficacy

(1) Procedure time

(2) Recovery time

(3) Discharge time

(4) Overall patient satisfaction

(5) Overall operator satisfaction

2) Items for safety

(1) Hypoxia (oxygen saturation less than 90%)

Table 1. Characteristics of included studies (ordered by study ID)

Author year (country)	Clinical Characteristics		Participants			Interventions	Selected Outcomes				Quality Score
	Procedure	Setting	Age (year) (mean)	Sample size (Male %)	ASA PS		measures	PPF groups	Other agents groups	Notes	
Arya[16] 2002 (India)	Pediatric dental Tx.	NS	2–5	30	1	Group A (N = 15) : MDZ (0.02 mg/kg +0.005 mg/kg); IV Group B (N =15) : PPF (3 mg/kg +0.4 mg/kg); IV	1. Operator satisfaction	12/15 (n/N)	15/15 (n/N)	Houpt "overall Behavior" score	0
Cohen[14] 1996 (USA)	Third molar Ext.	unclear	18 over	40	1–2	Group A (N = NS) : FTN (0.0007 mg/kg) + MDZ (1 mg/2 min) + MTH (0.3 mg/kg); IV Group B (N = NS) : FTN (0.0007 mg/kg) + MDZ (1 mg/2 min) + PPF (0.5 mg/kg + 0.066 mg/kg/min); IV	1. Procedure time (min)	20.73	19.45	Mean (SD)	3
Gillo[23] 2005 (USA)	Full face laser resurfacing	Outpatient	51–80 (62)	41 (100%)	2–3	Group A (N = 15) : MDZ (6.2 mg) + FTN (291 mcg); IV Group B (N = 26) : MDZ (3.8 mg) + FTN (86.5 mg) + PPF (300–400 mcg + 30–40 mcg/kg/min); IV	1. Hypotension (mmHg) 2. HR (beat/min) 3. SPO_2 (%) 4. RR (br/min) 5. Procedure time (min)	123.5 79.1 95 14.7 85.7	132 86 95.3 13.5 95	BP<90 Mean Mean Mean Mean	2
Johns[15] 1998 (USA)	Third molar Ext.	unclear	18–40 (24)	75 (46%)	1–2	Group A (N = 35) : MDZ (0.05 mg/kg) + FTN (1.5 mcg/kg) + MTH (50–100 mcg/kg/min); IV Group B (N = 35) : MDZ (0.05 mg/kg) + FTN (1.5 mcg/kg) + PPF (50–100 mcg/kg/min); IV	1. Procedure time (min) 2. HR (beat/min) 3. SBP (mmHg) 4. SPO_2 (%) 5. Pt. satisfaction (VAS) 6. Operator satisfaction (VAS)	44.7 82.3 123.4 98 8.9 8.5	49.5 89.9 129.4 98 9.3 8.3	Mean Mean Mean Mean Mean Mean	3
Leitch[17] 2004 (UK)	Third molar Ext.	Outpatient	17–49 (28)	110 (19%)	1–2	Group A (N = 55) : MDZ (2 mg +1 mg); IV Group B (N = 55) : PPF (1.0 mcg/ml + 0.2 mcg/ml, lockout 2 min, maximum 3.0 mcg/ml); IV PCS	1. Hypoxia 2. HR (beat/min) 3. SBP (mmHg) 4. SPO_2 (%) 5. Procedure time (min) 6 Discharge time (min) 7. Pt. satisfaction 8. Level of sedation	0/55 97 136 99.5 14 18 49/53 2.25	1/55 92 135 99.2 14 25 35/45 2.51	SPO_2<90% Mean Mean Mean Mean Mean sedation score	3
Lee[36] 2008 (USA)	Oral & Maxillofacial operation	Outpatient	1–101 (28.5)	47,710 (57%)	1–2 (98%) 3 (1.8%) 4–5 (0.1%)	Group A (N = 26,147) : PPF IV Group B (N = 15,859) : MTH IV Group C (N = 5,704) : BNZ IV	1. Arrhythmia 2. Apnea or Hypoventilation	3/ 26,147 5/ 26,147	19/ 21,599 15/ 21,599		3

Author year (country)	Clinical Characteristics		Participants			Interventions	Selected Outcomes				Quality Score
	Procedure	Setting	Age (year) (mean)	Sample size (Male %)	ASA PS		measures	PPF groups	Other agents groups	Notes	
Lee[22] 2008 (Korea)	Oral minor surgery	Outpatient	(31.5)	34 (44%)	NS	Group A (N = 5) : MDZ (2 ml + 1-2 ml/2 min) Group B (N = 8) : MDZ (2 ml + 1-2 ml/2 min) + FTN (1 ml) Group C (N = 7) : MDZ (2 ml + 1-2 ml/2 min) + PPF (15-20 ml/hr) Group D (N = 14) : MDZ (2 ml + 1-2 ml/2 min) + FTN (1 ml) + PPF (15-20 ml/hr)	1. Recovery time (min)	18.8	34.1	Mean	2
Meyers[24] 1994 (USA)	Third molar Ext.	Outpatient	18over	40	1-2	Group A (N = NS) : MDZ (5 mg/min) + MTH (3 mg/kg); IV Group B (N = NS): MDZ (5 mg/min) + PPF (5 mg/kg); IV	1. Arrhythmia	+13.9%	+26.7%	HR change %	3
Okawa[25] 2009 (Japan)	Chair side dental Tx.	Unclear	Adult	25 (100%)	1-2	Group A (N = 25) : PPF (0.7 mcg/ml) ; IV TCI Group B (N = 25) : DEX (0.1 mcg/kg + 0.4 mcg/kg/h); IV	1. SPO2 (%) 2. Pt Dissatisfaction 3. Level of sedation	96.9 1.6 79.4	97.5 3 79.6	Mean FAS score Mean	3
Parworth[8] 1998 (USA)	Third molar Ext.	Unclear	16-47	57	1-2	Group A (N = 24) : PPF (300 mcg/kg/ min) + FTN (100 mcg); IV Group B (N = 33) : MDZ (75 mcg/kg/ min) + FTN. (100 mcg); IV	1. Apnea 2. Procedure time (min)	1/24 20.6	2/33 21	 Mean	5
Rai[18] 2007 (India)	Oral rehabilitation	Outpatient	3-6	30	1-2	Group A (N = 10) : MDZ (0.1 mg/kg + 0.004 mg/kg/min); IV Group B (N = 10) : PPF (1 mgkg-1 + 0.06 mg/kg/min); IV Group C (N = 10) : Ketamine (0.5 mg/kg + 0.01 mg/kg/min); IV	1. Level of sedation 2. Operator satisfaction	2.4 3.43	2.6 4.26	"SLEEP" score score	3
Rudkin[19] 1992 (Australia)	Third molar Ext.	Outpatient	Adult (22)	40	1	Group A (N = 20) : FTN (0.7 mcg/kg)+ PPF (20 mg + 1200 ml/h, lockout 1 min); IV PCS Group B (N = 20) : FTN (0.7 mcg/kg) + MDZ (0.5 mg + 1200 ml/h, lockout 1 min); IV PCS	1. Procedure time (min) 2. Discharge time (min) 3.Level of sedation	33.6 113.3 2.7	35.6 113.1 3.15	Mean Mean sedation score	3
Sarasin[26] 1996 (US)	Oral surgical procedure	NS	(23.4)	28 (35%)	1-2	Group A (N = 14) : MDZ (0.1 mg/kg); IV Group B (N = 14) : PPF (1.0 mg/kg + 65 mcg/kg/min); IV	1. Procedure time (min)	14.3	13.9	Mean	5
Shimada[37] 2007 (Japan)	Scaling	Outpatient	21-25 (23)	12 (100%)	NS	Group A (N =12) : PPF (8 mg/kg/hr for 10 min + 4 mg/kg/hr for 20 min); IV Group B (N =12) : DEX (6 mg/kg/hr for 10 min + 0.2 mcg/kg/hr for 20 min); IV	1. Hypoxia 2. Level of sedation	0/12 2.88	2/12 3.74	SPO2 drop Ramsay score	3
Stephens[9] 1993 (UK)	Restorative dental Tx. & Tooth Ext.	Outpatient	5-26 (11.6)	18 (67%)	1-3	Group A (N = 16) : MDZ (0.02 mg/kg + 0.4 mg/kg/h); IV Group B (N = 16) : PPF (0.2 mg/kg + 4.0 mg/kg/h); IV	1. Recovery time (min) 2. Hypotension 3. Operator satisfaction	22.97 2/16 16/16	84.98 5/16 3/16	Mean SBP drop	5

Author year (country)	Clinical Characteristics		Participants			Interventions	Selected Outcomes				Quality Score
	Procedure	Setting	Age (year) (mean)	Sample size (Male %)	ASA PS		measures	PPF groups	Other agents groups	Notes	
Takaishi[13] 2007 (Japan)	Oral & Maxillofacial Surgery	NS	25–80 (25.5)	14 (50%)	1–2	Group A (N = 7) : DEX (6 mcg/kg/hr over 10 min + 0.2–0.7 mcg/kg/hr); IV Group B (N = 7) : PPF (10 mg +1–6 mg/kg/hr); IV	1. Procedure time min) 2. Arrhythmia 3. Level of sedation	71 0/7 82.4	64 1/7 72.6	Mean HR <50 Lowest BIS score	3
Tan[10] 2000 (Singapore)	Third molar Ext.	Outpatient	15–26 (23.3)	10 (30%)	1	Group A (N = 10) : PPF (20 mg/6 sec, no lockout time); IV PCS Group B (N = 10) : Alfentanil (0.1 mg/6 sec. no lockout time) IV PCS	1. Procedure time (min) 2. Recovery time 3. Discharge time (min) 4. Pt dissatisfaction 5. Level of sedation	20.5 7.6 30.8 3 3	20.5 6.1 27.3 6 2	mean mean mean VAS sedation score	3
Taniyama[38] 2009 (Japan)	Minor oral surgery	NS	(30.3)	14 (21%)	1	Group A (N = 7) : DEX (6 mcg/kg/h + 0.4 mcg/kg/h); IV Group B (N = 7) : PPF (0.5 mcg/kg/h + 4 mg/kg/h); IV	1. Pt satisfaction(cm)	8.7	7.1	10cm VAS	3
Tomoyasu[20] 2007 (Japan)	Sedation following oral & Maxillofacial surgery	Inpatient	16–17 (32.8)	30 (40%)	N/S	Group A (N = 19) : DEX (0.3–1.2 mcg/kg/h); IV Group B (N = 11) : PPF (1–4 mg/kg/h); IV	1. Pt. satisfaction	14/19	3/11		2
Tsugayasu[21] 2010 (Japan)	Chair side dental sedation	Outpatient	(27)	7 (100%)	1	Group A (N = NS) : MDZ (0.01 mg/kg/min); IV Group B (N = NS) : PPF (0.7 mcg/ml); IV TCI	1. HR (beat/min) 2. Pt dissatisfaction	76.25 2.1	76.35 1.4	Mean FAS score	3
Valtonen[11] 1989 (Finland)	Third molar Ext.	Outpatient	(24.4)	12	1	Group A (N = NS) : PPF (10 mg/min + within 6 mg/kg/h); IV Group B (N = NS) : Diazepam (5 mg/min); IV	1. Procedure time (min) 2. Operator satisfaction (cm)	27.9 9.51	26.6 9.51	Mean 10cm VAS	4
Win[12] 2005 (Japan)	Dental implantation surgery	Outpatient	30–62	30	1–2	Group A (N =15) : PPF (1 mcg/ml + within 0.5 mcg/ml); IV TCI Group B (N =15) : MDZ (0.5 mg over 30s within 0.075 mg/kg)	1. HR (beat/min) 2. SBP (mmHg) 3. Level of sedation 4. Procedure time (min)	73 104 72 51	82 112 77 40	Mean Mean BIS Mean	3

MDZ: midazolam, PPF: propofol, FTN: Fentanyl, MTH: methohexital, Tx.: treatment, Ext.: Extraction, BNZ: benzodiazepines, DEX: Dexmedetomidine

(2) Apnea or Hypoventilation

(3) Hypotension (systolic blood pressure less than 90 mmHg)

(4) Arrhythmia (heart rate < 50/min or > 120/min)

3) Items for the sedation level

(1) Sedation score

(2) BIS (bispectral) index

5. Statistical analysis

Meta-analysis was performed only for the outcomes pertaining to at least two studies. Data combination and analysis were performed using comprehensive meta-analysis 5.0 (Biostat, NJ, USA). This software was designed to calculate the effect size using various statistical values, and allows a test of significance of the pooled effect sizes, and of the homogeneity of the data.

When the studies were combined, a weight was assigned to each of the studies, according to the number of samples. A test of homogeneity was performed using Cochrane Q test.

After the calculation of the heterogeneity χ^2, if the P value was > 0.10, the data were considered homogeneous [6]. The data were analyzed using a fixed-effect model for homogeneous data and random-effect model for heterogeneous data.

The effect size was obtained by calculating the standardized mean difference (SMD) for continuous outcomes. After combining the effect sizes, the significance of the total effect size was tested through the test of mean difference. A P value of < 0.05 was regarded as indicating a difference in effect size.

The effect size was obtained by calculating the odds ratio (OR) for dichotomous outcomes. After combining the effect sizes, the significance of the total effect size was tested via the relation test. A P value of < 0.05 was regarded as indicating a difference in effect size.

A sensitivity test for assessing the publication bias was carried out using Fail-Safe Number (Nfs), and was performed only for the outcome that contained at least three studies .Fail-Safe Number shows that the significant outcome obtained via meta-analysis will become non-significant if a few studies with non-significant outcomes will be added to the analysis [7].

RESULTS

1. Description of included study (Table 1)

Twenty two RCTs were included, with 48,397 subjects undergoing variety procedure. Of these studies, one was conducted on 47,710 subjects, accounting for 98.6% of the entire sample size. Most of the studies were conducted on healthy adults belonging to ASA 1-2, although four studies included pediatric patients, one included disabled patients, and three included systemic-disease patients. Four studies included only male patients. Thirteen studies were conducted only on outpatients, and one study only on inpatients. The study settings were unclear or nonspecific in nine studies. The subjects ranged in age from 1 to 101 years.

Propofol was administered alone in 14 studies and in combination with other agents in eight studies. The method of administration of propofol was IV Bolus in three studies, IV infusion in one study, target controlled infusion (TCI) in three studies, and patient controlled sedation (PCS) with lock out pump in three studies. The intervention dose varied according to the administration method (Table 1). In one study, the method of administration was not described. In most of the studies, the patients were supplied with an adequate amount of oxygen through a nasal prong, under blood pressure, oxygen saturation, and pulse rate monitoring during the sedative state.

2. Effects of interventions (Table 2)

1) Procedure time

(1) Propofol alone (Fig. 1)

In the meta-analysis in this study, a total of five studies were included [8,9,10,11,12]. All the studies were homogeneous, with Cochrane Q = 1.367 and P = 0.850. Thus, analysis was performed considering the fixed-effect model. No significant difference was found between the studies with pooled SMD = 0.256 (95%CI; −0.111, 0.622) and P = 0.172.

(2) Propofol combined other agent (Fig. 2)

Meta-analysis of this item was performed on five studies [2,6,13,14,15]. All the studies were homogeneous, with Cochrane Q = 1.3576 and P = 0.852. Thus, analysis was performed considering fixed-effect model. There was no significant difference between the studies with pooled SMD = −0.128 (95%CI; −0.349, 0.094) and P = 0.260.

(3) All studies (Fig. 3)

Meta-analysis of this item was performed on 10 studies [2,6,9,14,16,17,18,19,20,21]. All the studies were homogeneous, with Cochrane Q = 5.797 and P

Table 2. The result of Meta−analysis

Outcome or subgroup title	No. of studies	Statistical method	Effect size (95% CI)	Nfs
1. Procedure time (all)	10	SMD	0.256 (−0.111, 0.622)	0
1−1. Propofol alone	5	SMD	−0.128 (−0.349, 0.094)	0
1−2. Propofol combined with another agent	5	SMD	−0.025 (−0.215, 0.165)	0
2. Recovery time	2	SMD	−1.442 (−2.060, −0.824)	−
3. Discharge time	3	SMD	−0.504 (−0.816, −0.913)	0
4−1. Patient satisfaction (continuous outcomes)	2	SMD	1.248 (0.779, 1.716)	−
4−2. Patient satisfaction (dichotomous outcomes)	2	OR	4.575 (1.691, 12.379)	−
4−3. Patient dissatisfaction	3	SMD	−1.795 (; −2.338, −1.251)	32
5−1. Operator satisfaction (continuous outcomes)	2	SMD	0.803 (0.386, 1.220)	−
5−2. Operator satisfaction (dichotomous outcomes)	2	OR	3.857 (0.446, 33.386)	−
6. Hypoxia	2	OR	0.223 (0.024, 2.209)	−
7. Apnea or hypoventilation	2	OR	0.313 (0.123, 0.799)	−
8. Hypotension	1	−	−	−
9. Arrhythmia	2	OR	0.071 (0.013, 0.402)	7
10−1. Sedation score	4	SMD	−0.430 (−0.724, −0.136)	0
10−2. BIS index	3	SMD	−0.173 (−0.587, 0.241)	0

SMD: standardized mean difference, OR:odds ratio, Nfs: Fail−safe number

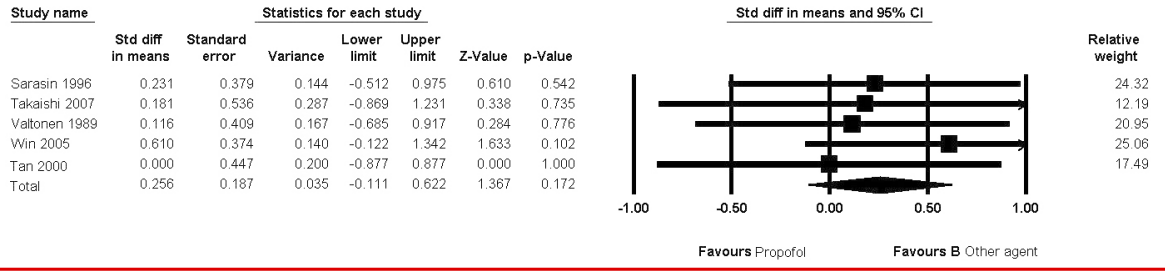

Fig. 1. Metagraph for procedure time (propofol alone)

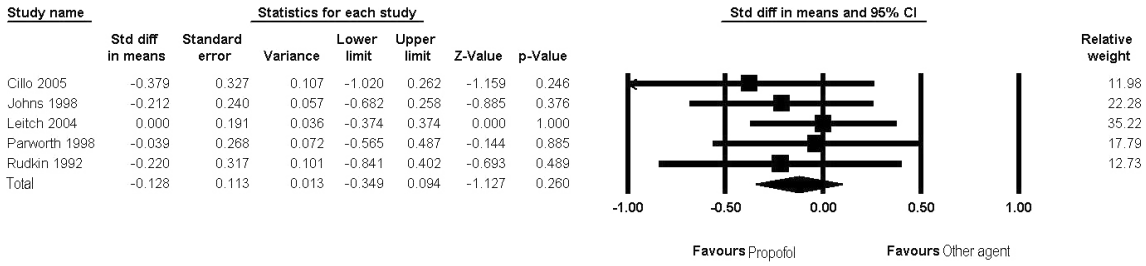

Fig. 2. Metagraph for procedure time (propofol combined other agent)

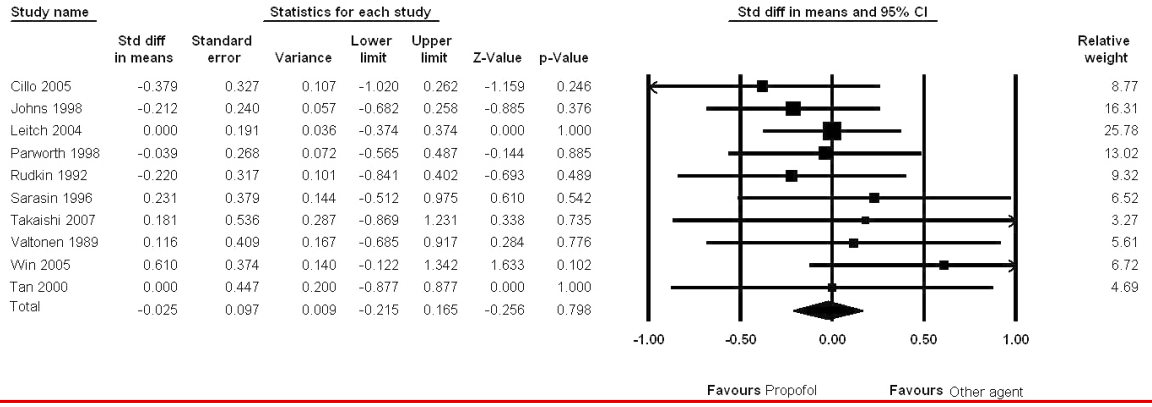

Fig. 3. Metagraph for procedure time (all studies)

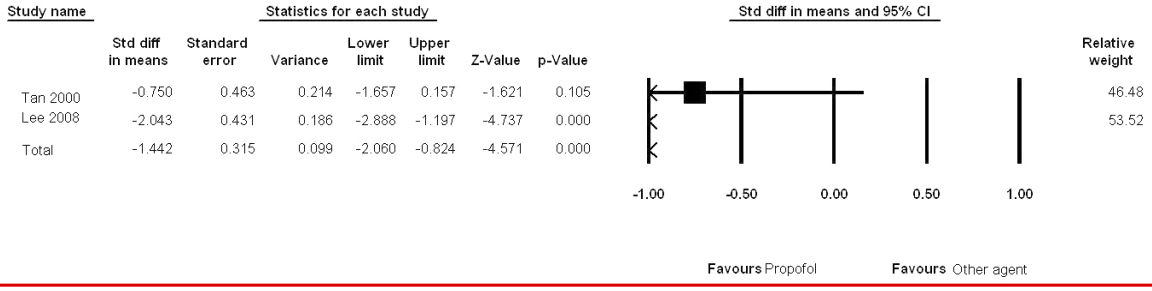

Fig. 4. Metagraph for recovery time

= 0.760. Thus, analysis was performed considering the fixed-effect model. There was no significant difference between the studies with pooled SMD = −0.025 (95%CI; −0.215, 0.165) and P = 0.798.

As a result, there was no significant difference in the procedure time between the propofol and control groups when propofol was used alone or in combination with other agents.

2) Recovery time (Fig. 4)

Meta-analysis of this item was performed on two studies: one with propofol alone and one with propofol in combination with other agents [7,22]. The two studies were homogeneous, with Cochrane Q = 4.177 and P = 0.041. Thus, analysis was performed considering the fixed-effect model. There was a significant difference between the studies with pooled SMD = −1.442 (95%CI; −2.060, −0.824) and P = 0.000. That is, the recovery was significantly faster in the

propofol group than in the control group.

3) Discharge time (Fig. 5)

Meta-analysis of this item was performed on three studies: one with propofol and two with propofol in combination with other agents [9,16,23]. All the studies were homogeneous, with Cochrane Q = 14.031 and P = 0.001. Thus, analysis was performed considering the fixed-effect model. There was a significant difference between the studies with pooled SMD = −0.504 (95%CI; −0.816, −0.913) and P = 0.002. That is, the patients in the propofol group were discharged significantly earlier than those in the control group.

4) Overall patient satisfaction

(1) Patient Satisfaction (continuous outcomes, Fig. 6)

Meta-analysis of this item was performed on two studies: one with propofol alone and one with propofol in combination with other agents [6,24]. Not all the studies were homogeneous, with Cochrane Q = 0.575 and P = 0.44. Thus, analysis was performed considering the random-effect model. There was a significant difference between the studies with pooled SMD = 1.248 (95%CI; 0.779, 1.716) and P = 0.000. That is, the

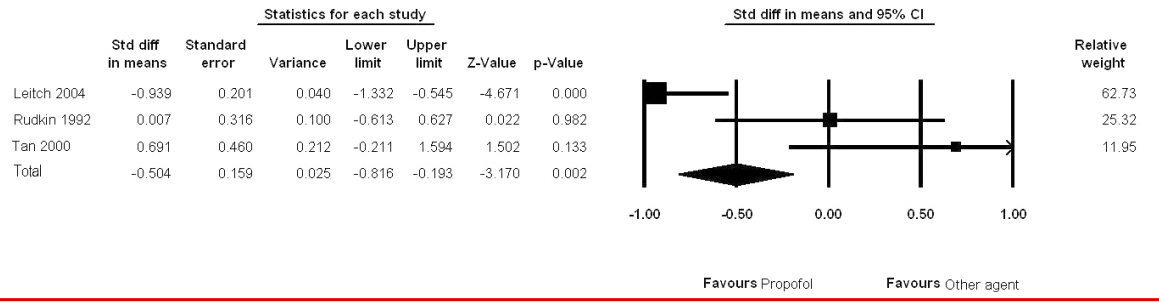

Fig. 5. Metagraph for discharge time

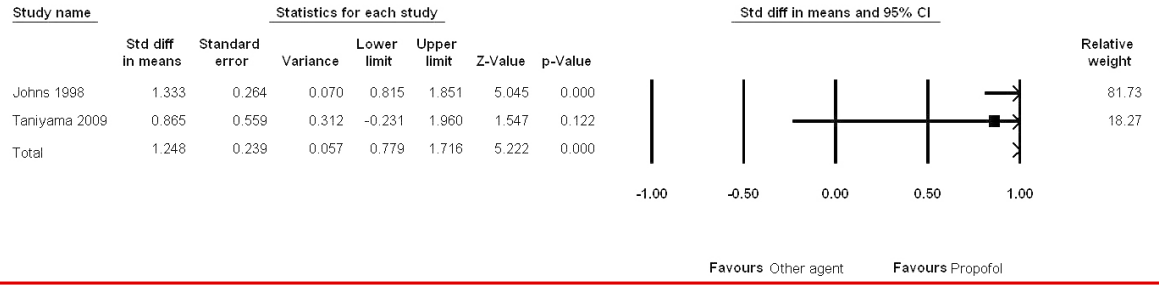

Fig. 6. Metagraph for patient satisfaction (continuous outcomes)

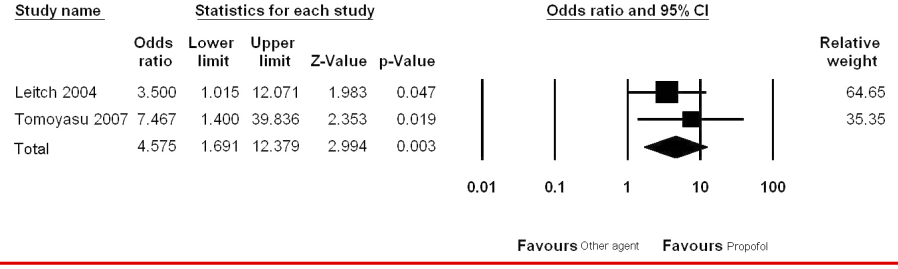

Fig. 7. Metagraph for patient satisfaction (dichotomousoutcomes)

patient satisfaction was significantly higher in the propofol group than in the control group.

(2) Patient Satisfaction (dichotomous outcomes, Fig. 7)

Meta-analysis of this item was performed on two studies: one with propofol alone and one with propofol in combination with other agents [9,25]. All the studies were not homogeneous, with Cochrane Q = 0.509 and P = 0.476. Thus, analysis was performed considering the random-effect model. There was a significant difference between the studies, with pooled odds ratio (OR) = 4.575 (95%CI; 1.691, 12.379) and P = 0.003. That is, the patient satisfaction was significantly higher in the propofol group than in the control group.

(3) Patient Dissatisfaction (Fig. 8)

Meta-analysis of this item was performed on three studies where propofol was used alone [13,24,26]. None of the studies was homogeneous, with Cochrane Q = 2.178 and P = 0.33. Thus, analysis was performed considering the random-effect model. There was a significant difference between the studies with pooled SMD = −1.795 (95%CI; −2.338, −1.251) and P = 0.000. That is, the patient dissatisfaction was significantly lower in the propofol group than in the control group.

5) Overall operator satisfaction

(1) Operator satisfaction (continuous outcomes, Fig. 9)

Meta-analysis of this item was performed on two studies where propofol was used in combination with other agents. All the studies were homogeneous, with Cochrane Q = 3.982 and P = 0.46. Thus, analysis was performed considering the fixed-effect model. There was a significant difference between the studies with pooled SMD = 0.803 (95%CI; 0.386, 1.220) and P = 0.000. That is, the operator satisfaction was significantly higher in the propofol group than in the control group.

(2) Operator satisfaction (dichotomous outcomes, Fig. 10)

Meta-analysis of this item was performed on two

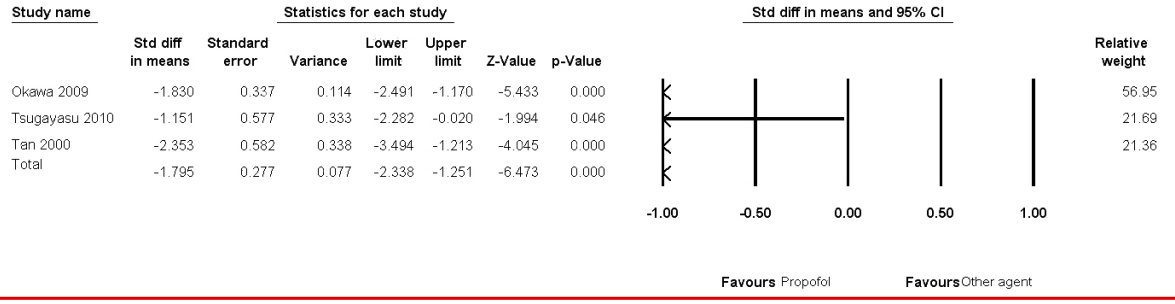

Fig. 8. Metagraph for patient dissatisfaction

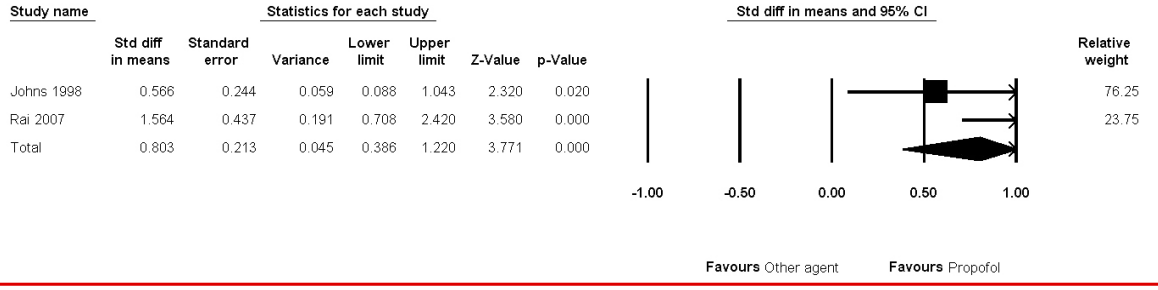

Fig. 9. Metagraph for operator satisfaction (continuous outcomes)

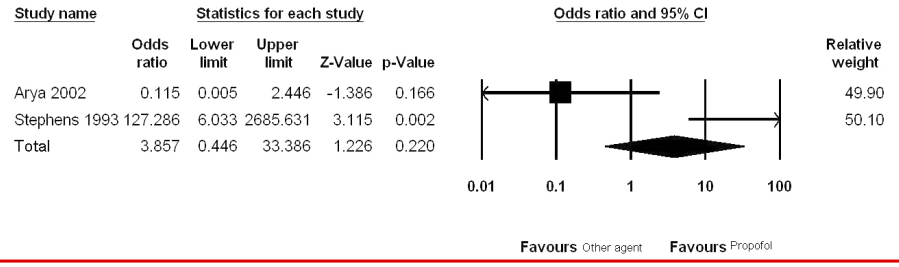

Fig. 10. Metagraph for operator satisfaction (dichotomous outcomes)

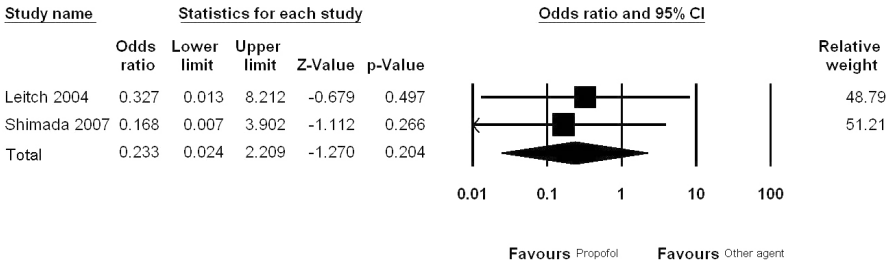

Fig. 11. Metagraph for hypoxia

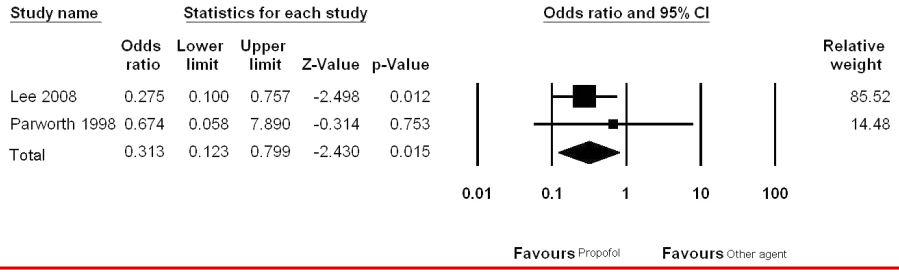

Fig. 12. Metagraph for apnea or hypoventilation

studies: one with propofol alone and one with propofol in combination with other agents. All the studies were homogeneous, with Cochrane Q = 10.123 and P = 0.001. Thus, analysis was performed considering the fixed-effect model. There was no significant difference between the studies with pooled OR = 3.857 (95%CI; 0.446, 33.386) and P = 0.220. That is, there was no significant difference in the operator satisfaction between the propofol and control groups.

6) Hypoxia (Fig. 11)

Meta-analysis of this item was performed on two studies: one with propofol alone and one with propofol in combination with other agents. None of the studies was homogeneous, with Cochrane Q = 0.084 and P = 0.772. Thus, analysis was performed considering the random-effect model. There was no significant difference between the studies with pooled OR = 0.223 (95%CI; 0.024, 2.209) and P = 0.20. That is, there was no significant difference in the incidence of hypoxia between the propofol and control groups.

7) Apnea or Hypoventilation (Fig. 12)

Meta-analysis of this item was performed on two studies: one with propofol alone and one with propofol in combination with other agents. None of the studies was homogeneous, with Cochrane Q = 0.435 and P = 0.509. Thus, analysis was performed

considering the random-effect model. There was a significant difference between the studies with pooled OR = 0.313 (95%CI; 0.123, 0.799) and P = 0.015. That is, the incidence of apnea or hypoventilation was significantly lower in the propofol group than in the control group.

8) Hypotension

Meta-analysis could not be performed on this item as there was only one study that investigated it. In that study, however, the incidence of hypotension was 2/16 in the propofol group and 5/16 in the control group (Stephens et al., 1993).

9) Arrhythmia (Fig. 13)

Meta-analysis of this item was performed on two studies where propofol was used alone. None of the studies was homogeneous, with Cochrane Q = 0.896 and P = 0.334. Thus, analysis was performed considering the random-effect model. There was a significant difference between the studies, with pooled OR = 0.071 and P = 0.003. That is, the incidence of arrhythmia was significantly lower in the propofol group than in the control group.

10) Level of sedation

(1) sedation score (Fig. 14)

Meta-analysis of this item was performed on four studies: one with propofol alone and three with pro-

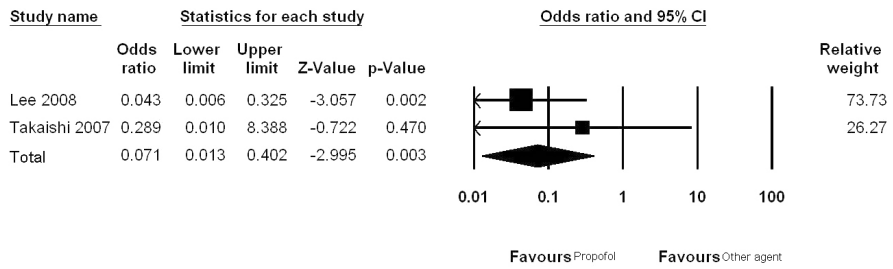

Fig. 13. Metagraph for arrhythmia

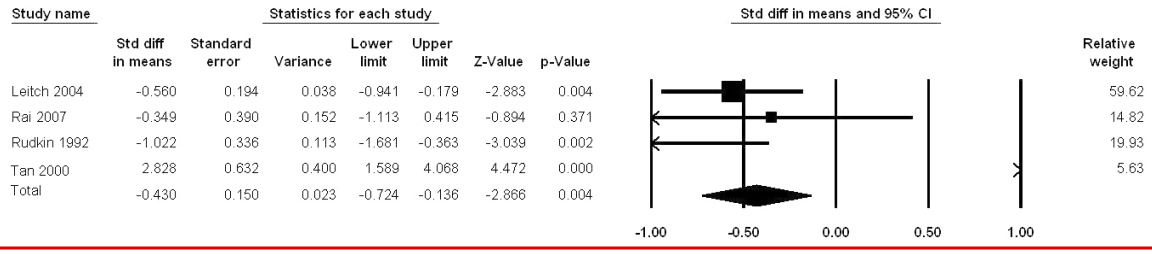

Fig. 14. Metagraph for sedation score

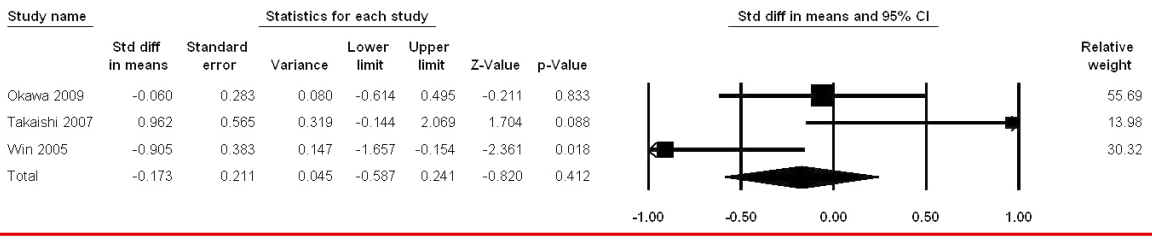

Fig. 15. Metagraph for bispectral (BIS) index

pofol in combination with other agents. All the studies were homogeneous, with Cochrane Q = 30.134 and P = 0.000. Thus, analysis was performed considering the fixed-effect model. There was a significant difference between the studies with pooled SMD = −0.430 (95%CI; −0.724, −0.136) and P = 0.004. That is, the sedation score was significantly lower in the propofol group than in the control group.

(2) BIS (bispectral) index (Fig. 15)

Meta-analysis of this item was performed on three studies where propofol was used alone. All the studies were homogeneous, with Cochrane Q = 7.852 and P = 0.02. Thus, analysis was performed considering the fixed-effect model. There was no significant difference between the studies with pooled SMD = −0.173 (95%CI; −0.587, 0.241) and P = 0.412. That is, there was no significant difference in BIS index between the propofol and control groups.

3. Risk of bias in included studies

The overall quality of the studies was good. In the Jadad scale, one study scored 0 point, three studies scored 2 points, and 14 studies scored 3 points. One study scored 4 points and three studies scored 5 points. Seventeen studies mentioned that allocation concealment was used. Four studies used double-blinding. The mean score for the study quality was 3.05.

A publication bias sensitivity test was performed only on the items that had three or more relevant studies (Table 2). The results of the sensitivity test showed that the studies did not appear to be free from publication bias. As the fail safe number was found to be 0-32, indicating that if 0-32 non-significant studies will be added to the meta-analysis, the significant effect size can change into a non-significant one, the outcomes presented through such meta-analysis are regarded as having a risk of publication bias.

DISCUSSION

The development of local anesthesia in dentistry provided a foothold for stable dental treatment. As the dental-treatment environment continuously develops, however, the patients' expectations also rise, and the control of stress, fear, and phobia arising from dental treatment is leading another paradigm.

Patients who experienced severe pain or stress during dental treatment may have developed phobia for the next treatment or may fail to receive the planned treatment. In addition, child or disabled patients who lack experience in or understanding of dental treatment may develop more severe stress, fear, and phobia. To address this concern, sedation is considered in dental treatment [27]. In particular, if patients have a history of hyperventilation or syncope due to severe stress, they should be made to feel more comfortable by reducing the risk of such events, which can be done by minimizing the stress that the patients may receive during the treatment and by informing the patients in advance of the pain that may occur during the treatment [28]. Sedation used for this purpose can reduce fear, can make the patients comfortable and stable, and can reduce the unexpected movements or reactions of the patients during treatment. It also has the advantages of increasing the patients' cooperation during the treatment as well as patience with the long treatment time, through communication with the patients [29].

Various sedatives and administration routes (e.g., oral administration, inhalation, intravenous injection, etc.) are currently being used for dental sedation. Among these, intravenous sedation is most advanta-

geous in that it is effective for administering sedatives and the other agents required for the patients' safety through the veins. Traditionally, benzodiazepines were used for intravenous sedation in dental treatment. Benzodiazepines as diazepam and midazolam have the advantage of good stability but are disadvantageous in that their adequate dose greatly varies by patient and they have a longer induction and recovery time compared to the propofol [30].

Dental sedation using propofol has seen great advances in the technical aspects. In its early days, propofol was injected in bolus dose, but nowadays, various devices (e.g., infusion pump) and protocols for safety and efficiency are being used. In accordance with the advances in the related equipment, professionalism is required on the part of the clinicians performing sedation.

As meta-analysis yields outcomes through the analysis of within- and between-study factors, it provides statistical markers that enable objective outcome prediction by expressing the intervention or drug effects when the occurrence of a random situation in the clinical setting is to be predicted. In meta-analysis, each investigator combines two or more independent outcomes (e.g., odds ratio and relevant confidence interval) using certain methods (e.g., weighted-average method), to obtain answers to the clinical questions raised by them. The sample size and precision (mostly standard deviation) are used as weighted values.

The disadvantages of meta-analysis are the publication bias and the drawer -effect. This is because articles whose outcomes are contrary to those of past related studies with positive outcomes are mostly rejected by the publishers and end up in the drawer, or because editors who review articles are likely to have a bias against publishing articles with opposite outcomes. If such bias exists, the effect of an intervention or a drug will become greater than it actually is [31].

Another disadvantage of meta-analysis is the "Garbage in Garbage out" effect. This means that no matter how precise an analysis is, if the objects of the analysis are low-quality studies, the outcome of the analysis may make it seem that what were analyzed were high-quality studies [32].

Thus, for genuine meta-analysis, unpublished articles and articles with opposite outcomes should be included in the analysis, and the quality of the studies should be strictly assessed to ensure the reliability of the outcome.

The meta-analysis that was conducted in this study showed that the use of propofol alone or in combination with other agents for dental sedation resulted in a shorter recovery time, faster hospital discharge, and a high satisfaction levels on the part of the patients and clinicians, without any difference in the complications. Instead, the incidence of arrhythmia and apnea / hypoventilation was significantly lower in the propofol group than in the control group. The same is true with regard to the incidence of hypotension, although meta-analysis for the incidence of hypotension could not be performed because there was only one study related with hypotension.

The sensitivity test that was used in the meta-analysis in this study showed, however, that there is a risk of publication bias arising from the shortage of relevant RCTs. The studies that were included in the analysis were of good quality, however, and the sensitivity test was only an additional analysis modality for determining the reliability of the outcome but was not an obstacle for accepting the outcome of the analysis. Thus, if further studies will be performed with more RCTs, the reliability will be improved.

In addition, in terms of the surgeons' satisfaction, unlike the analysis of continuous data, the analysis of dichotomous data in the meta-analysis conducted in this study showed that there was no significant difference between the propofol and control groups. This, however, was considered an medium effect based on Cohen's standard (1988) for the interpretation of the effect size because the SMD was 3.857 [33].

On the sedation level, unlike BIS index, the sedation score was significantly lower in the propofol group than in the control group. This is an small effect based on Cohen's standard for the interpretation of the effect size considering that the OR was −0.430. In the assessment of the sedation level, the sedation score is an objective marker while BIS index is a subjective marker. In sedation in clinical practice, however, both objective numerical values as well as the surgeons' subjective judgment can be important. The correlation between the sedation score and BIS index was established in previous studies, and particularly for propofol, BIS index was reported to more accurately predict responsiveness to verbal instructions compared to the plasma concentration [34]. In the administration of propofol, the BIS index is known to more accurately predict the depth of sedation compared to other agents [35]. The sedation score is graded subjectively and can thus be a marker for the efficacy and safety of sedation. As the efficacy and safety of sedation, however, were not clearly distinguished in relation with the sedation score in this study, the sedation score was presented only as a reference.

This study is the first meta-analysis of the use of propofol in dental sedation. As a characteristic of meta-analysis, the shortage of RCT that could be included in the analysis limited the completeness of the present study. If more RCT will be included in the further study on the same theme, this limitation will be overcome.

The present analysis showed that the use of propofol resulted in high satisfaction levels on the part of the patients and operators, a shorter recovery time, and faster hospital discharge. The incidence of complications, however, was lower in the propofol groups or not much different between the propofol and control groups. Thus, the adequate use of propofol in dentistry is believed to be helpful for the effective and safe sedation of the patients.

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