



Evaluation of hemodynamic changes and patient-reported outcome measures in surgical therapy with or without intravenous sedation: a prospective controlled clinical study

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Abstract

Objectives To determine whether intravenous (IV) sedation would contribute to the stabilization of patients' hemodynamics during periodontal and oral surgical procedures, and to evaluate the patient-reported outcome measures (PROMs).

Materials and methods Periodontal or oral surgery patients were recruited and distributed into two groups: (1) sedation group (SG): intravenous sedation plus local anesthesia; (2) control group (CG): local anesthesia only. Systolic and diastolic blood pressure (SBP, DBP), heart rate (HR), and oxygen saturation (SaO₂), were monitored at 15-min intervals from sitting in the dental chair (baseline) until the end of the treatment. In addition, a subjective assessment of PROMs was obtained through a post-operative questionnaire.

Results Forty-nine patients (25 in SG and 24 in CG) were included. The highest SBP and DBP were significantly higher in CG compared to the SG (141.1 ± 18.4 and 133.6 ± 15.1 , respectively in SBP; and 85.5 ± 11.0 and 82.9 ± 10.1 , respectively in DBP), but no mean significant differences were found between groups (*P* value of 0.85 and 0.72 for systolic and diastolic BP, respectively). HR and SaO₂ did not show statistical intra- and inter-group differences. The overall patient satisfaction score was significantly higher in the SG group compared to CG.

Conclusions Intravenous moderate sedation seems to contribute to the stabilization of patient's hemodynamics, especially the systolic blood pressure, although small differences have been found.

Clinical relevance Intravenous sedation seems to contribute to stabilize the hemodynamic values, and enhances the patient satisfaction after periodontal and oral surgical treatment in the dental office.

Keywords Intravenous sedation · Hemodynamics · Dental implants · Patient satisfaction · Local anesthesia · Anxiety

Introduction

The patient's stress pertinent to oral surgical procedures often collaborates with a sense of fear, anxiety, and uncertainty. The physical and mental stress incurred during dental treatment often triggers cardiovascular changes [1]. Hence, the stress has been evaluated by a variety of means, such as blood pressure (BP), oxygen saturation (SaO₂), and heart rate (HR) [2, 3]. It is not surprising that dental anxiety and pain can lead to hemodynamic changes such as increased HR and BP, but they can also be affected by certain individual factors such as age, gender, previous experience with dental treatments, and psychological background [1]. Additionally, the use of local anesthetics with vasoconstrictors can also induce hemodynamic changes in the same way as other factors, such as patient anxiety or stress [4,

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5], and all these hemodynamic changes can be controlled and even modified with sedation approaches [6, 7].

Moderate sedation (conscious sedation) is defined as a minimally depressed level of consciousness that retains the patient's ability to maintain inhalation and exhalation independently and continuously, and patient stays awake and alert during the procedure which responds to physical stimulation and/or verbal command [6, 7]. It has become the second safest, convenient, and effective anesthetic technique after inhalation, and offers several advantages to both patients and dentists [8]: (1) decreasing patient anxiety level [8, 9]; (2) dealing with patients who have dental phobias, involuntary movements, and/or intellectual disability [10, 11]; (3) providing a certain level of comfort especially long and difficult procedures [12]; (4) offering patient's benefits through depressing the central nervous system, minimizing pain perception in conjunction with local anesthesia, relieving anxiety, and helping to maintain cardiovascular stability [13–15].

Subsequently, moderate sedation with intravenous medications may enhance the patient's positive perception related to the surgical experience by reducing the patient anxiety throughout the procedure. This congruently may also favor the clinical outcomes of dental surgical procedures [16, 17]. The most crucial aspect regarding the cardiovascular stability assessment is following a global standard method of monitoring and observation of data recording [18]. The advantages of cardiovascular stability monitoring are the ability to detect, evaluate, and prevent emergency situations in clinical practice [19]. Basic monitoring provides essential information such as vital signs, BP, and HR, both circulatory and respiratory [19]. A pulse oximetry is also used to record HR and SaO₂ since stress and anxiety increase respiratory rate but being less effective to properly increase the oxygen saturation in the blood [20]. Additionally, respiratory depression induced by IV sedation must be monitored through a pulse oximetry to avoid critical situations.

Therefore, the primary aim of the present prospective study was to determine whether intravenous sedation during surgical therapies would contribute to the stabilization of patient's hemodynamics. And the secondary aim is to evaluate the patient-reported outcome measures (PROMs) pertaining to the patient's satisfaction after surgical therapy with intravenous (IV) moderate sedation, compared to patients whose surgical therapy will be performed with local anesthesia alone.

Materials and methods

Study design and patient selection

This prospective controlled study obtained human subject's Institutional Review Board (IRB) approval from the

University of Michigan (USA) (Ref. HUM00172521), and it was conducted in consonance with the Helsinki Declaration of 1975, as revised in 2013 [21]. Also, the study was conducted based on the principles of the STROBE statement for improving the quality of observational studies (Appendix A).

The minimum number of patients needed to be enrolled in this study resulted to be 35 considering a sample size calculation with a power to detect a clinically significant difference of 10% ($\alpha=0.05$), adding a 10% of incrementing the sample for possible dropouts. As a result of this calculation, a total of 50 patients were already have been selected for this study. Patients that were treated for periodontal and oral surgery procedures from the University of Michigan School of Dentistry, Department of Periodontics and Oral Medicine were recruited.

The patients' inclusion criteria were the following:

- 1) ≥ 18 years of age, who agreed to take part in this study and signed the informed consent;
- 2) American Society of Anesthesiologists physical status classification (ASA) I (a normal healthy patient); and ASA II (a patient with mild systemic disease) [22];
- 3) need of periodontal or oral surgical treatment with or without IV sedation using midazolam;
- 4) receiving 10.8 ml or less local anesthetic (max. 6 carpules of 1.8 ml each).

Patients who reported the use of any medications that may influence hemodynamic changes including anxiolytic medication (last intake <48 h before intervention) as well as pain medication (last intake <48 h) or BP medication, pregnant patients or unsure of pregnancy status (self-reported), individuals with uncontrolled systemic diseases or known conditions capable of influencing the results of the study, such as reported cardiovascular disorders, especially those already diagnosed with arterial hypertension or showing basal values above 90 mmHg or 140 mmHg for diastolic or systolic pressures, respectively, and patients receiving more than 10.8 ml (6 carpules of 1.8 ml each) of local anesthesia, were excluded.

The cohort of patients was enrolled consequently after their surgeries were already scheduled, with or without IV sedation, regardless of the type of scheduled surgery. After subjects have consented during the screening visit, their health history was screened, and if they did not meet any exclusion criteria, individuals were allocated into one of the following study groups: (1) sedation group (SG): IV sedation plus local anesthesia administration; (2) control group (CG): local anesthesia administration only.

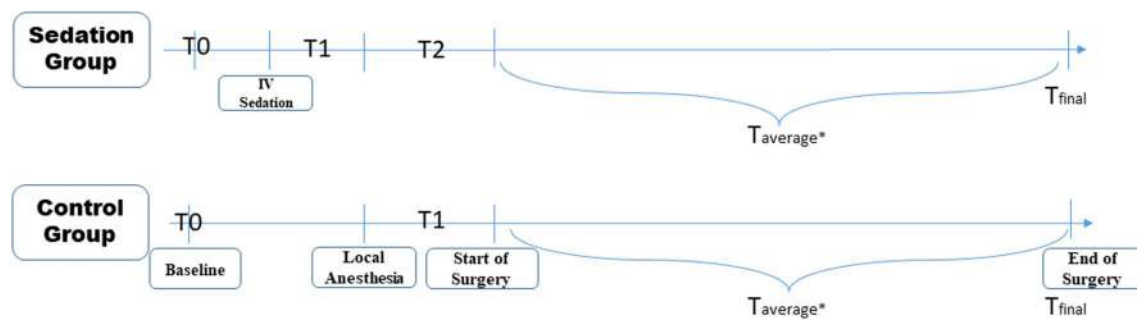


Fig. 1 Timeline of the study and data collection intervals. (IV, intravenous; *average amount of 15-min intervals was calculated)

Intravenous sedation and local anesthesia agents

Administration of conscious IV sedation was performed using midazolam 0.05 mg/kg. Then, sedation was maintained with midazolam 1 mg every 30 or 60 min considering the patients' state and sedation depth needs. Local anesthesia through lidocaine hydrochloride 2% with epinephrine 1:100,000¹ was used in both groups.

Data collection

Patients completed a Dental Anxiety Scale (DAS) [1] (Appendix B) to appraise the preoperative surgical anxiety during in the waiting room. DAS involved four questions related to the stress associated with a specific dental situation. Each question contained five multiple-choice responses numbered from 1 to 5. The number obtained after the total sum of the results of each question served to assess the preoperative patient's anxiety: (1) low anxiety: when the total scores are less than 9; (2) moderate anxiety: scores between 9 and 12; and (3) severe anxiety (dental phobia): with scores between 13 and 20. Neither minimum DAS score was used to include or exclude patients nor to distribute them into the groups.

During the surgical therapy, the hemodynamic values were monitored using a vital sign monitoring device², at 15-min intervals from sitting in the dental chair (first record—baseline) until the end of the treatment. In the conscious IV sedation group, the second record was taken after the induction of sedation, the third record after the injection of local anesthesia, and then every 15 min until the end of the treatment. In the control group, the second record was taken after the local anesthesia infiltration, and then every 15 min until the end of the treatment.

Hemodynamic values evaluated were systolic and diastolic blood pressures (SBP, DBP), HR, and SaO₂. The average values throughout the surgery (after the local anesthesia

injection and before the post-op measurement) and the maximum value for each variable were recorded. The total amount of local anesthesia utilized and complications during or after surgical therapy were also recorded. The timeline of the data collection is presented in Figure 1.

In addition, subjective assessment of PROMs was obtained through a post-operative questionnaire. When the subjects returned for their 2-week post-operative visit, they were asked to complete a written questionnaire regarding their experience and level of satisfaction from 1 (lowest) to 5 (highest). The patient satisfaction questionnaire consisted of five paramount questions as follows:

- 1.How satisfied are you with how your pain was controlled during surgery?
- 2.How satisfied are you with the surgical therapy?
- 3.How satisfied are you with how your pain was controlled when you returned home?
- 4.Would you recommend dental surgery to friends and relatives?
- 5.Would you choose dental surgery again?

Data processing and statistical analysis

Descriptive statistics were used to illustrate age, gender, quantity (in milliliters) of local anesthesia employed, duration of the surgery, preoperative anxiety scores, and to demonstrate the gathered continuous variables (BP, HR, and SaO₂). The collected data were entered into spread sheets. Descriptive statistics were used for presenting the retrieved data at baseline as means $\pm$ standard deviations (SD). The statistical analysis was performed by a single author (H.S), and a commercially available software³ was employed. The association of the study parameters with conscious IV sedation was examined. Changes in the parameters over time within the two groups as well as differences between groups were analyzed using a repeated measure of analysis of variance.

All variables were tested for normal distribution by the Shapiro-Wilk test. Paired-samples *t* test was performed to compare the means within each group of each variable.

¹ (Xylocaine®, Dentsply Sirona, Charlotte, NC, UUEE)

Likewise, the independent samples *t* test was used for comparison of the parameters between the two study groups, whereas the Mann-Whitney *U* test was used for comparing two groups of quantitative data that did not show normal distribution. Significances of the data were set at 5% (*P* value < 0.05).

Results

Descriptive analysis

Out of the 50 individuals initially assessed for eligibility, 49 patients (25 corresponding to SG and 24 to CG) were finally included in the study. One patient was excluded from the CG group because he requested nitrous oxide after administration of the local anesthetic.² The mean age of the included subjects was 54.76 ± 9.95 and 55 ± 15.93 for the SG and CG, respectively, and gender distribution was 12 (48%) and 13 (52%) for men and women, respectively in the SG, while 9 (37%) and 15 (63%) of men and women, respectively in the CG. Seven (28%) patients of the SG corresponded to ASA I considered as a normal healthy patient [22], while 18 (72%) corresponded to ASA score II considered as a patient with mild systemic disease. On the other hand, CG involved 5 (20.83%) and 19 (79.17%) patients corresponded to ASA I and ASA II, respectively.

When it comes to the type of the procedures, the subjects in SG underwent guided bone regeneration (4), implant placement (5), extractions (4), lateral sinus augmentation (8), transcrestal sinus augmentation and implant placement (1), and soft tissue grafting (3). Regarding the CG, the patients underwent guided bone regeneration (3), implant placement (6), extractions (5), transcrestal sinus augmentation and implant placement (3), periodontal flap surgery (6), and soft tissue grafting (1). The total mean local anesthesia injected was 9.21 ± 2.39 ml (5.12 ± 1.33 carpules) and 8.46 ± 2.44 ml (4.7 ± 1.36 carpules) for SG and CG, respectively, and the total duration of the surgery resulted to be 189.6 ± 39.1 and 129.4 ± 29.1 min for the SG and CG, respectively. Regarding the amount of midazolam administered in the SG patients, 8.1 ± 3.6 mg was the mean quantity employed.

Regarding the preoperative anxiety evaluation, the majority of patients showed mild to moderate scores according to Corah's anxiety scale [1]. Nevertheless, the SG revealed a significantly higher total mean score than CG (9.68 ± 3.04 vs 7.08 ± 2.06 , respectively), indicating that the mean

Table 1 Preoperative anxiety evaluation based on the scores of the Corah's anxiety scale [2]. (SG, sedation group; CG, control group; *statistical significance *P*<0.05)

Preoperative anxiety	SG (n)	CG (n)
Mild (0–8)	8	15
Moderate (9–12)	10	8
High (13–14)	7	1
Severe (15–20)	-	-
Mean total anxiety scores	$9.68 \pm 3.04^*$	$7.08 \pm 2.06^*$

preoperative anxiety of the patients undergoing IV sedation (SG) was allocated to the moderate score, while it was allocated to the mild score in CG. Complete preoperative anxiety evaluation is shown in Table 1.

Hemodynamic evaluation

SBP was the hemodynamic parameter analyzed which showed more variations, increasing significantly from the baseline (134.2 ± 13.6) to the maximum value reached within the surgery (141.1 ± 18.4) in the CG. In contrast, this parameter did not reveal such variation in the SG (from 129.3 ± 14.8 in baseline to 133.6 ± 15 in the maximum value reached). Additionally, the highest SBP was significantly higher in CG compared to the SG (141.1 ± 18.4 and 133.6 ± 15.1 respectively). However, the mean difference in SBP was not significant between the two groups. Likewise, the highest DBP was statistically significantly higher in CG (85.5 ± 11.0) when compared to SG (82.9 ± 10.1), although in baseline and regarding the intergroup mean difference the variation resulted not to be statistically significant. Figure 2 illustrates the mean BP (systolic and diastolic) changes throughout the surgery in both groups, showing that data lines of the BP in the SG were below those of the CG during the entire surgery.

HR and SaO₂ did not show statistical intra- and inter-group differences. While HR is lower in SG than CG, however no statistical difference was reached. For SaO₂, it was consistent with less fluctuations in both intra- and inter-groups.

All the data regarding hemodynamic evaluation at different time points during surgical therapies was shown in Table 2, and intra- and inter-group evaluation of mean differences between the baseline, and the maximum value of each variable within the surgery is fully depicted in Table 3.

Figure 2 illustrates the mean blood pressure (systolic and diastolic) changes throughout the surgery in both groups. It can be observed that both SBP and DBP parameters in SG always remained lower than the parameters found in CG.

² %IBM® SPSS Statistics® 24.0.0 (Chicago, IL)

Fig. 2 Mean blood pressure (systolic and diastolic) changes throughout the surgery in both groups (SBP, systolic blood pressure; DBP, diastolic blood pressure; SG, sedation group; CG, control group)

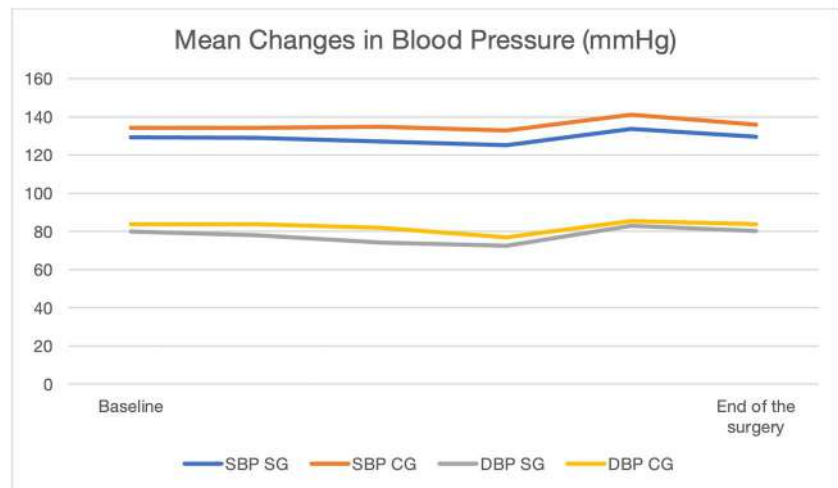


Table 2 Hemodynamic evaluation at different time points during surgical therapies (SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SaO_2 , oxygen saturation; SG, sedation group; CG, control group; IV, intravenous)

		Baseline	Measurement points			
			IV infusion	Local anesthesia injection	15-min intervals	End of the surgery
SBP (mm Hg)	SG	129.3 ± 14.8	128.8 ± 15.4	127.1 ± 13.5	125 ± 11.4	129.6 ± 16
	CG	134.2 ± 13.6	-	134.8 ± 18.3	132.9 ± 14.8	135.7 ± 18.3
DBP (mm Hg)	SG	79.9 ± 10.4	78.1 ± 10	74 ± 10.2	72.4 ± 9.2	80.2 ± 11.8
	CG	83.9 ± 10.9	-	81.8 ± 10.8	76.9 ± 11	83.7 ± 11.5
HR (beats/minute)	SG	75.4 ± 14.2	76.1 ± 13.1	81.8 ± 17.4	78.5 ± 15.8	74.2 ± 12.3
	CG	79.7 ± 18.2	-	77.4 ± 11.4	75.9 ± 13.4	69.7 ± 10.1
SaO_2 (%)	SG	97.3 ± 1.6	97 ± 1.8	97 ± 1.5	95.8 ± 1.8	96.7 ± 1.9
	CG	97.6 ± 1.2	-	97 ± 1.3	96.9 ± 1.7	97.3 ± 1.6

Table 3 Intra- and inter-group analyses of mean differences between the baseline and the maximum value of each variable within the surgery. (SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SaO_2 , oxygen saturation; SG, sedation group; CG, control group. Bold letters represent statistically significant differences; *statistically significant, paired samples *t* test; ^statistically significant, independent samples *t* test)

			Measurement points		Mean difference	P value
			Baseline	Maximum within the surgery		
SBP (mm Hg)	SG		129.3 ± 14.8	133.6 ± 15.1	4.3 ± 11.8	0.17
	CG		134.2 ± 13.6	141.1 ± 18.4	6.8 ± 15.2	0.03*
	Inter-group comparison		0.11	0.03^	0.85	
DBP (mm Hg)	SG		79.9 ± 10.4	82.9 ± 10.1	2.9 ± 9.3	0.13
	CG		83.9 ± 10.9	85.5 ± 11.0	1.6 ± 10	0.44
	Inter-group comparison		0.85	0.02^	0.72	
HR (beats/minute)	SG		78.5 ± 17.7	75.4 ± 14.2	-3.1 ± 12.8	0.51
	CG		79.7 ± 18.2	81.4 ± 11.4	1.6 ± 14.2	0.44
	Inter-group comparison		0.11	0.36	0.09	
SaO_2 (%)	SG		97.3 ± 1.6	97.1 ± 1.9	-0.3 ± 1.2	0.22
	CG		97.6 ± 1.2	96.9 ± 1.7	-0.7 ± 1.7	0.06
	Inter-group comparison		0.57	0.08	0.12	

Table 4 Post-operative patient reported outcome measures. (SG, sedation group; CG, control group; *statistical significance $P < 0.05$)

	Study groups		<i>P</i> value
	SG	CG	
How satisfied are you with how your pain was controlled during surgery? (out of 5)	4.76 ± 0.42	3.58 ± 0.57	0.001*
How satisfied are you with the surgical therapy? (out of 5)	4.56 ± 0.49	3.62 ± 0.56	0.002*
How satisfied are you with how your pain was controlled when you returned home? (out of 5)	4.28 ± 0.72	3.75 ± 0.72	0.452
Would you recommend dental surgery to friends and relatives? (out of 5)	3.96 ± 0.72	2.83 ± 0.68	0.345
Would you choose dental surgery again? (out of 5)	4.24 ± 0.76	2.83 ± 0.74	0.03*
Overall satisfaction score (out of 25)	21.76 ± 2.17	16.62 ± 1.84	0.001*

Patient-reported outcome measures

Based on the post-operative questionnaire, the overall PROMs were significantly higher in the SG group when compared to CG. More specifically, the patients reported statistically higher satisfaction regarding the pain control during surgery, the surgical therapy, and improved predisposition to undergoing surgical therapy again when conscious IV sedation was employed in contrast with local anesthesia only. On the contrary, no statistical significance was reached in relation to how pain was controlled at home or about the predisposition to recommending the procedure to friends or relatives. Table 4 illustrates information relating the patient's satisfaction outcomes in the CG and SG.

Discussion

This prospective clinical study revealed that using conscious IV sedation in combination with local anesthesia during surgical therapy seems to help in decreasing both SBP and DBP when compared to using local anesthesia alone, especially noted in maximum values measurements, although small difference has been found between groups. It also helps to maintain SBP under control during surgical therapy. In addition, PROMs revealed a statistically higher satisfaction with IV sedation adjunct to local anesthesia than when local anesthesia alone was used. In general, patients reported better satisfaction outcomes about the surgical therapy, better perception of pain control during surgery, and better predisposition to perform another surgical therapy in the future with the IV sedation group.

It is well known that dental anxiety is a common phenomenon in the dental office that often complicates proper dental treatment [1]. According to Corah [2] and Shepherd [3], a decrease in the blood pressure of the patient can also be indicative of a reduction in their stress levels. Therefore, this study revealed that IV sedation may decrease patients' stress during surgical therapy versus only local anesthesia was

used. Furthermore, this study also revealed that the patients displayed certain levels of anxiety before dental procedures, presenting a mean Corah's scale score of 9.68 ± 3.04 in the SG and 7.08 ± 2.06 in the CG, corresponding to moderate and mild preoperative anxiety respectively. This is in agreement with the data reported in the previous studies [6].

Severe hemodynamic fluctuations during dental treatment may cause undesirable physical reactions as cardiac rhythm alterations, angina, or myocardial infarction [1, 13]. Brand et al. [1] reported an increase in BP and HR during dental treatment, potentially affecting the patients with established cardiovascular disorders or even affecting healthy patients. This present study showed that using moderate IV sedation during surgical therapy seems to help in stabilizing SBP and DBP when compared to using local anesthesia alone, although only SBP and DBP maximum values reached showed statistically significant differences between both groups.

In contrast, Saravia et al. [23] and Patterson et al. [24] reported fluctuations in SBP during dental treatment under sedation in children; nonetheless, they could not find any statistical differences between the pre- and intra-operative readings, and emphasized that even IV sedation procedures may punctually increase SBP in pediatric patients associated to environmental stimuli [23].

Studies have found a higher SBP during local anesthesia injection, followed by during tooth extraction procedure in non-sedated patients [4, 23]. The possible mechanisms underlying these findings may be related to emotional stress and fear with sympathetic activity (tachycardia) that leads to an increase in plasma concentrations of adrenaline and norepinephrine or both [25]. However, Liao et al.'s [4] article reported that the increase of SBP and HR during the local anesthesia injection was due to endogenous epinephrine release as a result of the emotional stress and not from the effect of the local anesthetic. Nonetheless, Patterson et al. [24] and Sanadhya [25] did report a significant increase in DBP related to the injection of local anesthesia or during dental manipulation, both in

sedated and non-sedated pediatric patients. Interestingly, the effect of increasing BP during anesthesia injection was not observed in our study. Although, no explanation can be made for this observation, we felt that as being part of the research, participants may somehow calm the patient to ensure their treatment was closely watched and monitored, a so-called Hawthorn effect.

Our data also found that no statistically significant differences were found in terms of gender. This is contradictory to some reported finding that showed BP was higher in males than females, while women showed higher HR values and anxiety levels [19].

This study could not find any differences between sedated and non-sedated patients in terms of HR and SaO₂, even though patients may develop moderate to severe hypoxia due to compromise of oxygen saturation [23]. While SG group had lower HR when compared to the CG, SaO₂ remained stable in both groups and without intragroup variations. This is different than Sanadhya et al. [25] who found HR reach maximum during local anesthetic injection, followed by during tooth extraction in non-sedated pediatric patients. Once again, these effects can be explained by the association between emotional stress and fear with sympathetic activity [1] that causes an increase in plasma concentrations of adrenaline and norepinephrine [25].

Needless to mention that although this study did not show any side effects associated to conscious IV sedation, side effects such as hypoxia, nausea, vomiting, or tachycardia, have been previously reported, including some risk of morbidity and mortality associated to anesthetic agents [23, 26–29]. This indicates that conscious IV sedation requires proper training to administer, involving a more complex procedure requiring a continuous patient monitoring, and an extra cost. Taking into account that the effect in hemodynamic stabilization is very little, therefore the use of IV sedation in non-anxious patients has to be properly evaluated.

Besides hemodynamic parameters and stress, the patients' willingness to repeat surgical treatments could be considered one of the key factors to determine patients' satisfaction towards to our treatment. Ganzberg et al. [30] and Garip et al. [31], obtained a mean of 84.1% and 95% patient satisfaction after performing dental treatment under conscious IV sedation, respectively. This implies conscious IV sedation

should be recommended in patients that need oral and periodontal surgeries to not only reduce stress during the therapy but also enhance patient's satisfaction towards to treatment as reflected by the patients' willingness to accept more treatments in the future.

Lastly, this study is not exempted from having limitations, including the difficulty to obtain a homogenous distribution of oral and periodontal surgical therapies, and the lack of randomization which can influence the pre-operative anxiety results and the final data outcomes. In this regard, patients from the SG showed a higher pre-operative mean anxiety score in comparison to CG group individuals, indicating that probably patients with a higher pre-anxiety score likely to opt for the IV sedation treatment. However, results revealed that even with higher pre-anxiety scores, conscious IV sedation has helped to maintain hemodynamic parameters under control and lowering BP than when local anesthesia alone was employed. Additionally, selected patients were not checked for blood pressure measurements before conducting the study, which could have influenced to the mean values recorded if preexisting cardiovascular alterations already affected the regular blood pressure levels. Also, the findings reported in this study regarding outcome measurements and post-operative satisfaction have to be considered with caution, taking into account that patients were not blinded, and they probably were positively influenced by receiving the IV sedation drugs. Finally, it is imperative to acknowledge that further research is warranted to investigate whether the use of IV sedation introduces additional challenges in the context of oral and periodontal surgery, as well as its potential impact on clinical outcomes.

Conclusions

Within its limitation, this prospective clinical study revealed that the use of intravenous moderate sedation adjunct to local anesthesia during various oral and periodontal surgical therapies seems to contribute to the stabilization of patients' hemodynamics, especially the systolic blood pressure, although small differences have been found. Additionally, sedation clearly enhances the post-operative overall patient satisfaction, incrementing the patients' predisposition to accept other surgical therapies in the future.

Appendix A

STROBE statement—Checklist of items that should be included in reports of case-control studies

	Item no	Recommendation	Page no
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	5
		(b) For matched studies, give matching criteria and the number of controls per case	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6, 7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	7
		(d) If applicable, explain how matching of cases and controls was addressed	7
		(e) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	8, 9
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers in each exposure category, or summary measures of exposure	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, 9
		(b) Report category boundaries when continuous variables were categorized	N/A
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	8, 9

	Item no	Recommendation	Page no
Discussion			
Key results	18	Summarize key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11,12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9,10,11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11,12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

Appendix B

Corah's Dental Anxiety Scale (DAS) 1 for preoperative dental anxiety evaluation: (a = 1; b = 2; c = 3; d = 4; e = 5; Total possible = 20: < 9 = mild anxiety; 9–12 = moderate anxiety; 13–14 = high anxiety; 15–20 = severe anxiety (or phobia)

1. If you had to go to the dentist tomorrow for a check-up, how would you feel about it?
 - a. I would look forward to it as a reasonably enjoyable experience
 - b. I wouldn't care one way or the other
 - c. I would be a little uneasy about it
 - d. I would be afraid that it would be unpleasant and painful
 - e. I would be very frightened of what the dentist would do
2. When you are waiting in the dentist's office for your turn in the chair, how do you feel?
 - a. Relaxed
 - b. A little uneasy
 - c. Tense
 - d. Anxious
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick
3. When you are in the dentist's chair waiting while the dentist gets the drill ready to begin working on your teeth, how do you feel?
 - a. Relaxed
 - b. A little uneasy
 - c. Tense
 - d. Anxious
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick
4. Imagine you are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist or hygienist is getting out the instruments which will be used to scrape your teeth around the gums, how do you feel?
 - a. Relaxed
 - b. A little uneasy
 - c. Tense
 - d. Anxious
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick

Author contributions J. GA: study design and conceptualization, manuscript writing, data interpretation, final revision, final approval.

E. D: data collection, data interpretation, initial draft preparation, final approval.

H. S: data collection, statistical analysis, manuscript writing, illustrations, final revision, final approval.

L. S: study design and conceptualization, final approval.

S. PG: study design and conceptualization, manuscript writing, final approval.

HL. W: study design and conceptualization, critical revision, final approval.

Data availability The data that supports the findings of this paper is available from the corresponding author upon request.

Declarations

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the Research Medical Ethical Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from all individual participants included in the study.

Competing interests The authors declare no competing interests.

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