Effects of intravenous sedation on autonomic nerve activity and the psychological state during tooth extraction: A prospective non-randomized controlled trial

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Abstract

Purpose

Intravenous sedation is considered to decrease patient anxiety and tension during dental treatment, thereby reducing fluctuations in autonomic nerve activity and the risk of medical emergencies. We hypothesized that intravenous sedation would suppress the sympathetic nervous system during tooth extraction and relieve patient anxiety. Accordingly, the purpose of this study was to investigate the effects of intravenous sedation on autonomic nerve activity and psychological state during impacted mandibular third molar (IMTM) extraction.

Methods

This prospective study included 40 healthy women scheduled for IMTM extraction under local anesthesia alone (control group; n = 20) or local anesthesia and intravenous sedation (sedation group; n = 20); of these, 34 women were evaluated. Heart rate variability (HRV) was analyzed to evaluate autonomic nerve activity. HRV and circulatory dynamics were measured during the treatment. The Modified Dental Anxiety scale and State-Trait Anxiety Inventory (STAI-S and STAI-T) scores were obtained before treatment. STAI-S scores were also obtained after treatment. Descriptive and bivariate statistical analyses were conducted, and a *P*-value <.05 was considered statistically significant.

Results

The low frequency/high frequency ratio was lower in the sedation group than in the control group (*P* < .01). Compared with the control group, the sedation group showed a significantly greater decrease in post-treatment STAI-S scores relative to pretreatment scores (*P* < .01).

Conclusions

The findings suggest that sedation suppresses the sympathetic nervous system during IMTM extraction and decreases anxiety after the extraction. Further research should elucidate the mechanisms by which sedation suppresses the sympathetic nervous system.

Key words: Intravenous sedation, anxiety and tension, tooth extraction, autonomic nerve activity, psychological state

Introduction

Patient anxiety and tension during dental treatment may cause acute fluctuations in the activity of autonomic nerves and result in a medical emergency.[1,2] Therefore, it is important to analyze changes in the autonomic nervous activity and psychological states such as anxiety and tension.[3] Intravenous sedation with midazolam and propofol is often used to reduce anxiety and tension in patients during dental treatment.[4-6] Midazolam exhibits good amnesic and anxiolytic effects, and propofol has hypnotic and antiemetic effects[5,7]; they are often used together for stable and secure sedation.[5] However, the effect of intravenous sedation on autonomic nerve activity and psychological states remains unclear.

Changes in the autonomic nervous activity can be analyzed by assessing the heart rate variability (HRV).[8-10] This method has recently been used in a study where dental treatment was administered under intravenous sedation.[4] The power spectrum of heartbeat intervals is divided into low frequency (LF: 0.04–0.15 Hz) and high frequency (HF: 0.15–0.4 Hz) via frequency domain analysis. The LF is mediated via the sympathetic and parasympathetic nerves, while the HF is mediated via the parasympathetic nerves. Therefore, the LF/HF is used as a sympathetic nerve index, and the HF is used as a parasympathetic nerve index.[11]

Among the different types of dental treatments, extraction of the impacted mandibular third molar (IMTM) is associated with the highest anxiety[10-13]; however, no study has investigated the changes in the autonomic nerve activity during this procedure when patients are under intravenous sedation. Therefore, we evaluated the effects of intravenous sedation on autonomic nerve activity, cardiovascular parameters, and the psychological state during IMTM extraction.

Materials and Methods

Participants

This study was approved by the Ethics Committee on Epidemiological Studies, Kagoshima University (No. 190172). Written informed consent was obtained from all participants. All procedures were conducted in accordance with the Declaration of Helsinki.

A total of 40 healthy adult women aged between 20 and 40 years were scheduled for IMTM extraction between December 2019 and May 2020 at Kagoshima University

Hospital. The angulation of the IMTM was classified by winter's classification (Vertical, horizontal angulation, distoangular angulation, mesioangular angulation, transversal angulation, inverse angulation). All IMTMs in this study were classified as horizontal angulation. The position of the IMTM in relation to the mandibular ramus was classified by Pell and Gregory's classification.[14] We determined the required sample size by power analysis ($\alpha = 0.05$, $\beta = 0.2$). The patients scheduled for extraction under local anesthesia constituted the control group, while the patients scheduled for extraction under local anesthesia and intravenous sedation constituted the sedation group. The decision regarding the need for sedation was based on the clinical judgment of the dentist after a thorough discussion with the patient. The dentist explained the details related to intravenous sedation, and only the patients who voluntarily opted for the procedure were assigned to the intravenous sedation group.

The patients were not smokers and were not using any regular medications. Consumption of water within 2 hours, eating and exercising within 6 hours, and consumption of caffeine and alcohol within 24 hours before surgery were prohibited.[15-18]

Experimental procedures

The patients were in a semi-Fowler position on the dental chair in a noise-free clinic room, which was maintained at 24°C.[15] All procedures were initiated at 2:00 pm to minimize the effects of the circadian rhythm.[15,18] HRV, systolic blood pressure (SBP), heart rate (HR), and oxygen saturation (SpO_2) were measured throughout the procedure. These measurements were started 15 minutes before treatment initiation. The level of sedation was evaluated by the bispectral index (BIS) (70–80) using a BIS monitor (Nihon Kohden, Tokyo, Japan) and the Observer's Assessment of Alertness/Sedation (OAA/S) score (1 to 2).[4,5] Anxiety levels before treatment were evaluated using the Modified Dental Anxiety Scale (MDAS) and the State-Trait Anxiety Inventory (STAI-S and STAI-T). These were noted just before IMTM extraction.

In addition, STAI-S scores were calculated after the treatment.[3] The respiratory rate was determined by observing the patient and counting the number of breaths drawn during the treatment.

In the sedation group, a 22-gauge catheter was inserted into the left-hand vein, and acetated Ringer's solution was infused. The participants were instructed to close their eyes and rest until treatment initiation, and midazolam (0.05 mg/kg) and propofol were administered as a bolus so that the BIS was 70–80. The propofol maintenance concentration was adjusted to maintain the BIS at 70–80 during treatment. A specialist in oral surgery performed all tooth extractions to standardize the stress level of patients.[3]

The HRV was measured every 2 seconds using the software MemCalc-Makin2 (GMS, Tokyo, Japan). The HRV parameters included the LF, HF, LF/HF, and HR. The autonomic nerve activity analysis was initiated after the participant had been at rest for 15 minutes in the control group. Based on previous studies, we defined the data recorded during a 5-minute period after a 15-minute rest period as resting data in the control group.[3,11,16,18] In the sedation group, the measurements recorded during the first 5 minutes of sedation (as the BIS decreased to 70–80) were classified as data obtained at rest.

Based on previous study protocols, we evaluated autonomic nerve activity and circulatory dynamics at a point during each surgical step (local anesthesia injection, flap incision and reflection, bone removal, separation of the tooth crown, and suturing).[9] The relative ratios of LF/HF, HF, HR, and SBP at the different time points were compared with those at rest.

SBP, a cardiovascular parameter, was measured noninvasively every 2 minutes. BIS, which reflects the pharmacodynamic anesthetic effect on the central nervous system, was used to monitor the sedation level.[19] OAA/S was used to measure the sedation level by assessing a participant's response to stimuli.[19]

Two questionnaires were used to evaluate the patient's psychological state. The MDAS consists of five questions, which evaluate dental anxiety. The STAI consists of 20 self-reported items used to evaluate state anxiety (STAI-S) and 20 self-reported items used to evaluate trait anxiety (STAI-T).[20]

Statistical analyses

The Mann-Whitney U test, Friedman test, and Steel-Dwass test were used for statistical analysis. A *P*-value <.05 was considered statistically significant. Statistical analysis was performed using the GraphPad Prism version 6 (San Diego, CA).

Results

Participants

Among the 40 female patients recruited in the study, 6 withdrew, and thus, a total of 34 participants were included in the final analysis (17 participants in each group) (Fig. 1); the 6 female patients did not wish to participate, and hence opted out of the study.

Prior to the procedure, there were no significant differences in physical characteristics (mean age, height, and weight), treatment-related parameters (volume of local anesthetics), and psychological states (treatment time) between the two groups (Table 1). All subjects were classified as CLASS Ⅱ /PositionB by Pell and Gregory's classification (Table 2).

Relative ratios of LF/HF

In the control group, LF/HF at all the procedure steps showed significant increases relative to the value at rest. In the sedation group, significant increases in LF/HF were observed during incision and flap reflection. The LF/HF at all the steps was significantly lower in the sedation group than in the control group (Fig. 2a).

Relative ratios of HF and HR

No significant within-group differences were observed in either group. No significant between-group differences were observed during any of the steps (Fig. 2b and 2c).

Relative ratios of SBP

In the control group, SBP during all steps of the extraction procedure was significantly higher than that at rest. Notably, the SBP during flap incision and reflection, bone removal, and separation of the tooth crown was significantly lower in the sedation group than in the control group (Fig. 2d).

Postoperative STAI state anxiety scores

Between the control and sedation groups, the latter exhibited a significantly larger reduction in STAI-S scores after treatment (Fig. 3).

Discussion

The results of this study indicate that intravenous sedation during IMTM extraction can effectively suppress sympathetic nervous activity and relieve anxiety. The decrease in sympathetic nerve activity during surgery may be due to decreased anxiety and tension owing to the loss of consciousness and drug use. Notably, midazolam and propofol (both used in the present study) have been reported to reduce sympathetic nervous activity.[17,21] Therefore, the use of intravenous sedation during IMTM extraction might be important for the prevention of medical emergencies.

The MDAS and STAI scales are widely used to determine the fear and anxiety of patients during dental treatment.[3,22] Midazolam and propofol have anxiolytic and amnestic effects.[6,23,24] Accordingly, the amnestic effect of midazolam and propofol might significantly reduce the STAI anxiety score in the sedation group. As BIS and OAA/S scores are valid and widely used measures for the evaluation of the sedation level during intravenous sedation,[4,25] both scores were utilized in the present study. The OAA/S score during the patient's treatment was maintained at 1-2, indicating that the patient's mental stress with treatment under sedation could be significantly lower than that before surgery or with treatment without sedation. Our study suggests that sedation during IMTM extraction may help reduce patient anxiety.

HRV is the most commonly used method for assessing autonomic nerve activity.[8-10] Based on prior studies,[4,6] we used HRV analysis to evaluate autonomic nerve activity during sedation. In our study, the respiratory rate was nine or more in the control and sedation groups; this finding indicated that parasympathetic nervous activity was accurately assessed.[4] Therefore, this protocol, which evaluated the activity of the autonomic nerves, was considered appropriate for evaluating autonomic nerve activity in patients under sedation.

No significant difference in HF was found between the two groups, probably due to individual differences in the reactivity of parasympathetic nerve activity to sympathetic nervous system stimulation. The HR rhythm is controlled by sympathetic and parasympathetic activity,[26] and the human autonomic nervous system is dominated by the parasympathetic nervous system. The myocardial contractile force and cardiac output increase with an increase in the activity of the sympathetic nerves distributed in the myocardium.[3] When sympathetic activity decreases, myocardial contractility decreases, resulting in a decrease in cardiac output and blood pressure. Moreover, the decrease in peripheral vascular resistance in the circulatory system, in which the sympathetic nerves are distributed, also contributes to the reduction in blood pressure. While peripheral vascular resistance was not evaluated in the present study, it might have been decreased by the use of sedation. Taken together, the decrease in blood pressure is likely caused by decreases in both cardiac output and peripheral vascular resistance owing to a decrease in myocardial contractility due to decreased sympathetic activity.

While previous studies have assessed autonomic nervous activity in patients undergoing some types of dental treatment while under sedation,[27,28] no investigations concerning IMTM extraction have been conducted. Additionally, the experience of the surgeon, the evaluation of the sedation level, and the type of anesthetic drugs used were not standardized in previous studies.[4,7,9,10,28] The stress level of patients during extraction is thought to depend on the experience level of the surgeon; thus, in our study, a single oral surgery specialist performed the treatment procedures for all patients in order to standardize the stress level of patients.[3]

Generally, lidocaine with epinephrine is used during the extraction of impacted third molars. Lidocaine suppresses sympathetic nervous system activity during impacted third molar extraction and has been shown to be more effective than prilocaine-felypressin. Therefore, we used 2% lidocaine with epinephrine in this study.

Limitation

One limitation of this study is that all the participants were healthy adult women aged between 20 and 40 years. Therefore, further studies involving male participants at different ages are needed to confirm the present findings.

Conclusion

Our study suggests that sedation suppresses the activity of the sympathetic nervous system during IMTM extraction and relieves anxiety after treatment. Additional studies are needed to investigate the underlying mechanisms and to develop approaches to prevent the onset of medical emergencies.

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Table 1. Clinical characteristics of the participants

	Control (n = 17)	Sedation (n = 17)	Total (n = 34)	*P*
Age (years)	25.17 ± 3.86	27.88 ± 5.09	26.53 ± 4.66	0.08
Height (cm)	160.76 ± 5.84	160.17 ± 5.22	160.46 ± 5.47	0.87
Weight (kg)	49.71 ± 6.61	53.51 ± 8.81	51.6 ± 7.9	0.54
Local anesthesia (mL)	4.76 ± 0.90	5.28 ± 1.47	5.02 ± 1.23	0.42
Operation time (min)	37.4 ± 10.66	42.17 ± 10.89	40.32 ± 1.88	0.11
MDAS scores	13.71 ± 4.27	14.59 ± 5.36	14.15 ± 4.79	0.75
STAI-S scores	49.71 ± 5.97	51.29 ± 11.67	50.5 ± 9.16	0.07
STAI-T scores	55.71 ± 6.66	51 ± 9.84	53.35 ± 8.61	0.09

MDAS: Modified Dental Anxiety scale; STAI-S: State-Trait Anxiety Inventory – State anxiety; STAI-T: State-Trait Anxiety Inventory – Trait anxiety.

Table 2. The position of the IMTM in relation to the mandibular ramus

	Control	Sedation
CLASS Ⅱ/PositionB	17	17

CLASS Ⅱ : Small space for IMTM(root/crown is partially located in the ramus).

PositionB : The highest portion of the IMTM was below the occlusal plane but above the cervical line of the second molar.

Figure Legends

Figure 1. Protocol of this study.

BP: Blood pressure; HR: Heart rate; HRV: Heart rate variability; local: Local anesthetic injection; Separation: Tooth crown separation; Extraction: Extraction of the impacted mandibular third molar.

Figure 2. (a) Comparisons of low frequency/high frequency (LF/HF) ratios during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM. Comparison between groups: $**P < .01$. Comparison within groups: control, †$P < .05$ and ‡$P < .01$ (vs. Rest); sedation, § $P < .05$ (vs. Rest).

(b) Comparisons of the HF component during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM.

(c) Comparisons of heart rate (HR) during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM.

(**d**) Comparisons of systolic blood pressure (SBP) during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM. Comparison between groups: $*P < .05$; comparison within groups: †$P < .05$, ‡$P < .01$ (vs. rest).

Figure 3. Comparison of decreases in the STAI-S scores between the control group and the sedation group. Data are presented as means and SEM. Statistical significance: $**P < .01$.

Table and Figure

Table 1

Table 1. Clinical characteristics of the participants

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Table 2

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Fig. 1

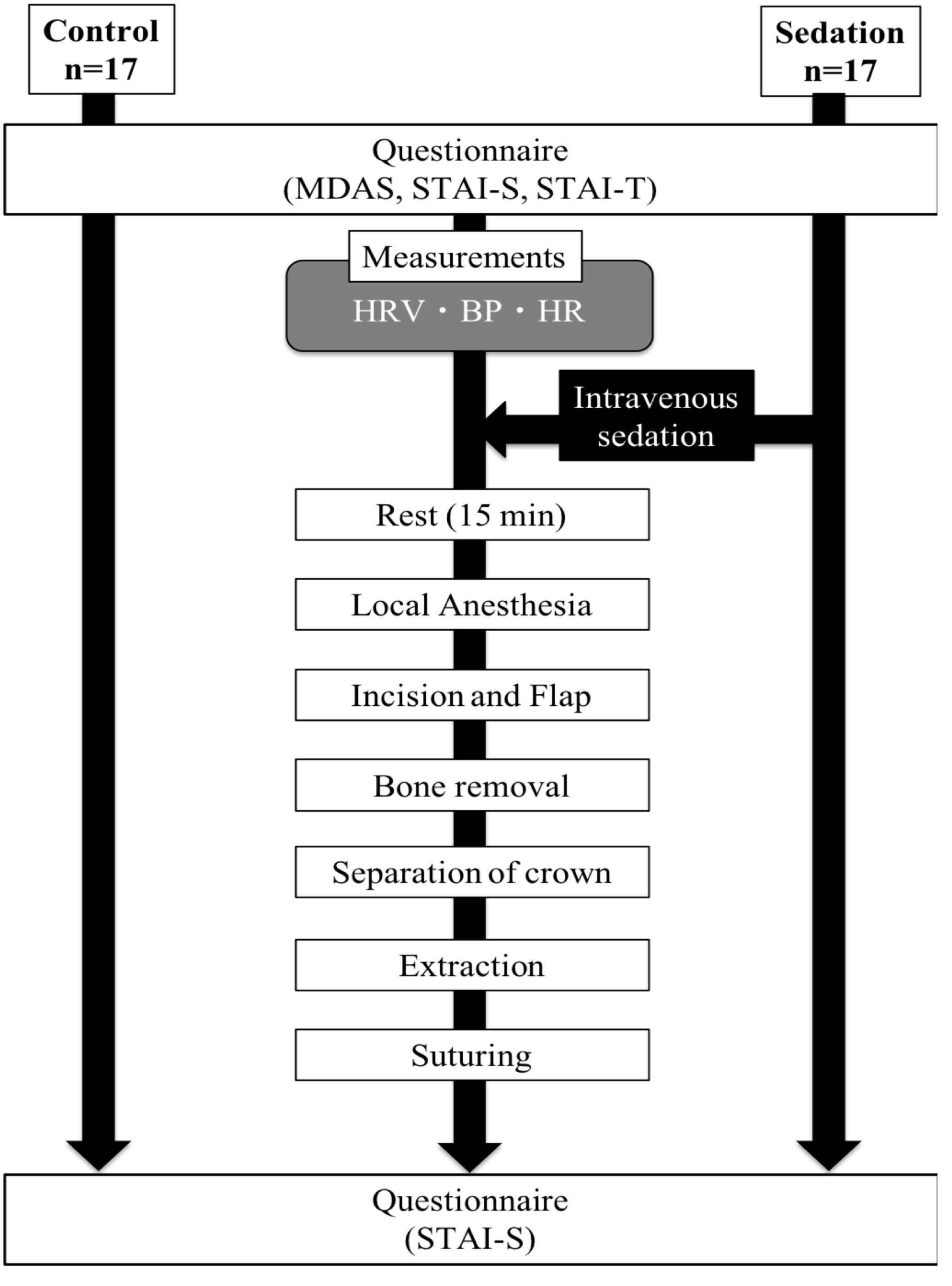

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Fig. 2 (a)

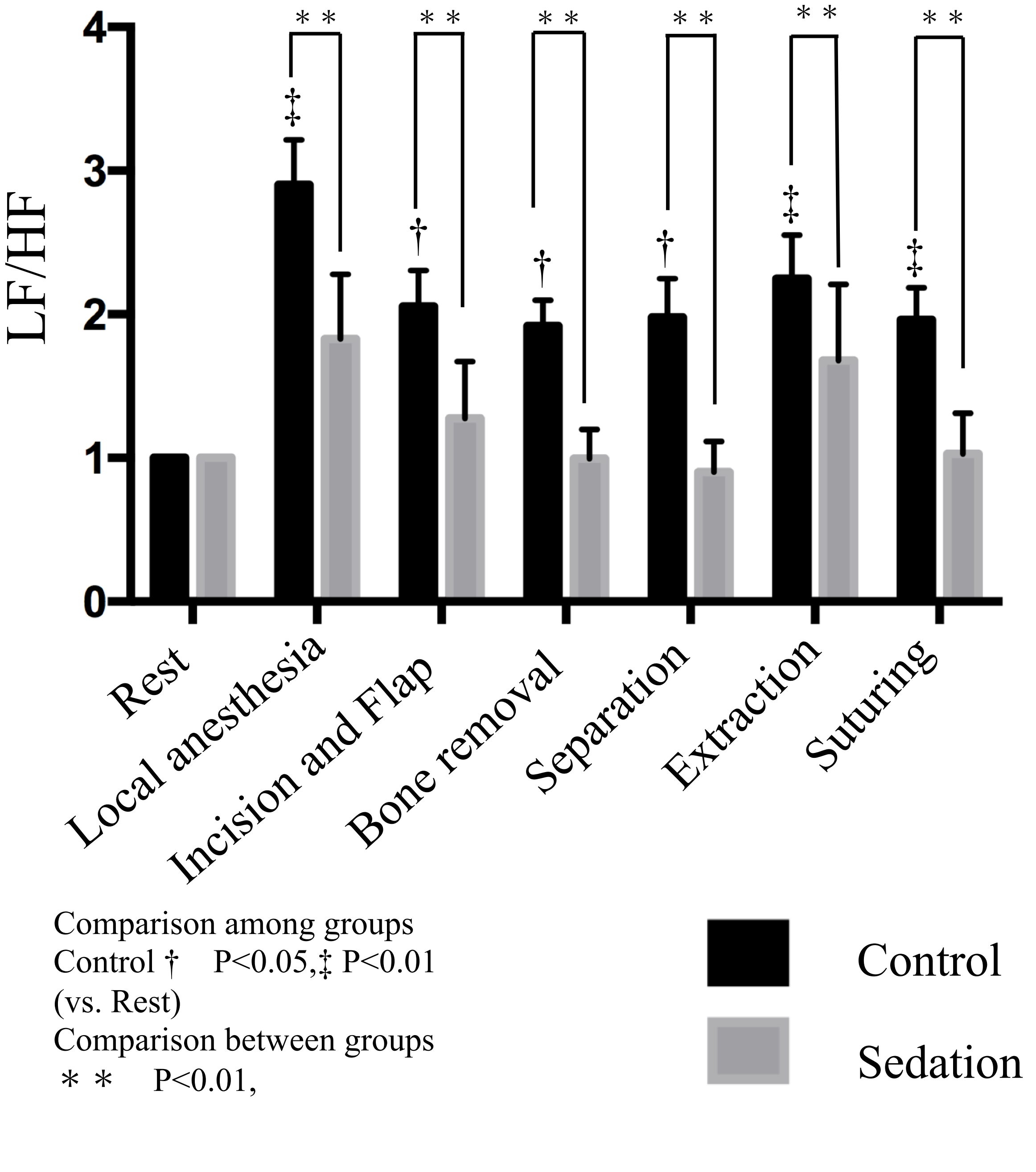

Figure 2. (a) Comparisons of low frequency/high frequency (LF/HF) ratios during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM. Comparison between groups: ∗∗$P < .01$. Comparison within groups: control, †$P < .05$ and ‡$P < .01$ (vs. Rest); sedation, § $P < .05$ (vs. Rest).

Fig. 2 (b)

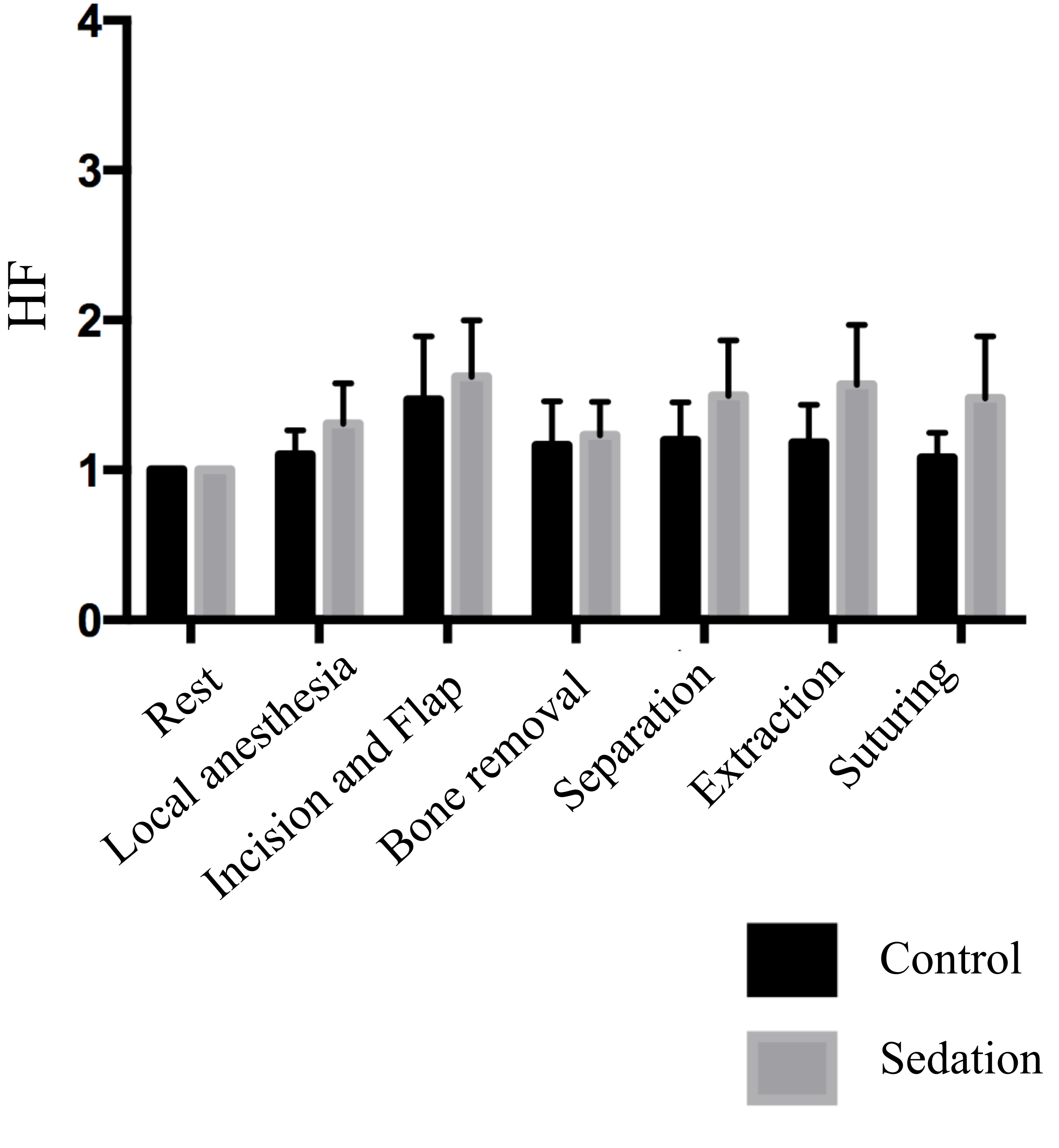

Fig. 2 (b) Comparisons of the HF component during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM.

Fig. 2 (c)

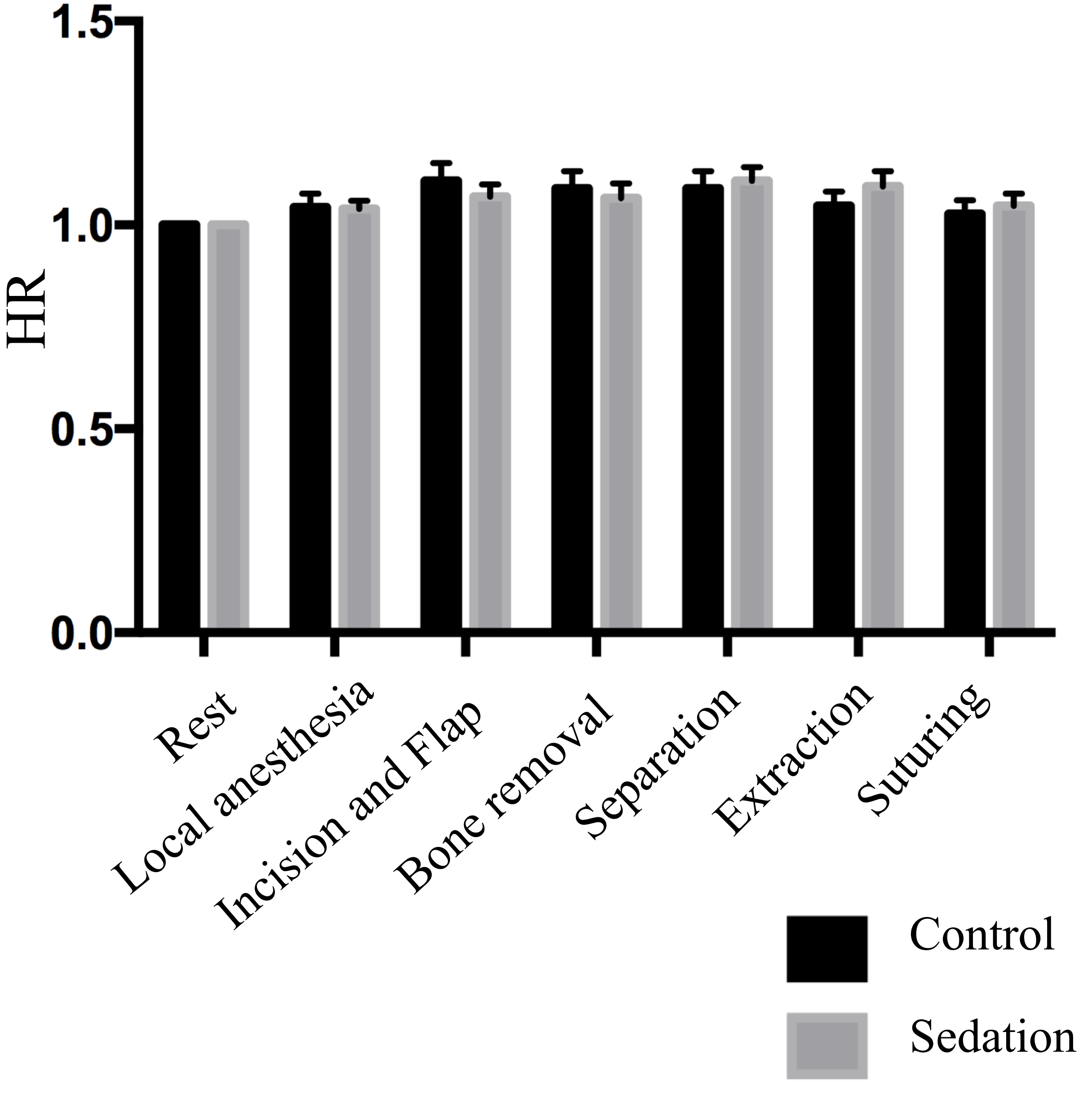

Fig. 2 (c) Comparisons of heart rate (HR) during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM.

Fig. 2 (d)

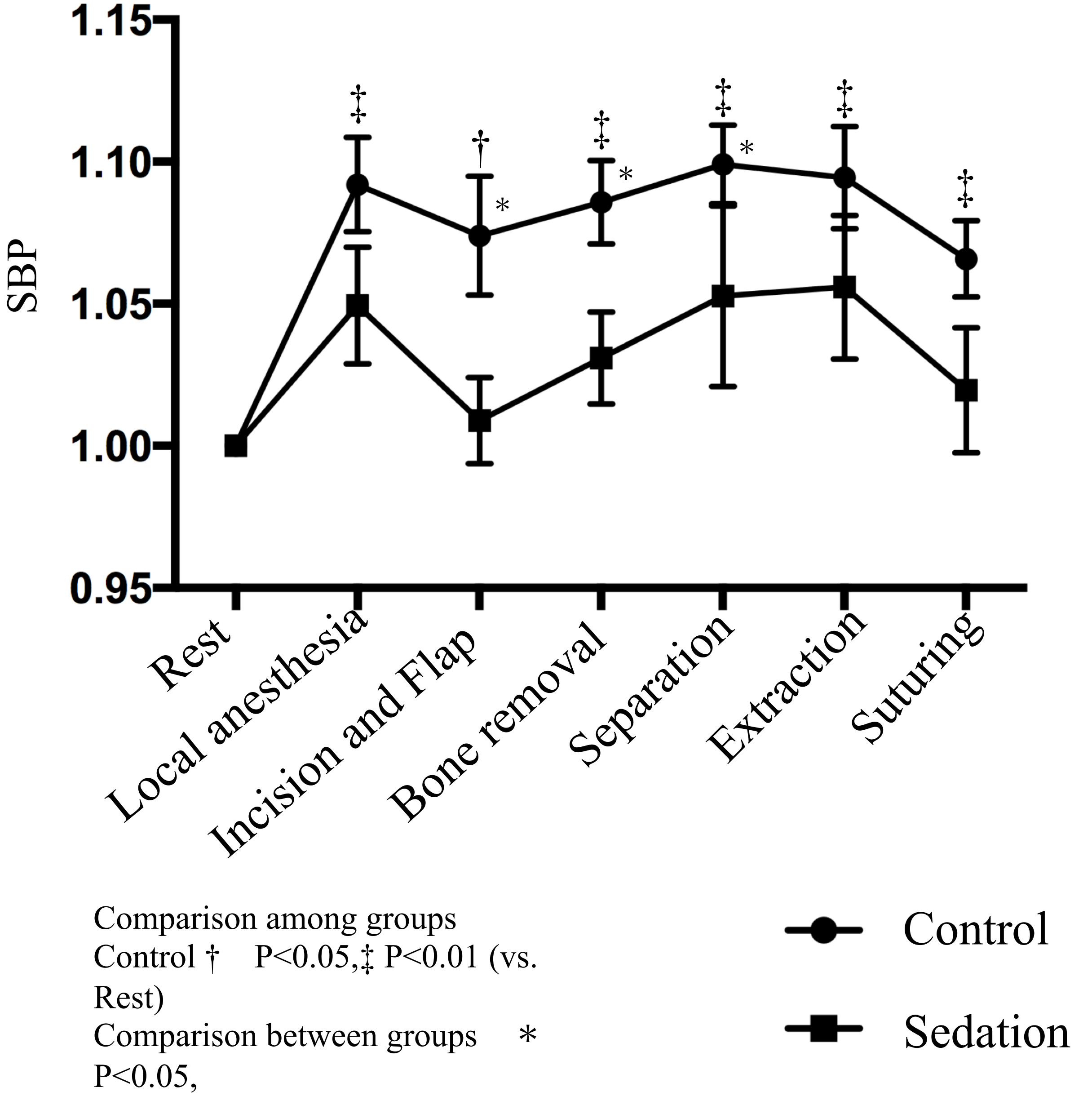

Fig. 2 (d) Comparisons of systolic blood pressure (SBP) during tooth extraction between the control and sedation groups, as well as within each group, at different stages. Data are presented as means and SEM. Comparison between groups: $*P < .05$; comparison within groups: $\dagger P < .05$, $\ddagger P < .01$ (vs. rest).

Fig. 3

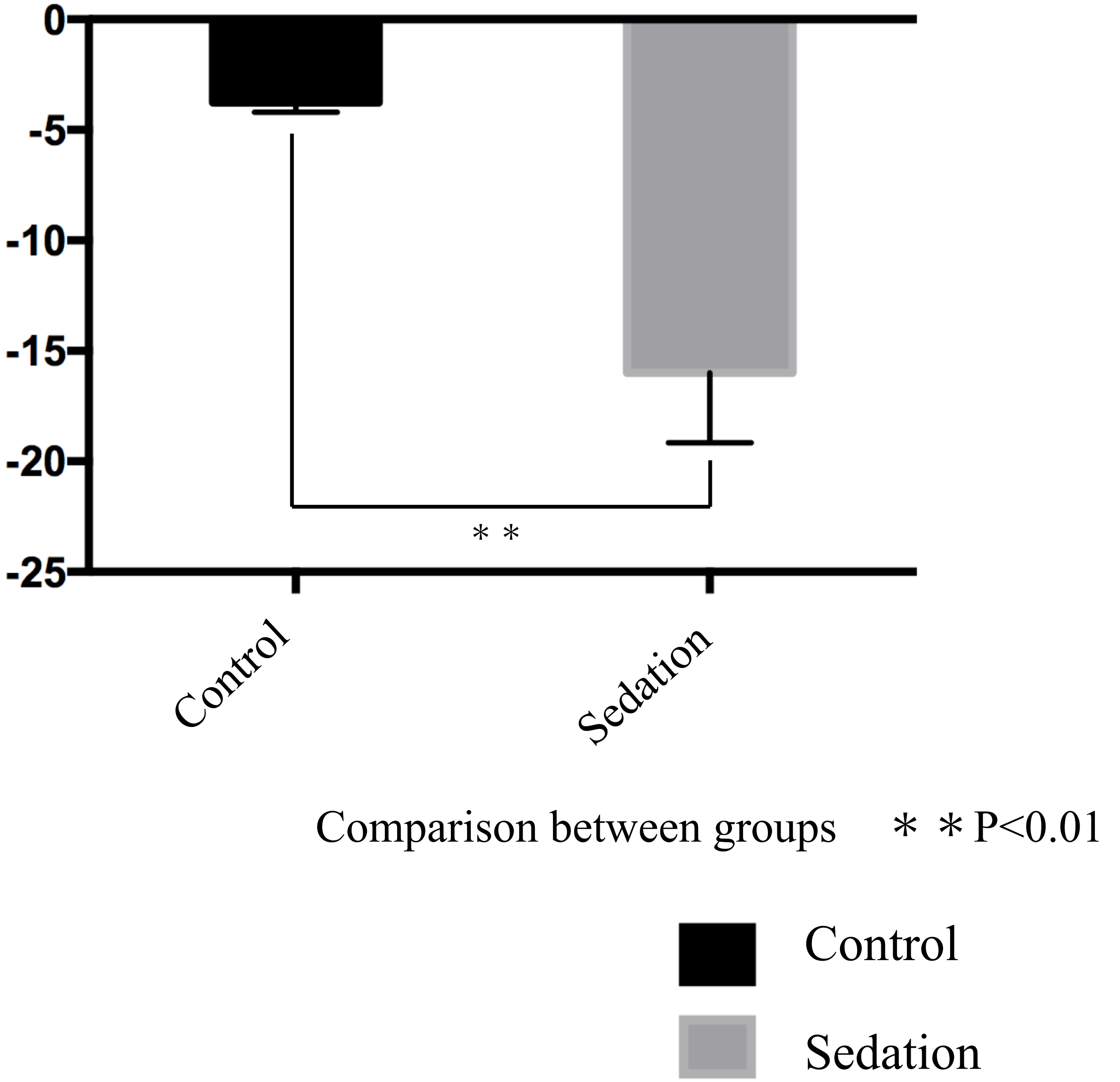

Figure 3. Comparison of decreases in the STAI-S scores between the control group and the sedation group. Data are presented as means and SEM. Statistical significance: $**P < .01$.