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# Effects of cranial electrotherapy stimulation on preoperative anxiety and blood pressure during anesthetic induction in patients with essential hypertension

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## Abstract

**Objective:** Cranial electrotherapy stimulation (CES) is a non-invasive treatment that improves symptoms such as anxiety and pain. The purpose of this study was to analyze the effect of CES pretreatment on levels of preoperative anxiety, pain, and hemodynamic responses—especially changes in blood pressure—during anesthetic induction in patients with essential hypertension.

**Methods:** Eighty patients undergoing general anesthesia were randomly assigned to receive either no pretreatment (control group, n = 40) or CES pretreatment (CES group, n = 40). Anxiety scores, systolic and diastolic blood pressures, mean arterial pressure, and heart rate were measured in the general ward the evening before surgery, as well as in the preoperative holding area, operating room, and after intubation. Withdrawal responses to rocuronium injection were also measured.

**Results:** Anxiety scores in the operating room were significantly lower in the CES group. Withdrawal responses to rocuronium injection were also significantly lower in the CES group. There were no significant differences in hemodynamic values between the two groups.

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**Conclusions:** CES pretreatment reduces both preoperative anxiety levels and withdrawal responses to rocuronium injection. However, it does not have a significant effect on hemodynamic responses.

**Keywords**
Anxiety, blood pressure control, cranial electrotherapy stimulation, essential hypertension, rocuronium injection, hemodynamic responses

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## Introduction

Cranial electrotherapy stimulation (CES) is a method by which an electrode is attached to the earlobe to deliver a microcurrent to the cranium, thereby providing a non-pharmacological treatment that can relieve symptoms such as anxiety, depression, insomnia, and stress.[1] No serious side effects associated with CES have yet been reported. However, there have been reports of skin irritation caused by electrodes, as well as headache and dizziness.[2] Because CES is effective in treating anxiety, insomnia, and fatigue, it has also been used for the treatment of various medical and psychiatric disorders.[3–5] In addition, by increasing the potency of anesthetic agents by up to 37%, CES can be used to reduce anesthetic drug doses during operations.[1] Moreover, patients who undergo CES before surgery or on the day of surgery have relaxation reactions that relieve anxiety symptoms, such as decreasing blood pressure, respiratory rate, and heart rate.[6] Although the mechanisms underlying the effects of CES have not yet been elucidated, several studies have suggested that the inflow of microcurrents during CES can cause changes in brain waves, thus affecting brain activity.[5]

Hypertension is a very common disease in adults, with a 2013 prevalence of 25.76% among Korean adults aged between 40 and 64 years.[7] Hypertension is defined as systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg.[8] Hypertension is the main cause of coronary artery disease, which is one of the most common cardiovascular, cerebrovascular, and renal diseases.[9] The need to control blood pressure in patients with hypertension has already been highlighted in many studies, and is not an exception in patients under general anesthesia. In particular, the control of blood pressure before and after surgery is more important in patients with a previous history of hypertension than in normal patients.[10,11] Patients undergoing surgery may have preoperative anxiety caused by an unfamiliar environment, fear of their own disease or anesthesia, or fear of surgery. This anxiety increases patients' blood pressure before surgery. In particular, hypertension is exaggerated in patients with essential hypertension, and uncontrolled hypertension after entering the operating room is a common reason for delayed surgery.[10] Various methods have been proposed to control preoperative blood pressure because patients with relatively good preoperative blood pressure control have less changes in blood pressure during surgery. Primarily, it is important to maintain antihypertensive drugs that were administered before surgery.[12]

Furthermore, preoperative administration of anxiolytic medications, such as midazolam, may reduce anxiety and prevent mild-to-moderate preoperative increases in blood pressure.[13,14] In addition, Yuzkat et al.[15] suggest that showing patients the operating room the day before surgery decreases preoperative anxiety, as well as lowering blood pressure and heart rate inside the operating room. Anesthesia management in patients with hypertension should be performed by considering the dysfunction of each organ, the use of current anti-hypertensive treatments, and the preoperative baseline blood pressure. In patients with hypertension, changes in blood pressure during anesthesia should be minimized. The ideal range of blood pressure during surgery should be maintained within approximately 20% of the preoperative blood pressure, to prevent ischemia of important organs.[16] Intraoperative hypertension is often caused by painful stimuli, for example as a result of laryngoscopic manipulation, intubation, skin incision, or shallow anesthesia. This phenomenon is especially common in patients with a preoperative history of hypertension.[17] In such cases, blood pressure can be controlled by increasing the concentration of the inhalation anesthetic agent or adding an opioid or a short-acting beta-blocker.[18]

Patients undergoing surgery under general anesthesia are admitted the day before surgery, and an anesthesiologist evaluates the patient's condition and forms a relationship of trust with the patient through preoperative visits. To reduce postoperative and intraoperative pain and preoperative anxiety, benzodiazepines such as midazolam or opioids are commonly administered. However, these drugs may affect the cardiovascular system, and their effects can be severe in patients with hypertension.

Non-invasive CES treatment, which has no serious side effects, was therefore performed on both the day before surgery and the day of surgery. We evaluated its effect on pain, anxiety, and the degree of blood pressure increase during tracheal intubation.

## Materials and methods

### Patients

This study was approved by the hospital's Institutional Review Board (2018AS0209). The subjects were 20- to 65-year-old patients with a history of hypertension and American Society of Anesthesiologists Physical Class II, who were scheduled to undergo general anesthesia. Patients were excluded from the study if they had renal, endocrine, or musculoskeletal disease, or had a pacemaker. Patients taking any psychiatric medication or with a body mass index $> 35$ were also excluded. The purpose and method of the study were explained thoroughly to the patients, and they provided written informed consent for participation in the study. The included patients were divided into the control and CES groups using a computerized randomization method according to a table generated using www.randomization.com.

### Control and CES procedures

The patients in the CES group received preoperative CES for 20 minutes both on the day before surgery and on the morning of the day of surgery. A clip-type electrode of a microcurrent stimulator (Alpha-Stim 100, Electromedical Products International, Inc., Mineral Wells, TX, USA) was attached to the earlobe, and a microcurrent of less than 200 μA and 0.5 Hz was delivered via the electrode. We adjusted the current carefully until the patient experienced tingling or light dizziness (Figure 1). For patients in the control group, the electrodes were attached in the same way as in the CES group, but the power was turned off.

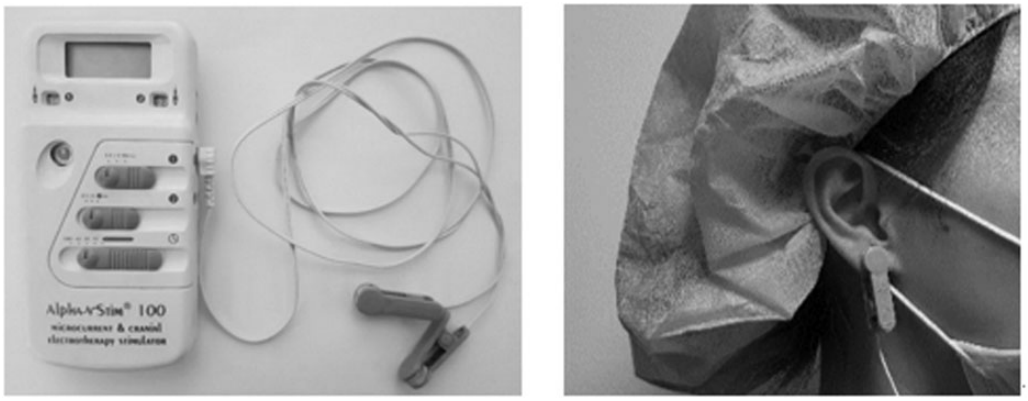


**Figure 1.** The Alpha-Stim 100 (Electromedical Products International Inc, Mineral Wells, TX, USA) cranial electrotherapy stimulation unit used in the study. Note: ear clips were worn on both ears.

## *Clinical measurements*

Pre-anesthesia visits, anxiety scores, CES pretreatment, and anesthesia induction were performed by different investigators. Preoperative anxiety, withdrawal responses to rocuronium injection, blood pressure, and heart rate were evaluated. Preoperative anxiety levels were assessed using a five-point Likert scale[19] (1: not at all; 2: mild; 3: intermediate; 4: moderate; 5: severe). Anxiety levels were measured three times: on the day before surgery, in the preoperative holding area on the day of surgery, and after entering the operating room. Anesthesia was induced via intravenous administration of propofol (2 mg/kg), followed by slow administration of rocuronium (0.9 mg/kg) for 5 s after the loss of consciousness. The withdrawal response to rocuronium was classified into four types, from no response to a severe response (Table 1). After anesthesia induction, intubation was performed after 2 minutes of mask ventilation at a fraction of inspired oxygen of 0.5, oxygenated air flow (6 L/min), and sevoflurane administration (3 vol%) until intubation. Breathing was controlled to maintain an end-tidal carbon dioxide level of 30 to 35 mmHg.

**Table 1.** Assessment of withdrawal responses of rocuronium.

| Withdrawal score | Withdrawal response |
|---|---|
| 0 (None) | No movement |
| 1 (Mild) | Movement at the wrist only |
| 2 (Moderate) | Movement below the elbow |
| 3 (Severe) | Movement above the shoulder, general response |

Blood pressure and heart rate were measured at the same time as the preoperative anxiety evaluations: in the ward on the day before surgery, in the preoperative holding area on the day of surgery, and after entering the operating room. Additionally, blood pressure and heart rate were measured a fourth time: immediately after tracheal intubation.

## *Statistical analysis*

Statistical analysis was performed using SPSS for Windows, version 12.0 (SPSS Inc., Chicago, IL, USA), and all results except sex are expressed as the mean ± standard deviation or frequency. The discrete demographic data were analyzed using the

chi-squared test or Fisher's exact probability test (sex, surgical site, and non-malignancy/malignancy), as appropriate. A P-value $< 0.05$ was considered statistically significant. Changes in blood pressure and heart rate in each group were calculated as a percentage change from the values measured in the ward on the day before surgery. We used the independent t-test to analyze the following: systolic blood pressure after entering the operating room and after tracheal intubation, diastolic blood pressure in the ward before surgery and in the operating room, mean arterial pressure after entering the operating room and after tracheal intubation, changes in the percentage of systolic blood pressure after entering the operating room and after tracheal intubation, and changes in the percentage of mean arterial pressure after tracheal intubation. The Mann–Whitney U test was used to analyze the other values. A P-value $< 0.005$ after Bonferroni correction was considered statistically significant. Anxiety scores and incidence of the rocuronium withdrawal response were compared using the chi-squared test. A P-value $< 0.05$ was considered statistically significant.

## Results

The required number of subjects in each group was calculated to be 40 on the basis of previous research results, with a significance level of 0.05 and power of 0.8. Considering potential dropouts, we recruited 90 patients who underwent surgery at our hospital. Of the 90 recruited patients, 10 refused to participate in the study and were excluded. Eighty patients participated in the study: 40 patients in each of the control and CES groups (Figure 2).

There were no significant differences in age, sex, height, body weight, surgical site, or malignancy between the two groups (Table 2). There were also no significant differences between the control and CES groups in anxiety scores on the day before surgery and in the preoperative holding area. However, anxiety scores after entering the operating room were significantly lower in the CES group than in the control group (Table 3, $P < 0.05$). Additionally, the number of patients with higher levels of anxiety was lower in the CES group than in the control group. There were no significant differences between the two groups in systolic blood pressures on the day before surgery, after entering the operating room, and immediately after tracheal intubation (CES group: $132.4 \pm 11.9$, $149.2 \pm 17.5$, and $175.0 \pm 23.3$ mmHg, respectively; control group: $131.1 \pm 11.8$, $154.4 \pm 18.9$, and $179.4 \pm 24.7$ mmHg, respectively). Diastolic blood pressures appeared to be lower in the CES group on the day before surgery, after entering the operating room, and immediately after tracheal intubation, but there were no significant differences between the two groups (CES group: $79.7 \pm 8.6$, $83.3 \pm 9.9$, and $108.8 \pm 23.5$ mmHg, respectively; control group: $82.9 \pm 9.2$, $86.9 \pm 9.0$ and $110.2 \pm 17.1$ mmHg, respectively). Heart rates also appeared to be lower in the CES group on the day before surgery, after entering the operating room, and immediately after tracheal intubation, but there were no significant differences between the two groups (CES group: $74.7 \pm 16.6$ and $67.3 \pm 10.0$, and $97.7 \pm 14.2$, respectively; control group: $77.4 \pm 10.3$, $75.2 \pm 12.4$, and $99.2 \pm 15.8$, respectively). There were also no significant differences in blood pressure changes between the CES and control groups (Table 4). Finally, the CES group had a significantly lower withdrawal response to rocuronium-induced pain after anesthesia induction compared with the control group (Table 5, $P < 0.05$).

## Discussion

Both the anxiety scores after entering the operating room and the withdrawal

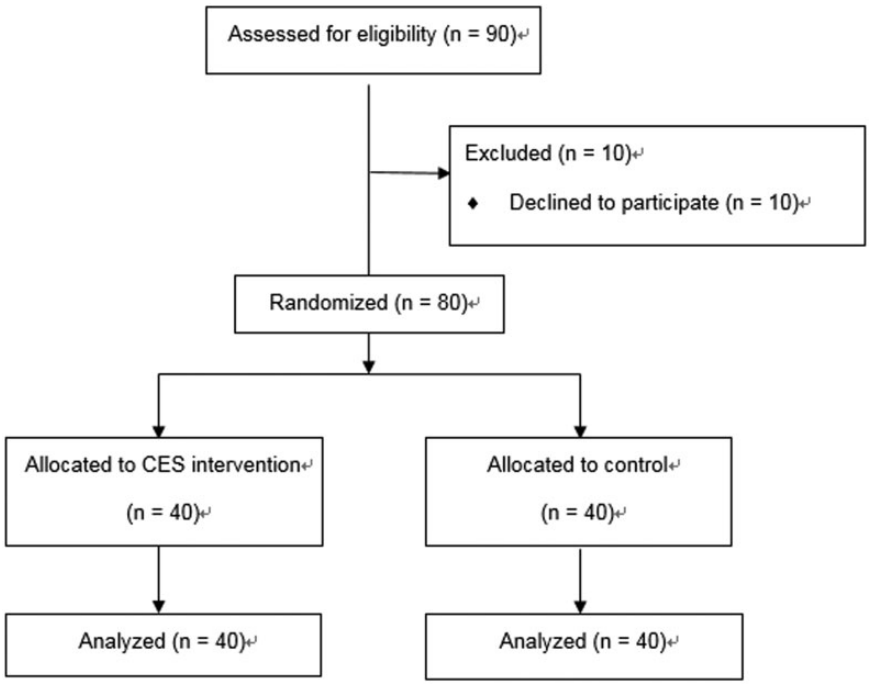


**Figure 2.** Flow diagram of the progression of patients undergoing elective surgery through this study.

**Table 2.** Demographic characteristics.

| | Control group (n = 40) | CES group (n = 40) | P-value |
|---|---|---|---|
| Age (years) | 54.8 ± 5.8 | 54.6 ± 7.3 | 0.798 |
| Sex (M/F) | 23/17 | 22/18 | 0.822 |
| Weight (kg) | 68.1 ± 10.7 | 69.1 ± 9.2 | 0.634 |
| Height (cm) | 161.2 ± 8.4 | 162.4 ± 8.3 | 0.518 |
| Surgical site | | | 0.259 |
| Head & neck | 13 (32.5%) | 16 (40.0%) | |
| Breast | 3 (7.5%) | 4 (10.0%) | |
| Spine | 2 (5.0%) | 3 (7.5%) | |
| Abdomen | 13 (32.5%) | 15 (37.5%) | |
| Extremity | 9 (22.5%) | 2 (5.0%) | |
| Non-malignancy/malignancy | 29/11 | 29/11 | 1.000 |

Values are expressed as the mean ± standard deviation or number of patients (percentages). Control group: no pretreatment; CES group: CES pretreatment. There were no significant differences between the two groups. CES: cranial electrotherapy stimulation.

responses to rocuronium administration were significantly lower in patients who underwent CES pretreatment compared with the control group. This finding is consistent with that of previous studies in which CES was effective in reducing anxiety and controlling pain. However, there were no significant differences in blood pressure

**Table 3.** Changes in anxiety scores.

| | Anxiety score | Control group (n = 40) | CES group (n = 40) | P-value |
|---|---|---|---|---|
| GW | 1 | 17 (42.5%) | 14 (35%) | 0.318 |
| | 2 | 13 (32.5%) | 12 (30%) | |
| | 3 | 4 (10%) | 11 (27.5%) | |
| | 4 | 3 (7.5%) | 1 (2.5%) | |
| | 5 | 3 (7.5%) | 2 (5%) | |
| PHA | 1 | 17 (42.5%) | 17 (42.5%) | 0.145 |
| | 2 | 10 (25%) | 12 (30%) | |
| | 3 | 3 (7.5%) | 7 (17.5%) | |
| | 4 | 5 (12.5%) | 4 (10%) | |
| | 5 | 5 (12.5%) | 0 (0%) | |
| OR | 1 | 14 (35%) | 17 (42.5%) | 0.040* |
| | 2 | 8 (20%) | 15 (37.5%) | |
| | 3 | 5 (12.5%) | 5 (12.5%) | |
| | 4 | 7 (17.5%) | 3 (7.5%) | |
| | 5 | 6 (15%) | 0 (0%) | |

Anxiety scores were graded using a five-point Likert scale (1: lowest to 5: highest). Values are presented as number of patients (percentages). Control group: no pretreatment; CES group: CES pretreatment. CES: cranial electrotherapy stimulation; GW: general ward; PHA: preoperative holding area; OR: operating room. *$P < 0.05$ compared with the control group.

**Table 4.** Changes in blood pressure and heart rate.

| | | Control group (n = 40) % change | CES group (n = 40) % change | P-value |
|---|---|---|---|---|
| SBP (mmHg) | GW–OR | 14.0 ± 11.9 | 10.4 ± 11.4 | 0.212 |
| | GW–after intubation | 25.4 ± 13.4 | 23.1 ± 12.5 | 0.412 |
| DBP (mmHg) | GW–OR | 3.9 ± 12.1 | 3.3 ± 14.0 | 0.988 |
| | GW–after intubation | 22.8 ± 15.3 | 8.4 ± 117.2 | 0.447 |
| MAP (mmHg) | GW–OR | 13.4 ± 12.5 | 10.2 ± 13.9 | 0.610 |
| | GW–after intubation | 26.1 ± 14.1 | 26.9 ± 12.1 | 0.491 |
| HR (beats/m) | GW–OR | –4.2 ± 13.8 | –7.3 ± 24.1 | 0.389 |
| | GW–after intubation | 20.8 ± 12.6 | 22.8 ± 16.3 | 0.942 |

Values are expressed as the mean ± standard deviation. Control group: no pretreatment; CES group: CES pretreatment. CES: cranial electrotherapy stimulation; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; GW: general ward; OR: operating room.

and heart rate between the two groups in our study. Nevertheless, the systolic and diastolic blood pressures and heart rate all appeared to be lower in the CES group than in the control group. Furthermore, the changes in diastolic blood pressure after intubation appeared smaller in the CES group, and heart rate in the preoperative holding area also appeared to decrease more in the CES group than the control group (Table 4). Therefore, CES may also be effective in controlling blood pressure, but further studies are needed to confirm this finding.

**Table 5.** Incidence and severity of withdrawal responses to rocuronium injection.

| Withdrawal score | Control group (n = 40) | CES group (n = 40) | P-value |
|---|---|---|---|
| 0 | 12 (30%) | 26 (65%) | 0.017* |
| 1 | 10 (25%) | 4 (10%) | |
| 2 | 7 (17.5%) | 4 (10%) | |
| 3 | 11 (27.5%) | 6 (15%) | |

Values are presented as the number of patients (percentages). Control group: no pretreatment, CES group: CES pretreatment. CES: cranial electrotherapy stimulation.
*$P < 0.05$ compared with the control group.

CES is a non-invasive device that is used to apply an electric current of 10 to 600 μA to the head via electrodes placed on the ear lobes. It is an effective treatment for insomnia, depression, and anxiety. Several studies have evaluated its efficacy, and have reported that CES treatment effects can last for 1 to 2 years following CES application for 5 to 10 days for approximately 30 minutes per day.[5] Although the mechanisms underlying its efficacy remain unclear, microcurrents are known to have a direct effect on the activity of the brain's limbic, hypothalamic, and reticular activating systems.[20] CES treatment decreases the delta and beta waves, and this effect is accompanied by a relative increase in alpha waves on electroencephalography. This increase in alpha waves contributes to a patient's relaxed mood. Accordingly, CES reduces stress and controls the perception and cognition of pain, thereby reducing anxiety and stabilizing the mood. Although this effect is observed even after one CES session, it is prolonged with repeated treatment.[4] In the present study, we tried to enhance this effect by performing CES twice: once on the day before surgery and once on the day of surgery.

Surgery and anesthesia cause stress to the patient, and anxiety before surgery is associated with postoperative hemodynamic changes as well as postoperative pain and complications.[21,22] Therefore, reducing anxiety before surgery is important not only for patient comfort, but also for reducing postoperative pain and complications. Patients do not just experience anxiety directly before their surgeries; anxiety increases from 2 days before surgery and continues until 2 days after surgery.[22] In particular, the degree of anxiety the evening before surgery is as severe as that 1 hour before surgery; hence, controlling anxiety the night before surgery may be an effective treatment strategy.

In the current study, we therefore performed two CES treatments, one on the day before surgery and one on the day of surgery. Our results revealed that patients who underwent CES pretreatment had significantly lower anxiety after entering the operating room compared with controls. Additionally, the number of patients with higher levels of anxiety was lower in the CES group than in the control group. Currently, preoperative patient visits are used to reduce anxiety before surgery, and benzodiazepine drugs are also widely used as medications before anesthesia. Several studies have reported that adjuvant therapies, such as music therapy, massage therapy, and humor therapy, have an effect on reducing preoperative anxiety.[22–24] In addition, anesthesiologists should consider various methods of reducing anxiety before surgery to minimize changes in blood pressure during surgery, especially in patients with hypertension. In particular, patients aged over 70 years may experience severe hemodynamic changes and respiratory depression as a result of anxiolytic drug administration.[25] Caution should therefore be exercised when administering midazolam, which is a commonly used premedication. In these patients, non-invasive CES treatment may be considered.

Rocuronium bromide is an aminosteroid non-depolarizing muscle relaxant. It is currently widely used because it enables rapid onset of relaxation and has a short duration of action.[26] However, rocuronium injection induces burning pain after 10 to 20 s in 50% to 80% of patients.[26,27] This pain has been observed to elicit withdrawal responses in 57% to 84% of patients, including the sudden flexion of the wrist and arm after loss of consciousness under general anesthesia. The withdrawal response is proportional to the intensity of pain. The cause of pain after intravenous rocuronium injection has not yet been elucidated, but Blunk et al.[28] have suggested the direct activation of C-type nociceptive receptors as the possible cause. Several studies have been conducted to reduce rocuronium-induced injection pain and withdrawal response. These studies have suggested administering local anesthetics,[29] opioids, or intravenous anesthetics in advance, or that a large vein is used for rocuronium injection.[30] In the present study, the withdrawal response to rocuronium injection was significantly reduced in the CES group.

The need to control blood pressure in patients with hypertension has been highlighted in many studies. In particular, the control of blood pressure before and after surgery is more difficult in patients with a previous history of hypertension than in normal patients.[10,11] Patients with relatively good preoperative blood pressure control have less changes in blood pressure during surgery. Anxiolytic medications, such as midazolam, are widely used as a premedication for blood pressure control.[14] A previous study reported that, in the CES group, anxiety scores decreased significantly after entering the operating room, and changes in systolic blood pressure and heart rate after entering the operating room were alleviated.[31] The purpose of the current study was to investigate the effects of CES pretreatment on blood pressure when inducing general anesthesia in patients with hypertension. To our knowledge, this is the first study to investigate these effects. There were no significant differences in hemodynamic changes between the two groups, but the systolic and diastolic blood pressures and heart rate appeared lower with CES pretreatment. Furthermore, in the CES group, the changes in diastolic blood pressure immediately after tracheal intubation appeared smaller, and the heart rate before entering the operating room appeared to decrease more compared with the control group. Therefore, CES seems to have a weak effect in controlling blood pressure before and after surgery.

In the present study, CES pretreatment significantly reduced both patient anxiety before surgery and the pain response to rocuronium bromide administration. However, there was no statistically significant evidence to support the hypothesis that pain and anxiety relief can reduce changes in blood pressure during tracheal intubation. Although pain reduction was observed after rocuronium administration following CES pretreatment, differences in stimulation intensity may be the reason for the lack of any decrease in blood pressure or heart rate during intubation. According to the results of Kimura et al.[32] and Yeom et al.[33], the 95% effective dose (ED95) of sevoflurane to inhibit rocuronium-induced withdrawal responses was 3.0 vol%, while the ED95 of sevoflurane for intubation was 8.07 vol%. That is, intubation is a much stronger stimulus for patients than the pain caused by rocuronium injection. In addition, studies comparing the intensity of various noxious stimuli during surgery have revealed that intubation has the greatest intensity.[34] Therefore, the CES pretreatment used in this study was able to reduce pain in response to the rocuronium injection, but may have been insufficient to reduce hemodynamic changes caused by

tracheal intubation. However, despite a lack of statistical significance, blood pressure and heart rate appeared lower in the CES group than in the control group. Therefore, we expect that significant results will be obtained if the CES pre-treatment effect is improved by increasing the pre-treatment frequency or duration. In addition, more meaningful results may be obtained regarding the anxiety-reducing effects of CES pretreatment if studies are conducted in a surgery group with a high anxiety index. Because patient anxiety may vary depending on the surgical site and whether the patient's diagnosis is malignant or not, we conducted our study without any significant differences in these features between the two groups. However, in a study conducted on patients undergoing the same operation, more accurate results may be obtained; this was therefore a limitation of the current study.

## Conclusion

In patients with a previous history of hypertension who underwent surgery under general anesthesia, CES pretreatment was effective in reducing preoperative anxiety and lowering the rocuronium withdrawal response. However, it had no significant effect on blood pressure and heart rate.

### Author contributions

Conceptualization: Kang HW, Kim WY. Data curation: Min WK, Kim JH, Min TJ. Formal analysis: Kang HW, Min WK, Kim WY, Lee YS, Kim JH, Min TJ. Writing - original draft: Kang HW, Kim WY. Writing - review & editing: Kang HW, Kim WY.

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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