Effect of Auricular Acupuncture on Propofol Induction Dose: Could Vagus Nerve and Parasympathetic Stimulation Replace Intravenous Co-Induction Agents?

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ABSTRACT

Objective: Auricular acupuncture, through a combination of several points, can produce sedative and analgesic effects. The aim of this study was to compare the induction dose of propofol required to obtain a loss of response to verbal commands, with and without a preoperative combination of auricular points.

Materials and Methods: This study involved American Society of Anesthesiologists physical status I and II patients, ages 18–65, of either sex, having elective ambulatory surgery (digestive or gynecologic) under general anesthesia. The subjects were allocated to 2 groups: (1) patients treated by auricular acupuncture (group AA), compared with (2) patients not treated by auricular acupuncture (group NA). Propofol injection was initiated in each group, 10 mg, every 5 seconds, in order for the anesthetist to determine the minimum dose until there was a loss of response to verbal commands (the clinical hypnotic endpoint). At this point, the main outcome—the dose of propofol given—was noted.

Results: There were 32 patients in this study (16 in each group). Age, height, weight, and body mass index were similar in the groups ($P \geq 0.05$). The required induction propofol dose was 17.7% lower in group AA than in group NA—a statistically significant difference ($P \leq 0.05$). The mean induction dose indexed to weight was 2.18 mg/kg (range: 1.53–3.13 mg/kg) in group NA and 1.79 mg/kg (range: 1.12–2.11 mg/kg) in group AA. There were no complications.

Conclusions: Auricular acupuncture is a method for stimulating the vagus nerve and parasympathetic nervous system. Preoperative auricular acupuncture enabled reductions of induction doses of propofol for general anesthesia without any clinically important side-effects.

Keywords: auricular acupuncture, vagus nerve stimulation, parasympathetic, propofol, co-induction, general anesthesia

INTRODUCTION

PROPOFOL IS ONE OF THE COMMONLY used hypnotic agents. The recommended intravenous (IV) induction dose is 1.5–2.5 mg/kg, corresponding to the dose producing unconsciousness in 95% of healthy subjects.¹ Unfortunately, the main side-effect of propofol is to decrease systemic vascular resistance, cardiac contractility, and

preload.² This results in a drop in blood pressure (BP) potentially deleterious for elderly or polymorbid patients with compromised cardiovascular status.³ The principle of co-induction is to combine other IV anesthetic agents in order to reduce the dose of propofol necessary for induction via synergism.^{4,5} Thus, the loss of consciousness can be achieved while minimizing cardiovascular adverse effects.⁶

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Acupuncture (body and auricular points) has been used in the Far East for more than 2000 years. Since the early 1970s, acupuncture has been gaining popularity in Western conventional medical settings, and the number of patients willing to allow use of these techniques is increasing.⁷ Several researchers have suggested that acupuncture might have beneficial effects on patients in the perioperative period.^{8–11} A number of studies have shown acupuncture's efficacy for reducing total consumption of opioids and hypnotics during surgery,^{12,13} and also for decreasing postoperative analgesic requirements.^{14,15}

Before surgery, auricular acupuncture (AA) can relieve anxiety naturally present in patients undergoing surgical interventions.¹⁶ However, so far, there is no literature regarding the effect of preoperative AA on the propofol dose required to induce general anesthesia. The current authors hypothesized that using a combination of auricular points, due to their sedative and analgesic effects, would reduce requirements of propofol at induction, compared to no use of acupuncture.

The aim of this study was to compare the induction doses of propofol required to obtain the clinical hypnotic endpoint, such as loss of response to verbal commands, with and without preoperative AA.

MATERIALS AND METHODS

This study protocol was approved by the institutional review board of Mont-Blanc Regional Hospitals, in Sallanches-Chamonix, France. As the current authors had conducted a pilot study, no *a priori* power analysis was performed. Between March and June 2018, a prospective and comparative investigation was conducted on American Society of Anesthesiologists physical status I and II patients, ages 18–65, of either sex, undergoing elective ambulatory surgery (digestive or gynecologic) under general anesthesia. All patients gave informed consent after the nature of the study was explained to them.

Exclusion criteria included patient's refusal; ear wound; history of cardiac, cerebrovascular, respiratory, hepatic, or renal diseases; allergy to propofol; risk of regurgitation, predicted difficult airway; obesity (body mass index [BMI] >30 kg/m²); and pregnancy. Patients premedicated with any sedatives before arrival in the operating room (OR); with histories of toxicomania, alcohol, or opioid abuse; and/or taking sedative or anxiolytic, anticonvulsant, antipsychotic, and antidepressant medications were also not included in the study.

The selected patients were consecutively included in a 1:1 process and allocated to 2 groups: (1) patients treated with auricular acupuncture (group AA); compared to (2) patients not treated with auricular acupuncture (group NA; the control group).

Surgical Procedure

After arrival in the OR, each patient was connected to a Datex Ohmeda S/5 monitor. Electrocardiogram, noninvasive BP, O₂ saturation, and end tidal CO₂ were monitored. Then, a 20-gauge IV cannula was placed in a forearm vein, and 500 mL of saline (0.9%) solution was infused. The patient did not receive IV premedication.

Immediately after the OR preoperative checklists were completed and signed, an experienced anesthetist (B.F.), who was trained in acupuncture, performed all the auricular acupuncture applications on the patients in the AA group, using a combination of 10 points known for their sedative and analgesic effects: (1) Thalamus; (2) Heart; (3) Brainstem; (4) Cervical; (5) Asthma-sedative; (6) *Shen Men*, (7) Point Zero; (8) Solar plexus; (9) Sacrum; and (10) Sympathique (Fig. 1).^{16–19} The needles were kept *in situ* for at least 20 minutes before starting propofol induction, and remained in each AA patient's ear until the end of the surgery (Fig. 2).

In both groups, at the beginning of preoxygenation, to avoid any pain in the arm during the propofol injection, each patient received 20 mg of lignocain. When preoxygenation was achieved, the patient was asked to open his or her eyes. Saline (0.9%) solution was interrupted and a 20 mL syringe

FIG. 1. Ear acupoints map: (0) Point Zero; (1) Solar plexus; (2) Sacrum; (3) *Shen Men*; (4) *Sympathique* point; (5) Thalamus; (6) Asthma-sedative; (7) Brainstem; (8) Cervical; and (9) Heart.

FIG. 2. Patient's ear with needles inserted.

of propofol 10 mg/mL (Fresenius, Fresenius Kabi, France) was connected directly to the IV cannula. Propofol injection was initiated, 10 mg every 5 seconds, enabling the anesthetist (B.F.) to determine the minimum propofol dose until there was a loss of response to verbal commands. When the patient started to close his or her eyelids, a simple command, such as "please, keep your eyes open," was asked. If there was a response such as moving, speaking, or opening the eyelids, the boluses of propofol were continued until there was no response to verbal commands and the patient's eyelids remained closed, corresponding to the study's clinical hypnotic endpoint. At this point, the total amount of propofol given was noted; this was the main outcome of this study.

Then the anesthesia management was pursued as planned for the surgical procedure being performed. A digital data collection form was used for recording the study observations. Adverse events—such as awareness, hemodynamic, or respiratory reactions (hypotension or hypertension, tachycardia, bradycardia, laryngospasm, cough)—were also recorded during the procedure.

Statistical Analysis

This was a proof-of-concept study to demonstrate feasibility and generate data to help design and power a subsequent clinical trial. Therefore, a convenience sample of 32 subjects

FIG. 3. Ear innervation: (1) Auriculotemporal nerve (branch of the mandibular nerve from the trigeminal nerve V-3); (2) concha of the ear supplied by the auricular branches of the facial nerve VII, the glossopharyngeal nerve IX, and the vagus nerve X; and (3) greater auricular nerve (superficial cervical plexus from spinal nerves C-2–C-3).

was enrolled. All continuous variables (i.e., patient's age, weight, BMI, and dose of propofol) were represented as mean $\pm$ standard deviation. Statistical analysis was performed using Statistical Product and Service Solutions (SPSS; version 13). Student's *t*-distribution (unpaired) was used to compare the mean ages, weights, BMIs, and doses of propofol. A *P*-value of <0.05 was considered statistically significant.

RESULTS

In total, 32 patients were included in this study, with 16 subjects in each group. An equal male and female distribution was kept between the 2 groups. Demographic parameters of age, height, weight, BMI were similar ($P \geq 0.05$; Table 1).

The required propofol-induction dose was 17.7% lower in group AA than in group NA, and the difference was statistically significant ($P \leq 0.05$). The mean induction dose, was 150.375 mg (range: 94–213 mg) in group NA, compared to 116.69 mg (range: 90–150 mg) in group AA. The mean induction dose indexed to weight, was 2.18 mg/kg (range: 1.53–3.13 mg/kg) in group NA, and 1.79 mg/kg (range: 1.12–2.11 mg/kg) in group AA (Table 2). No adverse events were

TABLE 1. DEMOGRAPHIC DATA FOR PATIENTS IN EACH GROUP

Characteristics	Group NA mean (SD)	Group AA mean (SD)	P-value
Age (yrs)	48.62 (12.03)	42.44 (12.90)	0.085
Weight (kg)	68.44 (10.61)	67.06 (14.27)	0.38
BMI (kg/m ²)	23.82 (3.16)	22.55 (3.97)	0.16

NA, no acupuncture; AA, auricular acupuncture; SD, standard deviation; yrs, years; BMI, body mass index.

noted in either group. No patient complained of intraoperative awareness. Less than 60 seconds were necessary to insert the 10 needles for each AA patient.

DISCUSSION

The required dose of propofol to obtain a loss of response to verbal commands in the AA group was significantly lower, compared to the NA group, 1.79 mg/kg (range: 1.12–2.11 mg/kg) versus 2.18 mg/kg (range: 1.53–3.13 mg/kg). Many investigators have already extensively studied co-induction with IV anesthetic agents (midazolam, fentanyl, ketamine) administered before general anesthesia, and reported that this approach was effective for decreasing the induction dose of propofol.^{4,5,20} The current study was consistent with these previous results, but the results were achieved by using a nonpharmacologic approach (auricular acupuncture).

Mechanism of Action: Vagus Nerve Stimulation

Multiple theories exist for body acupuncture; however the exact mechanisms of action are unknown at this time. Current explanations of the benefits experienced after acupuncture include Traditional Chinese Medicine and Western Medicine (WM) concepts.^{21,22} Acupuncture reduces central hyperexcitability, possibly by the central release of endorphins, so acupuncture could be an effective method of preemptive analgesia. Thus, during surgery and in intensive care units, acupuncture could be used to decrease the need for total doses of hypnotics, including propofol.¹⁰

Auricular acupuncture, or auriculotherapy, is defined as a form of acupuncture in which needles are placed in various positions of the external ear to affect the person. Proponents of this kind of acupuncture postulate that there is a correlation

TABLE 2. MEAN INDUCTION DOSE OF PROPOFOL IN TOTAL & INDEXED TO WEIGHT IN EACH GROUP

Doses	Group NA Mean (SD)	Group AA Mean (SD)	P-value
Induction dose: Total (mg)	150.375 (29.91)	116.69 (15.53)	0.00019
Induction dose: Indexed to weight (mg/kg)	2.18 (0.37)	1.79 (0.36)	0.00278

NA, no acupuncture; AA, auricular acupuncture; SD, standard deviation.

between the whole body and the surface of the external ear. In other words, an external ear somatotopy might exist, so that treatments performed upon the ear will have effects reflected on the corresponding body parts.¹⁷ No anatomical pathways exist to connect inner organs directly with the ear.¹⁹ Auriculotherapy is used in WM to address a wide range of conditions; examples include drug dependence, anxiety, and pain. In the perioperative period, auricular acupuncture could alleviate perioperative anxiety, and reduce anesthetic requirements during general anesthesia.^{16,23,24}

The auricle receives sensory innervation, mainly from the superficial cervical plexus (the greater auricular nerve, branching from spinal nerves C-2–C-3), and the trigeminal nerve V-3 (the auriculotemporal nerve, a branch of the mandibular nerve). The concha of the ear is supplied by the auricular branches of the vagus nerve X, the facial nerve VII, and the glossopharyngeal nerve IX (Fig. 3). The central parts of the neurons constituting the auricular branch of the vagal nerve are situated in the superior ganglion of the vagal nerve and nucleus tractus solitarius. The facial nerve and the glossopharyngeal nerve are also partially composed of parasympathetic neurons.^{25,26} Functionally, stimulation of the concha induces a significant increase in parasympathetic activity.^{27,28}

Thus, due to sensitive innervation of the concha by the vagus nerve, auricular acupuncture is a method of stimulating that nerve and subsequently the parasympathetic nervous system. Recently, many researchers have described stimulation of the vagus nerve with different methods and potential new ways of treatment for various conditions (refractory epilepsy, depression, fear and anxiety, pain, and inflammatory disorders of the gastrointestinal tract).^{29–33} The vagus nerve is the longest nerve of the body and is a major component of the parasympathetic nervous system. The parasympathetic and sympathetic nervous systems comprise the autonomic nervous system (ANS). There is, classically, an equilibrium between the sympathetic and parasympathetic nervous systems that is responsible for the maintenance of homeostasis. An imbalance of the ANS occurs in various pathologic conditions.²⁷ Stimulating the vagus nerve before surgery could reverse the preoperative anxiety naturally present in patients arriving in ORs. Therefore, the current study suggested that preoperative auricular acupuncture—through stimulation of the vagus nerve and subsequently the parasympathetic nervous system—by reducing anxiety, can help reduce the propofol induction dose needed to achieve general anesthesia.

Heart Rate Variability and Cardiac Output

A variety of factors affect the dose of propofol required to achieve the needed hypnotic state for induction of anesthesia. These include the patient's age, sex, and body weight; the rate of infusion; co-administered drugs; and the patient's anxiety.^{34,35} These phenomena can be partially explained by their

effects on the pharmacokinetics that modulate the concentration of propofol needed. It has been reported that cardiac output is a determinant of the initial plasmatic concentration of propofol after the administration of a short IV infusion.³⁴ Thus, the cardiac output at the induction of anesthesia is a major determinant of the hypnotic dose of propofol. The cardiac output at the induction of anesthesia varies among patients because it is regulated by numerous factors.³⁶ Auricular acupuncture, by stimulating the vagus nerve, would modulate the ANS by increasing the parasympathetic tone.³⁷ Thereby, this probably would prevent preoperative anxiety and induce positive effects on the patient's heart rate variability (HRV). Thus, auricular acupuncture might also regulate patient cardiac output and heart function indirectly before induction of general anesthesia, and thus diminish the interaction with the propofol-induction dose.

Application to the Perioperative Period

Accumulated evidence from clinical trials and updated reviews suggest that the role of acupuncture in perioperative medicine extends beyond the classical scope of anesthesia and has been underestimated.¹⁰ Acupuncture improves quality of perioperative care and reduces associated complications. Perioperative acupuncture is effective for reducing preoperative anxiety, as well as postoperative pain, nausea, and vomiting. These beneficial effects make acupuncture a promising approach to perioperative management, especially with respect to facilitating surgery recovery in specific surgical populations, such as elderly patients and polymorbid patients.^{10,11} Because the current authors hope to develop a system that can be incorporated into routine practice by anesthetists,³⁸ this article described an auricular acupuncture method that is relatively easy to use and that can be learned without special training. Body acupuncture would require a high level of expertise by the acupuncture practitioner, whereas auricular acupuncture seems to be easier to learn and apply.

Projection

This preliminary study focused on only one outcome—induction dose of propofol required to obtain the clinical hypnotic endpoint represented by a loss of response to verbal commands. Unfortunately, the study was not double-blinded, as the patients and anesthesiologist responsible for assessing the patients were not blinded to the auricular acupuncture.

Other outcomes should be observed and compared with group controls, to assess the potential global benefit of auricular acupuncture in the perioperative period and in the clinical setting. These outcomes could include hemodynamic variables (HRV, arterial pressure, cardiac output, hypertensive response to intubation), changes in O₂ saturation and bispectral index, opioid consumption, postoperative pain, nausea and vomiting, awareness, and rapid recovery. Healthcare expenditures consumption, hospital lengths of stay, and incidence of adverse events will also

need to be considered when assessing whether or not this nonpharmacologic technique can provide value in the management of patients. In addition, other ear points should be investigated to determine optimal ear-point combinations for co-induction; these points could be specific to patient types (sex, obese, hypertensive, etc.).

CONCLUSIONS

Preoperative auricular acupuncture, through vagus-nerve stimulation, helped reduce propofol-dose induction for general anesthesia without any clinically important side-effects. This is the first time that this result has been described in the literature.

Vagus-nerve and parasympathetic nervous system stimulation by auricular acupuncture is a promising intervention in the perioperative period. However, further, rigorously designed clinical trials are required to prove that auricular acupuncture is a safe, easy-to-learn, clinically feasible effective technique that should be promoted in the anesthesia field. The current authors believe that auricular acupuncture has the potential to revolutionize perioperative management of patients completely, as conventional medications have been used for the past century.

ACKNOWLEDGMENTS

The authors would like to acknowledge Mrs. S. Thomas for her contribution by rereading the manuscript for this article.

AUTHOR DISCLOSURE STATEMENT

No financial conflicts of interest exist.

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