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The Timing of Acupuncture Stimulation Does Not Influence Anesthetic Requirement

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Abstract

Studies suggest that acupuncture is more effective when induced before induction of general anesthesia than afterwards. We tested the hypothesis that electro-acupuncture initiated 30 minutes before induction reduces anesthetic requirement more than acupuncture initiated after induction. Seven volunteers were each anesthetized with desflurane on 3 study days. Needles were inserted percutaneously at 4 acupuncture points thought to produce analgesia in the upper abdominal area and provide generalized sedative and analgesic effects: Zusanli (St36), Sanyinjiao (Sp6), Liangqiu (St34), and Hegu (LI4). Needles were stimulated at 2-Hz and 10-Hz, with frequencies alternating at two-second intervals. On Preinduction day, electro-acupuncture was started 30 minutes before induction of anesthesia and maintained throughout the study. On At-induction day, needles were positioned before induction of anesthesia, but electro-acupuncture stimulation was not initiated until after induction. On Control day, electrodes were positioned near the acupoints, but needles were not inserted. Noxious electrical stimulation was administered *via* 25-G needles on the upper abdomen (70 mA, 100 Hz, 10 seconds). Desflurane concentration was increased 0.5% when movement occurred and decreased 0.5% when it did not. These up-and-down sequences continued until volunteers crossed from movement to no-movement 4 times. The P₅₀ of logistic regression identified desflurane requirement. Desflurane requirement was similar on the Control (5.2±0.6%, mean±SD), Preinduction (5.0±0.8%), and At-induction (4.7±0.3%, *P*=0.125) days. This type of acupuncture is thus unlikely to facilitate general anesthesia or decrease the need for anesthetic drugs.

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Implications: Electro-stimulation of the Zusanli (St36), Sanyinjiao (Sp6), Liangqiu (St34), and Hegu (LI4) acupuncture points, whether initiated 30 minutes before or at induction of anesthesia, did not reduce desflurane requirements in healthy volunteers. This type of acupuncture is thus unlikely to facilitate general anesthesia or decrease the need for anesthetic drugs.

Keywords

Anesthetic technique: Acupuncture, Electro-acupuncture; Potency: anesthesia requirement; Anesthetics, volatile: desflurane

Introduction

Acupuncture may alleviate postoperative nausea and vomiting (1) improve postoperative analgesia (2), and reduce intraoperative opioid requirement (3). Three studies have evaluated the use of acupuncture to reduce volatile anesthetic requirements. The first used electro-acupuncture of a single auricular acupoint and identified a statistically significant 11% reduction in anesthetic requirement (4). The second used needles at four auricular acupoints and identified a statistically significant 8% reduction in anesthetic requirement (5). The third study, which stimulated three acupoints on the leg, failed to reduce anesthetic requirement (6). In each of the three studies, (4-6) acupuncture was initiated after induction of general anesthesia to maintain complete double blinding. (These studies were arguably the first fully double-blinded acupuncture trials.) Nonetheless, aspects of this design might have obscured the potential influence of acupuncture on anesthetic requirement.

De-Qi is a typical sensation that is associated with proper acupuncture needle positioning. Patients variously report it as a soreness, numbness, warmth, heaviness, or distention around the area where the needle is inserted. *De-Qi* appears to be a slow pain sensation conducted by non-myelinated c fibers. Many practitioners consider this sensation to be crucial in achieving the effect of acupuncture (7). Because the *De-Qi* sensation cannot be elicited during anesthesia, the first limitation of previous studies of acupuncture and anesthetic requirement is that the needles may have been suboptimally positioned.

The endorphin hypothesis suggests that acupuncture activates type II muscle afferents that send signals to sites in the brain to release endorphins (8). These endorphins then suppress pain signals in the dorsal horn of the spinal cord. Emotional aspects of pain are also suppressed by endorphins acting in the limbic system. General anesthesia can block or attenuate these pathways (9,10), thus reducing the efficacy of subsequent acupuncture. There is considerable evidence to support this theory. For example, stimulation of the P6 acupuncture point reduces the risk of postoperative nausea and vomiting (11-13), except when acupuncture is started after induction of anesthesia (14-16).

The second limitation of previous studies of acupuncture and anesthetic requirement is that pre-existing general anesthesia may itself reduce the efficacy of acupuncture. Initiation of acupuncture after induction of general anesthesia has the advantage of permitting fully double-blinded trials. However, available evidence suggests that the efficacy of acupuncture — whether for analgesia or antiemetic effect — may be diminished when it is initiated after induction of general anesthesia. We, therefore, tested the hypothesis that acupuncture started 30 minutes before induction of anesthesia reduces anesthetic requirement more than acupuncture started at induction of anesthesia. We chose 30 minutes before induction because it takes ≈20 minutes after needle insertion to achieve maximum acupuncture analgesia (17).

Methods

With approval from the Human Studies Committee at the University of Louisville and written informed consent, we recruited 13 healthy volunteers aged 18-35 years. Exclusion criteria included a history of drug addiction or use of drugs other than oral contraceptives, or a history of chronic pain. Menstrual cycle was not controlled because cycle status has little or no influence on perception of electrical pain (18).

All volunteers underwent a needling test before they were included in the study with the aim of excluding potential subjects who were resistant to acupuncture and to familiarize the volunteers with the acupuncture procedure and the resulting De-Qi sensation.

Protocol

The volunteers fasted and refrained from smoking for at least eight hours before arriving at the laboratory. No premedication was given. The volunteers who completed the trial participated on 3 study days, separated at least 72 hours (8 ± 5 days). Each set of studies began at the same time of day because circadian rhythms can influence anesthetic requirement (19), as well as acupuncture efficacy (20).

On each study day, anesthesia was induced with approximately 3.5 mg/kg IV propofol. A laryngeal mask airway (The Laryngeal Mask Company Limited, Henley-on-Thames, UK) or perilaryngeal airway (*CobraPLA*, Engineered Medical Systems, Indianapolis, IN) was inserted. Ventilation was assisted until spontaneous breathing was re-established. Anesthesia was initially maintained with desflurane (5.0 volume-percent) in 80% oxygen and 20% air. Before induction of anesthesia on the initial study day, volunteers were randomly assigned to 30 minutes of electro-acupuncture before anesthesia induction (Pre-induction day), electro-acupuncture at anesthesia induction acupuncture (At-induction day), or no treatment (Control day). We used a crossover study design: each volunteer was thus given alternative treatments on subsequent study days.

We stimulated the Zusanli (St36), Sanyinjiao (Sp6), Liangqiu (St34), and Hegu (LI4) points. Zusanli is approximately 6 cm below the lower margin of the patella and 2 cm lateral to the tibia. Sanyinjiao (Sp6) is about 7 cm above the highest portion of the medial malleolus at the posterior border of tibia. Liangqiu (St34) is about 4.5 cm above superior-lateral border of the patella. Hegu (LI4) is in the middle of the second metacarpal bone, on the prominence of the first inner ossei dorsales, slightly towards the index finger (21). These points are thought to produce a generalized sedative and analgesic effect and to be effective for surgical procedures on the upper abdomen (22,23). Another advantage of these four points is that they are safe to needle since they are not adjacent to critical structures.

An acupuncturist (G.C.) with 15 years experience inserted AcuMaster acupuncture needles, which have a diameter of 0.22 mm and are 50 mm long (Helio Medical Supplies, Inc. USA). The needles were connected to an IC-4107 stimulator (ITO, Ltd. Tokyo, Japan). The stimulating frequency was set to 2 Hz and 10 Hz, with the frequencies being alternated at 2-second intervals (24). Pulse shape was bi-polar and asymmetric. The appropriate intensity was determined during the needling test before the first randomized study day. Stimulation intensity was set at the highest level that was well tolerated by the volunteers without provoking muscular twitching that might have unblinded the study. This stimulation intensity was then maintained for the duration of the study. The average stimulator output was 8 V at a current of 8 mA.

The acupuncture needles were inserted percutaneously (on appropriate days), and an unblinded investigator connected the electrodes. On the Pre-induction day, needles were inserted in appropriate points and the De-Qi sensation confirmed; electro-acupuncture stimulation was then initiated 30 minutes before anesthetic induction and maintained throughout the study. On the At-induction day, needles were inserted immediately before induction of general anesthesia, again eliciting the De-Qi sensation. But in this case, electro-stimulation of the acupuncture points was initiated only after induction of anesthesia. On the Control days, electrodes were insulated and taped to the skin without acupuncture needles having been inserted at all.

The stimulator was activated on all three study days to maintain blinding. Similarly, the acupuncture-insertion sites were kept covered during the entire procedure. Consequently, the investigators evaluating anesthetic requirement could not determine the treatment day. Volunteers were told that we were comparing the effectiveness of acupuncture depending on time of insertion and believed that we were using acupuncture on all 3 study days. The actual nature of the study was subsequently explained to each volunteer.

Anesthetic requirement was defined as the average partial pressure of desflurane required to prevent movement in response to noxious electrical stimulation. Electrical stimulation was *via* two 25-g sterile needles that were inserted intradermally into the upper abdomen. A bilateral 70 mA, 100-Hz tetanic electrical current, maintained for 10 seconds, provided the noxious stimulus. A tetanic stimulus even 20% of this intensity is unbearable to unanesthetized subjects. To prevent desensitization at the insertion site, the electrodes were moved by one cm after each stimulation. Stimulation was started one hour after anesthetic induction, to allow sufficient time for the effects of propofol to dissipate.

We used the “Dixon up-and-down” method, which is the standard paradigm for evaluating anesthetic depth (25). The initial end-tidal desflurane concentration (5.0 volume percent) was maintained for 10 minutes to assure alveolar-brain equilibration. If the subject moved in response to noxious electrical stimulation, the anesthetic concentration was subsequently increased by 0.5 volume percent. In contrast, the desflurane concentration was reduced by the same amount when the subject did not move. Purposeful movement of one or more extremities within one minute of stimulation defined a positive response to noxious electrical stimulation. Grimacing and head movement were not considered purposeful responses. The new steady end-tidal desflurane partial pressure was then maintained for 10 minutes, and the process repeated. This up-and-down sequence was continued until the subject “crossed-over” from movement to nonmovement 4 times.

Measurements

We recorded morphometric and demographic characteristics of the volunteers. End-tidal desflurane and carbon dioxide (CO₂) partial pressures were measured with an Ohmeda Rascal monitor (Ohmeda Inc, Salt Lake City, UT) that was calibrated daily. The resolution of this device is 0.1 percent desflurane. End-tidal concentrations of volatile anesthetics and carbon dioxide are virtually identical to alveolar concentrations (26).

All standard anesthetic safety values were monitored including heart rate and blood pressure, which were determined oscillometrically. The bispectrum of the electroencephalogram (BIS) was recorded from Zipprep™ electrodes (Aspect Medical Systems, Inc., Newton, MA). One active electrode was positioned 4 cm above the nasion, the other was situated midway between the preauricular point and outer malar bone of the right eye; the ground electrode was positioned on the temple just above the right eye. The electrodes were depressed as necessary to maintain impedance <5000 Ohms. Depth of hypnosis, quantified by BIS (revision 3.3), was displayed continuously on an A1050 BIS Monitoring System. A pulse oximeter continuously determined arterial oxygen saturation. Core body temperature was measured from the tympanic membrane using Mon-a-therm thermocouples (Tyco-Mallinckrodt, Inc. St. Louis, MO). Values were recorded at five-minute intervals and 60 seconds after each noxious electrical stimulation.

Data Analysis

All desflurane concentrations, as a function of movement, were entered into a logistic regression for each person and each study day. The model was used to determine the partial pressure of desflurane that produced a 50 percent likelihood of movement in response to noxious stimulation in each volunteer on each study day (P₅₀). Values on the two acupuncture

days and the Control day were compared with repeated-measures ANOVA. Results are presented as means $\pm$ SDs; $P < 0.05$ was considered statistically significant. Physiologic responses to noxious stimulation on each of the three study days were similarly compared with repeated-measures ANOVA, as were potential confounding factors.

Results

Eight women and 5 men were initially enrolled in the trial. Three women and 4 men completed all 3 study days; data analysis was restricted these 7 volunteers. These volunteers were 23 ± 4 (mean $\pm$ SD) years old, weighed 72.5 ± 15 kg, and were 170 ± 9 cm tall.

Total duration of the study was 4 ± 0.5 hours on the Pre-Induction day, 4.0 ± 1.0 hours on the At-induction day, and 3.7 ± 1.0 hours on the Control day ($P = 0.58$). Potential confounding factors were similar on the acupuncture and Control study days (Table 1).

Desflurane requirement on the Pre-induction acupuncture day was $5.0 \pm 0.8\%$; it was $4.7 \pm 0.3\%$ on the At-induction day and $5.2 \pm 0.6\%$ on the Control day ($P = 0.12$). Figure 1 shows within subject changes for the Pre-induction day compared to Control day. The average difference in MAC between these two days was $0.2 \pm 0.6\%$. Figure 2 shows within subject changes for the At-induction day compared to the Control day. The average difference between these two days was $0.5 \pm 0.4\%$. The P_{50} values were normally distributed. Using a repeated measures ANOVA to compare the three study days, these data provided an 80% power to detect a difference of 0.7 volume-percent among the days with $\alpha = 0.05$.

Neither type of acupuncture influenced the physiological response to noxious stimulation. Increases in mean arterial pressure, heart rate, and bispectrum of the electroencephalogram (BIS) one minute after noxious stimulation were similar on each of the 3 study days (Table 2).

Discussion

The primary mechanism of acupuncture analgesia is probably endogenous opioid release (8). Activation of μ opioid receptors markedly reduces the amount of volatile anesthetic needed to prevent movement in response to noxious stimulation (27). However, acupuncture also activates several other mechanisms, only a few of which have been characterized (28,29). For example, electro-acupuncture analgesia acts at three distinct anatomic levels: 1) In the spinal cord, it releases endorphin (dynorphin) to give segmental or localized pain relief (30). 2) In the midbrain and brain stem, it induces a regional analgesia through the enkephalin-dorsolateral funiculus (DLF)-serotonin system (31). And 3) in the hypothalamus and the pituitary, it produces a generalized increase in pain threshold mediated by the release of endorphins and adrenocorticotrophic hormone (ACTH) into the systemic circulation. ACTH stimulates the release of cortisol, which reduces inflammation (32). Both IV induction drugs and volatile anesthetics also influence each of these structures, mainly by suppressing them or disrupting their physiological integrity (9,10). It was thus reasonable to anticipate clinically important interactions between acupuncture and anesthetic requirement.

We nonetheless failed to identify statistically significant differences among any of the study days, not even finding a difference between the Preinduction and Control days. Our result is inconsistent with our hypothesis that initiating acupuncture 30 minutes before induction of anesthesia augments the effect of acupuncture and thus reduces anesthetic requirement.

Our observation that acupuncture did not reduce anesthetic requirement is similar to one previous study (6), whereas 2 others detected statistically significant 8 to 11% reductions in anesthetic requirement (4,5). The hope in each of these studies was to identify a combination of acupoints and stimulation methods that would provide a clinically important reduction in

volatile anesthetic requirement. After 4 studies, though, we are forced to conclude that common types of acupuncture do not reduce anesthetic needs by clinically important amounts. Similar results were found in recent randomized controlled study on surgical patients (33). These data suggest that the analgesic effect of acupuncture is comparatively weak and largely overshadowed by the effects of volatile anesthetics. Acupuncture in the perioperative setting might thus better be directed at providing postoperative analgesia (2) and ameliorating nausea and vomiting (1), both of which are better documented effects.

The conventional measure of volatile anesthetic potency is the minimum alveolar concentration (MAC) (34), which can most efficiently be determined by using the Dixon “up-and-down” method (25). MAC for a population is conventionally defined as the volatile anesthetic concentration preventing movement in response to surgical skin incision. An analogous concentration can be determined in individuals using repeated noxious electrical stimulation (35). The resulting partial pressures are uniformly lower than obtained with skin incision (36), but electrical stimulation nonetheless provides a reasonable measure of anesthetic need and has been used in previous studies (37).

We used this technique in the current study because it has the advantage of allowing crossover study designs that are especially sensitive for detecting treatment-induced changes in anesthetic requirement. Consequently, we had an 80% power to detect differences among the groups of only 0.7 volume-percent desflurane.

One might argue that the acupoints we used in our volunteers were suboptimal. However, the points we chose were located on the Stomach, Large Intestine, and Spleen meridians; all are closely related to each other and all 4 points are routinely used for pain in the epigastric area (where we positioned our noxious stimulation) and are recommended for abdominal surgery (22).

In conclusion, acupuncture initiated 30 minutes before induction of general anesthesia was no more effective than acupuncture initiated immediately before induction of general anesthesia. More importantly, neither was more effective than no treatment whatsoever. This result is consistent with three previous studies in which acupuncture induced after induction of general anesthesia produced little or no reduction in anesthetic requirement. We thus conclude that the effects of volatile anesthetics overshadow the analgesic effect of acupuncture. Consequently, acupuncture in the perioperative setting would more appropriately be directed at better-documented treatments including postoperative analgesia and ameliorating nausea and vomiting.

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Fig. 1.

Circles show the individual concentrations of desflurane required to prevent movement in response to intense electrical stimulation. Electro-acupuncture was started 30 minutes before induction of general anesthesia on the Preinduction day and avoided on Control day. Squares show the mean $\pm$ SD concentrations for each treatment; anesthetic requirements did not differ significantly.

Fig. 2.

Circles show the individual concentrations of desflurane required to prevent movement in response to intense electrical stimulation. Electro-acupuncture was started with induction of general anesthesia on the At-induction day and avoided on Control day. Squares show the mean $\pm$ SD concentrations for each treatment; anesthetic requirements did not differ significantly

Table 1.

Potential Confounding Factors.

	Control	Preinduction day	At-induction day	P
Mean arterial blood pressure (mmHg)	87 ± 13	85 ± 14	86 ± 13	0.685
Heart rate (bpm)	83 ± 17	81 ± 15	82 ± 21	0.612
Core temperature (°C)	36.4 ± 0.4	36.3 ± 0.4	36.2 ± 0.4	0.169
BIS	46 ± 16	45 ± 16	48 ± 17	0.281

BIS = Bispectrum of the electroencephalogram

Table 2.

Physiologic Response to Noxious Stimulation.

	Control	Preinduction day	At-induction day	P
Increase in mean arterial blood pressure (mmHg)	15.8 ± 12.0	13.3 ± 14.6	17.3 ± 11.2	0.148
Increase in Heart rate (bpm)	24 ± 12	23 ± 13	25 ± 13	0.394
Increase in BIS	9 ± 16	6 ± 14	7 ± 18	0.502

BIS = Bispectrum of the electroencephalogram. The increase in mean arterial blood pressure, heart rate, and BIS during the first minute after noxious electrical stimulation.