Electroacupuncture to reduce sedative and analgesic demands during endoscopic ultrasonography: a prospective, randomised, double-blind, sham-controlled study (abridged secondary publication)

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KEY MESSAGES

1. Electroacupuncture reduced sedative and analgesic demands, improved patient experience, and was associated with low risk of adverse events during endoscopic ultrasonography.
2. Electroacupuncture could reduce the use of propofol and the need of the presence of an anaesthesiologist during endoscopic ultrasonography. It could avoid the potential adverse effects related to propofol usage and improve the safety of sedation and analgesia.
3. The recovery time from anaesthesia could be significantly reduced.

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Introduction

The role of electroacupuncture in reducing sedative and analgesic requirements during endoscopy is uncertain. The aim of the current study is to investigate the efficacy of electroacupuncture in reducing procedure-related pain and discomfort, and the consumption of sedatives and analgesics during endoscopic ultrasonography (EUS). We hypothesised that electroacupuncture could reduce procedure-related pain and discomfort as well as consumption of sedatives and analgesics during EUS.

Methods

This double-blind randomised controlled study was conducted between March 2014 and July 2016, in accordance with the Declaration of Helsinki and the International Conference on Harmonization good clinical practice guidelines. Informed consent was obtained from all patients. Consecutive patients scheduled for diagnostic EUS for the first instance were recruited and assigned at random to the electroacupuncture group or sham-electroacupuncture group. The randomisation was stratified according to whether the patients recevied radial and linear EUS. Recruited patients, endoscopists, anaesthetists, endoscopy nurses, and the assessor were blinded to the type of intervention.

Patients were instructed by an anaesthetist on the use of the patient-controlled analgesia (PCA) when they experienced any discomfort during EUS. PCA was a mixture of propofol (200 mg in 20 mL) and alfentanil (0.5 mg in 1 mL) delivered via a 25-mL syringe pump to the patient's right arm. Each push of the button delivered 0.5 mL bolus of 4.8 mg propofol and 12 μg alfentanil. No loading dose was used, and the lockout time was set to 1 minute. 2 L/min of nasal oxygen was given to all patients. Their pulse rate and oxygen saturation were monitored continuously, and blood pressure was recorded every 5 minutes throughout the procedure and during the recovery period. An anaesthetist was present to monitor for any adverse events. After EUS, the syringe pumps were removed, and an endoscopy nurse monitored the patients closely until full recovery.

Patients were kept nil per oral for 6 hours prior to EUS. EUS was performed by two physicians who have performed >500 EUS procedures before. Conventional radial or linear echoendoscopes (GF-UE260-AL5, UM 2R/3R, GF-UCT260; Olympus Medical, Tokyo, Japan) were used. Patients were then subjected to 45 minutes of electroacupuncture or sham procedure before EUS and throughout the whole procedure. After EUS, the acupuncture needles were removed and discarded.

Electroacupuncture was at acupoints relevant to the treatment of abdominal pain and anxiety, including *Hegu* (large intestine meridian, LI-4),

Neiguan (pericardium meridian, PC-6), and *Zusanli* (stomach meridian, ST-36) [Fig]. These acupoints are most relevant to the organs in concern.[1] Sterile acupuncture needles (Hwato needles 0.22 × 25 mm, Suzhou Medical Appliance Factory, China) were inserted into the acupoints to a depth of 15 mm, via a sterile plastic tube stabilised by a foam block (Fig).[2,3] Regular electric stimulation was applied to the needles with the ES-160 6-channel programmable electroacupuncture device (Ito Company Limited, Tokyo, Japan). A stimulation protocol of frequency 2 Hz, pulse width 200 μs, and stimulation intensity "short of discomfort" was used. This setting was shown to be effective in relieving pain to the organs in concern.[2]

For sham procedure, sterile blunt-tip needles (self-prepared from Hwato needles 0.22 × 13 mm, Suzhou Medical Appliance Factory, China) were placed 15 mm from the acupoints. The needles were first inserted through a sterile plastic tube mounted on a foam block, and then pressed on the skin. The compression provided by the foam block gave a false impression that the needles were penetrating the skin, thus providing a sham acupuncture effect.[2,3] Electrical stimulation was simulated by connecting the needle to the incorrect output socket of the electroacupuncture device, resulting in absence of electrical current flow. Patients were also informed that the stimulation frequency was not perceivable by human and they would not be able to sense the stimulation.

The primary outcome was the dosage of PCA consumed. The secondary outcomes included pain, patient satisfaction, endoscopist satisfaction, patient willingness to repeat the procedure, total procedure time, episodes of hypotension (defined as systolic blood pressure of <90 mmHg), and desaturation (defined as SaO_2 of <90%).

In a study comparing the efficacy of electroacupuncture and sham procedure in reducing discomfort associated with colonoscopy, the mean maximal tolerable pressure/pain threshold was significantly higher in the electroacupuncture group (>20% difference).[2] Assuming that electroacupuncture during EUS reduced the consumption of propofol by 30% from 1 mg/kg to 0.7 mg/kg (standard deviation, 0.6 mg/kg), a sample size of 64 patients in each group is required to yield a power of 80% with a significance level of 0.05. The two groups were compared using Student's *t* test for parametric data and Mann-Whitney *U* test for non-parametric data. Categorical data were compared with Pearson Chi-squared test or Fisher's exact test. The pre- and intra-procedural scores were compared using Wilcoxon signed-rank test. The predictors to PCA consumption were analysed by multiple linear regression. A two-sided P value of <0.05 was considered statistically significant.

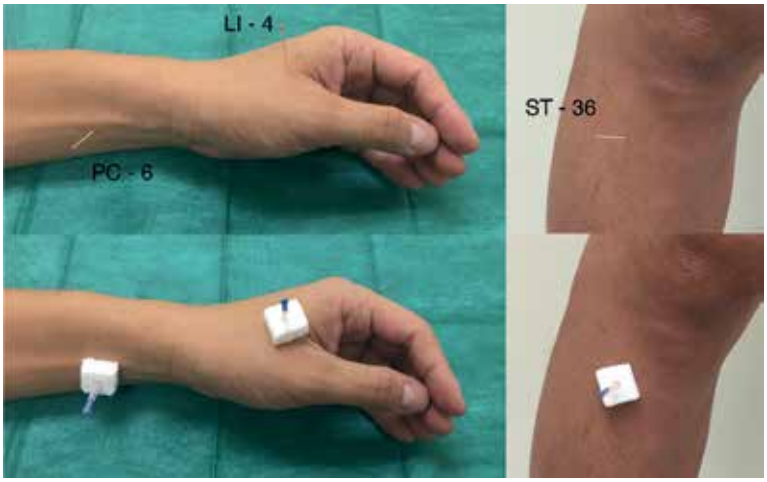

FIG. Acupoints of *Hegu* (LI-4) for large intestine meridian, *Neiguan* (PC-6) for pericardium meridian, and *Zusanli* (ST-36) for stomach meridian. Acupuncture needles inserted into the acupoints and stabilised by foam boxes. *Hegu* (LI-4) is located on the dorsum of the hand, between the 1st and 2nd metacarpal bones. *Neiguan* (PC-6) is located on the palmar aspect of the forearm, two cun above the transverse crease of the wrist between the flexor carpi radialis and palmaris longus tendons. *Zusanli* (ST-36) is located on the anterior aspect of the leg, three cun below the kneecap and one finger-breath from the anterior crest of the tibia. One cun is the distance between the interphalangeal creases of the subject's middle finger.

Results

A total of 128 patients were recruited. The two groups were comparable in terms of demographics, indications of procedure, and types of endoscopes used. Patients in the electroacupuncture group had significantly fewer demands for PCA (4.06±4.81 vs 28.27±30.43, P<0.001), fewer successful demands (2.73±2.30 vs 10.39±7.70, P<0.001), lower total dose of propofol (0.23±0.21 mg/kg vs 0.83±0.62 mg/kg, P<0.001), and lower total dose of alfentanil (0.58±0.53 mg/kg vs 2.07±1.54 mg/kg, P<0.001), compared with the sham procedure group (Table 1). Patients in the electroacupuncture group also had significantly lower procedural pain score (2.5±2.0 vs 6.1±2.9, P<0.001), lower anxiety score (2.4±2.5 vs 4.8±3.2, P<0.001), higher satisfaction score (8.7±1.4 vs 6.9±2.4, P<0.001), and they were more willing to repeat the procedure if required (P<0.001), compared with the sham procedure group. The endoscopist satisfaction score was also higher for patients in the electroacupuncture group (8.1±1.9 vs 7.1±2.7, P=0.003). The procedural time was shorter in the electroacupuncture group than in the sham procedure group (895.6±559.5 s vs 1265±841.3 s, P=0.007). No adverse events were observed in either group.

When comparing the pre-procedural and intra-procedural abdominal pain scores, both groups

TABLE 1. Comparison of outcomes between electroacupuncture and sham procedure groups.

	Electro-acupuncture (n=64)*	Sham procedure (n=64)*	P value
Highest systolic blood pressure, mmHg	156.52±26.57	157.14±30.56	0.819
Highest diastolic blood pressure, mmHg	83.98±17.10	90.20±21.81	0.083
Highest pulse rate, bpm	89.64±17.30	92.14±17.79	0.590
Total No. of demands for patient-controlled analgesia	4.06±4.81	28.27±30.43	<0.001
No. of successful patient-controlled analgesia demands	2.73±2.30	10.39±7.70	<0.001
Total dose of propofol consumed, mg/kg	0.23±0.21	0.83±0.62	<0.001
Total dose of alfentanil consumed, mg/kg	0.58±0.53	2.07±1.54	<0.001
Procedural pain score	2.5±2.0	6.1±2.9	<0.001
Procedural anxiety score	2.4±2.5	4.8±3.2	<0.001
Satisfaction score	8.7±1.4	6.9±2.4	<0.001
Patient willingness to repeat the procedure (yes/no)	32/32	12/52	<0.001
Endoscopists' satisfaction score	8.4±1.9	7.1±2.7	0.003
Procedural time, s	895.6±559.5	1265.4±941.3	0.007

* Data are presented as mean ± standard deviation unless otherwise specified

TABLE 2. Predictors for increased patient-controlled analgesia demands in multivariate linear regression analysis.

Parameter	Relative risk (95% confidence interval)	P value
Age	-0.65 (-0.14-0.11)	0.095
Male sex	1.17 (-1.03-0.67)	0.159
Body mass index	-0.50 (-0.27-0.17)	0.658
Type of echoendoscope	-0.05 (-1.08-0.98)	0.927
The need of fine needle aspiration cytology	-0.18 (-1.03-0.67)	0.679
Sham procedure group	5.83 (4.18-7.49)	<0.001
Procedural time	0.005 (0.004-0.006)	<0.001

had significantly more pain during the procedure but more so in the sham procedure group. The anxiety scores reduced significantly during the procedure in the electroacupuncture group (P<0.001), whereas the pre- and intra-procedural anxiety scores remained similar in the sham procedure group (P=0.257).

The predictors to PCA demands were analysed by linear regression analysis. Being in the sham procedure group and the procedural time were significant predictors to increased PCA demands (all P<0.001, Table 2).

Discussion

EUS is technically demanding and time-consuming. Electroacupuncture as a means to reduce analgesia and sedation during EUS was shown to be associated with fewer PCA demands, lower pain and anxiety scores, shorter procedural time, higher patient and endoscopist satisfaction scores, and more willingness to repeat the procedure. Electroacupuncture and the procedural time were significant predictors to increased PCA demands.

Sedation and analgesia for advanced endoscopic procedures is commonly achieved by the use of benzodiazepines and opioids.[4] In patients that require deep sedation, propofol is frequently used. However, the use of propofol can cause negative cardiac inotropy and respiratory depression. Furthermore, the drug has no reversal agent. Thus, trained personnel in the administration of propofol with the expertise in emergency airway management must be present. Patient physiologic parameters must be continuously monitored. Age-appropriate equipment for airway management and resuscitation must be available immediately if required. Post-procedurally, patients are required to be monitored in the recovery and are advised not to engage in activities that require a certain amount of concentration for the remaining of the day (eg, driving). These requirements add to the cost and inconvenience to the procedures.

Acupuncture has been used for curing diseases or promoting health. It involves insertion of needles into specific points in the body and manipulation of the needles (lifting, thrusting, twisting, twirling or other complex combination) to elicit a characteristic sensation called De-Qi,[5] which is believed to be responsible for causing the release of endorphins in the brain. Manipulation of the needles is an important aspect to promote further release of endorphins. However, the manipulation of acupuncture needles is operator-dependent and thus electroacupuncture has been introduced to provide a constant and reproducible stimulation with fixed frequency, pulse width, and current to the needles. Low-frequency electroacupuncture leads to supraspinal release of the μ opioid receptor ligand β-endorphin. This could positively influence a range of symptoms experienced during endoscopy including gagging, pain, and anxiety.

Acupuncture may have an effect on gastrointestinal motility and sensation, gastric acid secretion, anti-emesis, cancer pain management, postoperative ileus, and functional bowel disease.[2,3] Three randomised trials have investigated analgesia in gastroscopy or colonoscopy, and the results of these studies suggest that acupuncture may have a role in reducing discomfort or pain during endoscopy. However, these studies have methodological flaws,

including inappropriate and small sample size, unclear randomisation method, poorly defined outcomes, and unvalidated outcome measures.

In the current study, electroacupuncture was standardised by a programmable electroacupuncture device that delivered a fixed electric stimulation. In addition, pain experienced by patients during EUS was assessed objectively through the demand for PCA, which was compared among patients, and the results were highly reproducible. Furthermore, PCA demands were supplemented by subjective outcomes. However, there are drawbacks to the current study. The application of the acupuncture needles requires specific training, and trained acupuncturist may not be readily available. The need for an acupuncturist may also add to the cost of the procedure. There is no consensus or standardisation of electroacupuncture application and hence the acupoints and optimal duration of electroacupuncture prior to the procedure for maximal efficacy is uncertain. The anxiety, satisfaction, and willingness to repeat the procedure were not measured using a validated questionnaire and thus the results may not be reproducible.

Conclusions

Electroacupuncture reduced sedative and analgesic demands with low risk of adverse events and improved patient experience during EUS. Further studies are required to determine the optimal duration of electroacupuncture for the optimal efficacy.

Funding

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Disclosure

The results of this research have been previously published in:

1. Teoh AYB, Chong CCN, Leung WW, et al. Electroacupuncture-reduced sedative and analgesic requirements for diagnostic EUS: a prospective, randomized, double-blinded, sham-controlled study. Gastrointest Endosc 2018;87:476-85.

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