Acupuncture transcutaneous electrical nerve stimulation reduces discomfort associated with barostat-induced rectal distension: A randomized-controlled study

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Abstract

AIM: To explore the effectiveness of acupuncture transcutaneous electrical nerve stimulation (Acu-TENS), a non-invasive modality in reduction of rectal discomfort during barostat-induced rectal distension.

METHODS: Forty healthy subjects were randomized to receive 45 min of either Acu-TENS or placebo-TENS (no electrical output) over acupuncture points Hegu (large-intestine 4), Neiguan (pericardium 6) and Zusanli (stomach 36). A balloon catheter attached to a dual-drive barostat machine was then inserted into the subjects’ rectum. A step-wise (4 mmHg) increase in balloon pressure was induced until maximal tolerable or 48 mmHg. Visual analogue scale and a 5-point subjective discomfort scale (no perception, first perception of distension, urge to defecate, discomfort/pain and extreme pain) were used to assess rectal discomfort at each distension pressure. Blood beta-endorphin levels were measured before, immediately after intervention, at 24 mmHg and at maximal tolerable distension pressure.

RESULTS: There was no difference in the demographic data and baseline plasma beta-endorphin levels between the two groups. Perception threshold levels were higher in the Acu-TENS group when compared to the placebo group, but the difference reached statistical significance only at the sensations “urge to defecate” and “pain”. The distension pressures recorded at the “urge to defecate” sensation for the Acu-TENS and placebo-TENS groups were 28.0 ± 4.5 mmHg and 24.6 ± 5.7 mmHg, respectively (P = 0.043); and the pressures recorded for the “pain” sensation for these two groups were 36.0 ± 4.2 mmHg and 30.5 ± 4.3 mmHg respectively (P = 0.002). Compared to the placebo group, a higher number of participants in the Acu-TENS group tolerated higher distension pressures (> 40 mmHg) (65% in Acu-TENS vs 25% in placebo, P = 0.02). The plasma beta-endorphin levels of the Acu-TENS group were significantly higher than that of the placebo group at barostat inflation pressure of 24 mmHg (1.31 ± 0.40 ng/mL vs 1.04 ± 0.43 ng/mL, P = 0.044) and at maximal inflation pressure (1.46 ± 0.53 ng/mL vs 0.95 ± 0.38 ng/mL, P = 0.003).

CONCLUSION: Acu-TENS reduced rectal discomfort during barostat-induced rectal distension and concurrently associated with a rise in beta-endorphin level.

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Key words: Colonoscopy; Rectal discomfort; Transcutaneous electrical nerve stimulation; Acupuncture; Visceral pain
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INTRODUCTION

Early colonoscopy screening is encouraged in prevention of development of colorectal cancer[1]. However, the procedure is often associated with abdominal pain and discomfort[2]. The unpleasant feeling during examination may affect the patient's overall tolerance and thereby jeopardizing the accuracy of outcome findings. A combination of narcotic analgesia and benzodiazepines is often used to decrease the discomfort during colonoscopy[3,4]. However, these medications are also associated with gastrointestinal upset and although uncommon, respiratory and cardiac arrests during colonoscopy were reported[5,6]. Report of a European colorectal cancer screening project revealed that more than 50% of the subjects developed hypoxaemia and 6% had severe bradycardia after colonoscopy with sedation[7].

Electroacupuncture (EA) is widely accepted in China and is considered a possible treatment option for acute and chronic pain of various origins[8-10]. The role of acupuncture in managing pain and anxiety during colonoscopy however is unclear. A randomized sham-controlled study[11] suggested that patients receiving EA to acupuncture Zusanli (stomach meridian ST-36) and Hegu (large intestine meridian LI-4) experienced lower pain level during colonoscopy than those receiving sham acupuncture (SA), but the difference was non-significant statistically. Recently we have shown that application of EA to Hegu (large intestine 4), Neiguan (pericardium 6) and Zusanli (stomach 36) was able to effectively reduce rectal discomfort during Barostat-induced rectal distension[12]. Acupuncture however is invasive, and its application requires an experienced acupuncturist. Application of transcutaneous electrical nerve stimulation (TENS) over acupuncture points (Acu-TENS) is a non-invasive modality and a novel analgesic therapy that combines the advantages of acupuncture and TENS in management of painful conditions[13,14]. Acu-TENS has been shown to be effective in reducing postoperative analgesic requirement[14]. This pilot study aims to explore the potential of Acu-TENS in reduction of visceral pain. Prior to investigation of its role at the actual colonoscopy procedure, where the intraluminal pressures often varied in different subjects, it is necessary to first establish its role using a model which standardizes the intensity and duration of the stimulation. A dual drive barostat device was therefore used to mimic the discomfort caused by gaseous distension during colonoscopy, such model allows the nature of discomfort, distension pressure and duration of stimulation to be standardized.

MATERIALS AND METHODS

Subjects

Hong Kong Chinese subjects with age between 18 to 65 years registered for a screening colonoscopy examination (a free health care service provided by the Hong Kong Hospital Authority for all local permanent residents with family history of colorectal cancer) were invited to participate in the study prior to the actual colonoscopy screening procedure. Exclusion criteria included known cardiovascular dysfunction (American Society of Anaesthesiologists grade III or above), irritable bowel syndrome (Rome II classification[15]), renal impairment, previous abdominal surgery or experience of colonoscopy, gastrointestinal complaints, pregnancy or allergy to acupuncture needles. Subjects who met the inclusion criteria were randomized to either the Acu-TENS or placebo Acu-TENS (PA) group. The respective intervention code was generated randomly by a computer program (Random Allocation Software, Version 1.0, Isfahan University of Medical Sciences, Iran). The group allocation numbers were then placed in sealed opaque envelopes. An envelope was drawn and allocated to each subject by a secretary blinded to the groupings. The envelope was opened by the investigator who then applied the identified intervention accordingly. The subjects, surgeons and all other parties, including an independent outcome assessor, were blinded to the implementation of Acu-TENS or PA.

Bowel preparation

All subjects were instructed to have low fiber diet three days prior to the study. On the day before examination, all subjects underwent standard mechanical bowel preparation with 4 liters of polyethylene glycol (Klean-Prep, Norgine Ltd., Middlesex, United Kingdom) to induce bowel movement and to clear the bowel in preparation for the colonoscopy procedure. Participants were asked to empty their bowel at home before coming to the hospital for examination.

Equipment

A dual-lumen polyethylene catheter (Model CR3-0005, Mui Scientific, Mississauga, Ontario, Canada) was attached to a 10 cm long and 600 mL capacity polyethylene bag (Model CT-BP600R, Mui Scientific) using a sterile surgical silk suture (Ethicon, Mersilk Soie, Somerville, New Jersey, United States), with the surgical knots sealed by latex glue. One lumen of the catheter allowed passage of compressed air for bag inflation and the other was attached to a transducer for monitoring of the pressure inside the bag. The catheter was attached to the dual drive barostat (Distender Series II; G and J Electronics, Inc., Toronto, Canada) which controlled the rate of inflation and deflation of the bag electronically. To ensure
the bag attachment was airtight, the bag was inflated to 60 mmHg for 5 min and placed in sterile warm water to ensure there was no leakage of air from the system.

**Intervention protocols**

Acupuncture points Hegu (large-intestine 4), Neiguan (pericardium 6) and Zusanli (stomach 36) were first identified by the investigator before the procedure. LI 4 is located on the dorsum of the hand, between the 1st and 2nd metacarpal bones; Pericardium 6 is located on the palmar aspect of the forearm, 2 “cuns” above the transverse crease of the wrist between the flexor carpi radialis and palmaris longus tendons; ST 36 is located on the anterior aspect of the leg, at 3 cuns below the knee cap and one finger-breadth from the anterior crest of the tibia. One “cun” is the distance between the interphalangeal creases of the subject’s middle finger. These points were chosen because large-intestine 4 and pericardium 6 are reportedly used to reduce abdominal pain and ST36 was shown to regulate colorectal muscle contractility in conscious rats. All of the selected acupuncture points were swabbed with alcohol following a standard antiseptic process before the TENS electrodes were applied. Six gel pads were cut into size of 5 mm × 5 mm and placed over the subject’s acupuncture points (bilaterally). Each cleaned rubber electrode was placed over the small gel pad (HD-001, ITO Company Limited, Tokyo, Japan), this allowed electrical stimulation to be focused mainly over the acupuncture points. The electrodes were then attached to a dual channel TENS machine (Model 120Z, ITO Company Limited, Tokyo, Japan). Subjects in the Acu-TENS group received a constant mode of electrical stimulation at 2 Hz and pulse width at 200 μs for 45 min. Intensity was set to just initiate muscle contraction. This stimulation protocol has been shown to be effective in inducing endorphin production. Electrode placements were similar for subjects in the PA group, except that the electrical output from the TENS unit was disconnected. The output light however remained active and subjects were told that they may or may not feel the current.

**Experimental procedures**

All subjects arrived at the laboratory at 9 am on the assessment day. They were instructed to rest in the supine position for 15 min and randomized to receive 45 min of either Acu-TENS or PA in the supine position. The subject then adopted a left side-lying position with both knees flexed to 90°. The polyethylene bag which attached to the barostat was slowly inserted into subject’s rectum to a distance 10 cm from the anal verge. The tube was taped to the buttock with micropores and the subject then resumed the supine position. After rested in this position for 15 min the bag was inflated for 60 s and then completely deflated in 60 s, a resting period of 1 minute then followed, this constituted one complete cycle of inflation. An incremental stepwise increase in rectal pressure at 4 mmHg was instilled at subsequent cycles until a pressure of 48 mmHg or when the subject could not tolerate further discomfort. Acu-TENS or PA continued during the whole barostat procedure. When the maximal 48 mmHg or an intolerable pressure was reached, the stimulation was discontinued and all electrodes and gel pads removed.

**Outcome measures**

**Subjective discomfort scale:** During each 60-s phase of sustained incremental pressure, the subject was asked to rate their rectal sensation using an electronic panel attached to a computer. Ratings were “no perception”, “first perception of distension”, “urge to defecate”, “discomfort or pain” and “extreme pain”. Concurrently, each subject was also asked to rate the degree of rectal discomfort using a visual analogue scale (VAS)-a 10 cm ungraded line, with words “no discomfort at all” anchored to “0” end and “discomfort cannot be tolerated” anchored to the number “10”. The VAS and subjective discomfort scales were recorded by an independent research assistant who was blinded to the intervention allocation.

**Beta-endorphin measurement:** Venous blood (3 mL) was drawn (from a cannula inserted into the cubital vein of each subject under aseptic technique) before the randomization process, immediately after the 45 min intervention, at a distension pressure of 24 mmHg and at highest tolerable pressure. The blood samples were transferred to the biochemistry laboratory of the involved hospital in EDTA tubes stored in a 4 °C ice box. The blood sample was then centrifuged and frozen until further assayed. Batch analyzed for beta-endorphin (Human) were analyzed using EIA kit (Phoenix Pharmaceuticals Inc, 330 Beach Road, Burlingame, CA94010, United States). All subjects then undertook the colonoscopy screening procedure in the same afternoon following the barostat study.

**Sample size estimation**

Sample size estimation was based on the assumption that Acu-TENS could increase the mean pain threshold by 8 mmHg (this was based on our previous work which explored the effect of acupuncture in relief of discomfort induced by the barostat). To yield a power of 80% with a significant level of 0.05, a sample size of at least 17 subjects in each group was required (sample size estimation was determined by SPSS Version 15.0 for Windows, SPSS Inc., Chicago, IL, United States).

**Ethical approval**

This study was conducted at a local district hospital from September 2009 to May 2010. The protocol was approved by the Ethics Review Committees of the involved hospital and ClinicalTrials.gov prior to data collection (Approval numbers: NCT01551654 and CRE-2008.546-T). Written informed consent was obtained from each subject prior to commencement of the study.
### RESULTS

A total of 40 healthy subjects (16 male, 24 female; mean age 53.7 ± 3.62 years) were recruited to the study with 20 subjects randomized to either the Acu-TENS or PA group (Figure 1). The demographic data of all subjects were similar between the two groups (Table 1). All subjects completed the procedure and no adverse effects were reported. Colonic polyps were observed during the intervention. Results of the colonoscopy screening procedure for this subject constitute a possible mechanism of control of stimulation.

### DISCUSSION

To the best of the authors’ knowledge, this is the first report on the effect of Acu-TENS in reduction of rectal discomfort in human subjects. This study demonstrated Acu-TENS to large-intestine 4, pericardium 6 and stomach 36 reduced discomfort associated with rectal distension induced by a barostat. TENS is a non-invasive physical therapeutic modality commonly used for pain relief in conditions such as osteoarthritis and low back pain[23]. Although widely used in clinical situations, the working mechanism of TENS remains unclear. The pain-gate hypothesis proposed by Melzack and Wall[24] is considered a possible mechanism of control of stimulation.

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**Table 1** Demographic data of subjects in the transcutaneous electrical nerve stimulation over acupuncture points and placebo transcutaneous electrical nerve stimulation over acupuncture points groups (mean ± SD)

| Item                        | Acu-TENS group (n = 20) | PA group (n = 20) | P value |
|-----------------------------|-------------------------|------------------|--------|
| Age (yr)                    | 53.4 ± 3.8              | 53.9 ± 3.5       | 0.669  |
| Gender (male/female)        | 8/12                    | 8/12             | 1.000  |
| Body weight (kg)            | 63.9 ± 14.4             | 63.0 ± 9.35      | 0.825  |
| Body height (m)             | 1.62 ± 0.07             | 1.61 ± 0.07      | 0.692  |
| BMI (kg/m²)                 | 23.9 ± 3.61             | 24.0 ± 2.53      | 0.899  |

Acu-TENS: Transcutaneous electrical nerve stimulation over acupuncture points; PA: Placebo transcutaneous electrical nerve stimulation over acupuncture points; BMI: Body mass index.

**Table 2** Number of subjects in the transcutaneous electrical nerve stimulation over acupuncture points and placebo transcutaneous electrical nerve stimulation over acupuncture points groups identified with colonic polyps during the colonoscopy screening procedure

| Location of polyps                      | Acu-TENS group (n = 20) | PA group (n = 20) |
|-----------------------------------------|-------------------------|------------------|
| Right side (caecum, ascending colon, hepatic flexure, transverse colon) | 4                        | 3                |
| Left side (splenic flexure, descending colon, sigmoid) | 1                        | 1                |
| Rectosigmoid junction                   | 0                        | 0                |
| Rectum                                  | 0                        | 0                |
| No abnormality                          | 15                       | 16               |

Acu-TENS: Transcutaneous electrical nerve stimulation over acupuncture points; PA: Placebo transcutaneous electrical nerve stimulation over acupuncture points.

**Table 3** Perception threshold, distension pressures, levels of blood beta-endorphin in transcutaneous electrical nerve stimulation over acupuncture points and placebo transcutaneous electrical nerve stimulation over acupuncture points groups (mean ± SD)

| Item                        | Acu-TENS | PA | P value |
|-----------------------------|----------|----|--------|
| Perception threshold (mmHg) | 18.4 ± 4.2 | 16.8 ± 6.4 | 0.358   |
| Urge to defecate             | 28.0 ± 4.5 | 24.6 ± 5.7 | 0.043   |
| Discomfort or pain           | 36.0 ± 4.2 | 30.5 ± 4.3 | 0.002   |
| Extreme pain                 | 40.0 ± 6.7  | 35.4 ± 5.6  | 0.379   |
| Pressure (n = 20)            |           |    |        |
| 40 mmHg                     | 17 (85)   | 10 (50)  | 0.020   |
| 44 mmHg                     | 13 (65)   | 3 (15)   | 0.001   |
| 48 mmHg                     | 11 (55)   | 2 (10)   | 0.022   |
| Levels of blood beta-endorphin (ng/mL) |          |    |        |
| Baseline                    | 1.04 ± 0.35 | 1.22 ± 0.52 | 0.216   |
| After 45 min of intervention | 1.14 ± 0.41 | 1.13 ± 0.48 | 0.980   |
| At 24 mmHg pressure          | 1.31 ± 0.40 | 1.04 ± 0.43 | 0.044   |
| At maximal tolerable pressure or 48 mmHg | 1.46 ± 0.53 | 0.95 ± 0.38 | 0.003   |

Acu-TENS: Transcutaneous electrical nerve stimulation over acupuncture points; PA: Placebo transcutaneous electrical nerve stimulation over acupuncture points.
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Subject pathways during TENS. It was also believed that TENS inhibits pain signals via the descending pathway, the dorsal horn cell, and the spinothalamic tract. Another prevalent theory discussed in literature is the release of endogenous opioids such as beta-endorphins, enkephalins and dynorphin after TENS. Acu-TENS was previously shown to increase beta-endorphin levels in subjects with chronic respiratory disease; finding of this current study further confirms that application of 45 min Acu-TENS induced the release of beta-endorphins in subjects with rectal discomfort. Our Acu-TENS protocol adopts a low stimulation frequency at 2 Hz. It was believed that low frequency TENS was able to trigger μ- and delta opioid receptors, the correspondents of beta-endorphin. On the other hand, high frequency (100 Hz) stimulation was believed to trigger κ-opioid receptor and results in the release of dynorphin. Irrespective of the working mechanisms, this study has shown that Acu-TENS

Figure 1 Flow diagram of the study. Acu-TENS: Transcutaneous electrical nerve stimulation over acupuncture points.

Figure 2 Visual analog discomfort score recorded at different distension pressures (A) and mean beta-endorphin levels recorded at different time-points (B). Acu-TENS: Transcutaneous electrical nerve stimulation over acupuncture points.
TENS and placebo groups were included in the study, the
jects. Another limitation of this study is that only Acu-
colonoscopy screening to pay an extra visit to the theatre
at the VAS scores at any pressure level however did not
were reported with the use of Acu-TENS.
gel used in a very minority of subjects, no side effects
TENS machine is inexpensive, the Acu-TENS procedure
another advantage of employing Acu-TENS over acu
symptoms
stantial significant level at 90 min after stimulation. However,
in our previous study, the difference in change of beta-
level between acupuncture and placebo acupuncture was significant at immediately after 45 min of acupunc-
ture stimulation. This probably is associated with the
acupoints adopted in our studies, ST36, is situated in a much deeper anatomical position and because Acu-TENS works in a “transcutaneous” manner, more time is therefore required for Acu-TENS to achieve the expected effect. Interestingly the level of beta-endorphin remained high for a longer period of time after Acu-TENS when compared with acupuncture stimulation. Acupuncture points large-intestine 4, pericardi- cardium 6 and stomach 36 were selected in this study because stimulation of Hegu (large-intestine 4) was associated with excitation of sensory nerve fibers in the pelvic complex and induced regulation of pelvic floor muscle contraction. Stimulation of large-intestine 4 was also shown to be effective in management of labor pain and plantar fasciitis. Stimulation of Neiguan (pericardium 6) and Zusanli (stomach 36) were reported to have significant clinical results in management of gastrointestinal symptoms. Apart from being a non-invasive modality, another advantage of employing Acu-TENS over acupuncture is the low costing involved in Acu-TENS. The TENS machine is inexpensive, the Acu-TENS procedure is simple and experienced acupuncturists are not required for its application. Furthermore, apart from allergy to the gel used in a very minority of subjects, no side effects were reported with the use of Acu-TENS.
This study showed that while a higher distention pressure was tolerated during Acu-TENS, the difference at the VAS scores at any pressure level however did not reach a statistical difference. This could possibly be a consequence of both the slow release of endorphin during Acu-TENS, as well as the small sample size of this study. However convincing subjects who signed up for colonoscopy screening to pay an extra visit to the theatre for experimental recording of discomfort induced by a barostat machine was deemed demanding by many subjects. Another limitation of this study is that only Acu-TENS and placebo groups were included in the study, the
strength of the placebo effect cannot be accurately evalu-
ated without inclusion of a control group of no inter-
vention. Inclusion of a control group however requires
creasing the sample size, and as previously explained, this was difficult to comply. This study used the barostat model to mimic rectal discomfort. Previous reports on the use of the barostat model were mainly on patients with irritable bowel syndrome. The barostat-induced rectal discomfort cannot accurately reproduce the same painful sensation as the stretching of mesenteric tissues during actual colonoscopy procedure. However, gaseous distension during colonoscopy also creates visceral pain and discomfort. Our previous experience suggests that using the barostat model to mimic sensation of gaseous distension during colonoscopy appears to be a good model for evaluation of pain and distension discomfort under a standardized, controllable environment.
In conclusion, this study showed that 45 min of Acu-
TENS over large-intestine 4, pericardium 6 and stomach 36, compared to placebo Acu-TENS, appeared to reduce the level of rectal discomfort induced by barostat disten-
sion and allowed the subjects to withstand a higher disten-
ion pressure. Subjective toleration of a higher inflation pressure was shown to be accompanied with a significant increase in beta-endorphin level. The role of Acu-TENS in application during clinical colonoscopy warrants further investigation.

**COMMENTS**

**Background**
Colonoscopy procedure is often associated with abdominal pain and discom-
fort. Application of transcutaneous electrical nerve stimulation over acupoints (Acu-TENS) is a non-invasive treatment modality for management of musculo-
skeletal pain, but its role for pain relief in endoscopic procedure has not been investigated.

**Research frontiers**
TENS has extensively been used as a physical modality for pain relief for musculoskeletal condition, however, the mechanism of action remains unclear. Beta-endorphin is a natural painkiller and largely found in the hypothalamus and pituitary gland. In this study, employing the barostat, an electronic device as an experimental pain model to standardize and mimic visceral pain caused by gaseous distension, the authors demonstrated that application of Acu-TENS is associated with the release of beta-endorphin effecting pain relief.

**Innovations and breakthroughs**
Endoscopic procedure is often associated with abdominal pain and discomfort, especially when there is increased gaseous distension. The unpleasant feel-
during examination may affect the patient’s overall tolerance and thereby jeopardizing the accuracy of outcome findings. Electroacupuncture is consid-
ered worldwide as a possible treatment option for acute and chronic pain of various origins, however, acupuncture is invasive and require an experienced acupuncturist. Acu-TENS, on the other hand, is a novel non-invasive modality that combines the advantage of TENS and acupuncture in the management of acute painful conditions.

**Applications**
Findings of this study suggest that Acu-TENS is potentially a therapeutic, non-
invasive physical modality that could reduce rectal discomfort during an endo-
scopic procedure. The role of Acu-TENS during clinical colonoscopy warrants further investigation.

**Terminology**
Acu-TENS is the application of transcutaneous electrical nerve stimulation over acupoints. Visceral pain is an unpleasant sensation as a result of acti-
vation of nociceptors of the abdominal organs. Such type of pain is associated
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