

### **PAIN**

# Transcutaneous electric acupoint stimulation reduces intra-operative remifentanil consumption and alleviates postoperative side-effects in patients undergoing sinusotomy: a prospective, randomized, placebo-controlled trial

H. Wang<sup>1†</sup>, Y. Xie<sup>1†</sup>, Q. Zhang<sup>1</sup>, N. Xu<sup>1</sup>, H. Zhong<sup>1</sup>, H. Dong<sup>1</sup>, L. Liu<sup>2</sup>, T. Jiang<sup>1</sup>, Q. Wang<sup>1\*</sup> and L. Xiong<sup>1\*</sup>

# **Editor's key points**

- Transcutaneous electroacupuncture stimulation (TEAS) may provide non-invasive analgesia with minimal side-effects.
- Well-designed trials are needed to assess acupuncture-based techniques, such as TEAS, over placebo.
- This double-blind randomized controlled trial assesses the use of TEAS for acute perioperative pain.
- TEAS reduced remifentanil requirements and some side-effects compared with placebo.
- This simple, non-invasive technique needs further study of its role in acute pain management.

**Background.** Although opioids are widely used as analgesics in general anaesthesia, they have unpleasant side-effects and can delay postoperative recovery. Acupuncture and related techniques are effective for acute and chronic pain, and reduces some side-effects. We assessed the effect of transcutaneous electric acupoint stimulation (TEAS) on intra-operative remifentanil consumption and the incidences of anaesthesia-related side-effects.

**Methods.** Sixty patients undergoing sinusotomy were randomly assigned to TEAS or control group. TEAS consisted of 30 min of stimulation (6–9 mA, 2/10 Hz) on the Hegu (LI4), Neiguan (PC6), and Zusanli (ST36) before anaesthesia. The patients in the control group had the electrodes applied, but received no stimulation. Bispectral index was used to monitor the depth of anaesthesia. Perioperative haemodynamics were recorded, and peripheral blood samples were collected to measure the levels of mediators of surgical stress. The primary end point was intraoperative remifentanil consumption and the secondary endpoints were recovery quality and anaesthesia-related side-effects.

**Results.** Patients in the TEAS group required 39% less remifentanil during surgery than controls [0.0907 (sp 0.026)  $\mu$ g kg<sup>-1</sup> min<sup>-1</sup> vs 0.051 (0.018)  $\mu$ g kg<sup>-1</sup> min<sup>-1</sup>]. There were no differences in intra-operative haemodynamics or surgical stress between groups. However, the time to extubation and recall in the control group was 16.8 (6.8) min and 23.0 (5.0) min, respectively, significantly longer than that in the TEAS group (P<0.01). TEAS also decreased the incidence of dizziness and pruritus within the first 24 h after surgery (P<0.01).

**Conclusion.** The use of TEAS significantly reduced intra-operative remifentanil consumption and alleviated postoperative side-effects in patients undergoing sinusotomy.

Clinical trial registration. The trial was registered at clinicaltrials.gov (NCT01700855).

**Keywords:** electroacupucture; nausea; remifentanil; vomiting

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Pain relief during surgery is mainly achieved by the use of opioids, which are associated with undesirable side-effects such as nausea, vomiting, and decreased level of consciousness, leading to delayed postoperative recovery. Acupuncture, needling the specific points that restore health, has been used for more than 2500 yr in China. It has been shown to alleviate pain and regulate the physiological functions of the body. In the past decades, there has been an

increasing number of clinical trials evaluating the efficacy of acupuncture or electroacupuncture (EA) as a method supplementary to anaesthesia<sup>4</sup> and postoperative analgesia.<sup>5-7</sup> A randomized controlled trial (RCT) conducted by Sahmeddini and colleagues<sup>6</sup> found that either EA or morphine 0.1 mg kg<sup>-1</sup> given intra-operatively resulted in similar postoperative pain scores and analgesic requirements after nasal septoplasty. Wetzel and colleagues<sup>4</sup> found that

<sup>&</sup>lt;sup>1</sup> Department of Anesthesiology, Xijing Hospital, Fourth Military Medical University, Xi'an, 710032 Shaanxi Province, People's Republic of China

<sup>&</sup>lt;sup>2</sup> Department of Anesthesiology, School of Medicine, Stony Brook University, New York, NY 11794-8480, USA

<sup>\*</sup> Corresponding author. E-mail: wangqiang@fmmu.edu.cn (Q.W.); lxiong@fmmu.edu.cn (L.X.)

<sup>&</sup>lt;sup>†</sup> H.W. and Y.X. contributed equally to this work.



auricular acupuncture reduced fentanyl requirement during hip arthroplasty. However, they stated that the difference in fentanyl requirement was statistically significant, but not clinically important.

So far, the conclusions of studies have been conflicting. Several controlled clinical trials showed that acupuncture had no effects on postoperative pain or analgesic requirements after thoracotomy, abdominal surgery, and third molar extraction. On the other hand, others have demonstrated that acupuncture or EA has the potential to reduce perioperative analgesic requirements. However, in these trials, inadequate blinding of controls may have influenced the findings, as bias from anaesthesiologists or monitoring was not properly excluded. Moreover, these trials did not assess EA in the intraand postoperative settings. The relationship between the intra-operative consumption of opioids and postoperative side-effects such as postoperative nausea and vomiting (PONV), dizziness, and pruritus was also not examined.

Sinusotomy is now generally performed during total i.v. anaesthesia (TIVA) owing to its reliability and improved recovery profile. Transcutaneous electric acupoint stimulation (TEAS) can produce the same effects as those elicited by acupuncture or EA treatment. Compared with acupuncture or EA, TEAS is a non-invasive technique. It has no risk of infections, needleinduced contagious disease, and fear to stimulation. Thus, TEAS is an extremely reductionistic acupuncture technique and more 'user friendly'. Furthermore, it can potentially be applied by any anaesthesiologist or preoperative personnel with minimal training. We hypothesized that TEAS could reduce the intra-operative consumption of general anaesthetics and the incidence and severity of postoperative sideeffects. We conducted a randomized controlled clinical trial to evaluate the influence of TEAS on the consumption of remifentanil and incidence of side-effects in patients undergoing sinusotomy surgery.

### **Methods**

This is a double-blind RCT. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Clinical Research Ethics Committee. The trial was registered at clinicaltrials.gov (NCT01700855). Written informed consent was obtained from each participant.

### Patient population

Sixty patients undergoing elective sinusotomy at Xijing Hospital with an ASA physical status of I–II were recruited between August 2012 and November 2012. Their ages ranged from 29 to 60 yr. Exclusion criteria were pre-existing coagulopathy, peptic ulcer, hepatic dysfunction, confirmed renal impairment, use of  $\beta$ -blocker or anti-hypertensive drugs, and regular use of opioids.

### Randomization and blinding

Patients were assigned to either TEAS stimulus (TEAS group) or control group (Con group) on the basis of random numbers generated by a computer. Only the acupuncturist was informed the randomization allocation, just before the onset of TEAS. None of the anaesthesiologists, surgeons, physicians in the post-anaesthesia care unit (PACU), or participants were aware of the allocation. Blinding of the patients was ensured by using gel electrodes in the same therapeutic setting, which has previously been proved to be a successful strategy. <sup>12</sup>

### **TEAS** protocol

An experienced acupuncturist performed TEAS for 30 min before anaesthesia. According to the theory of traditional Chinese medicine, bilateral Hegu (LI4), Neiguan (PC6), and Zusanli (ST36) were chosen as the acupuncture points. These acupoints were identified according to the traditional anatomic localization (Fig. 1). Gel electrodes were applied to the skin after it had been cleaned with ethyl alcohol. The acupoints were then stimulated electrically with an intensity of 6-9 mA and densedisperse frequency of 2/10 Hz for 30 min, using the Hwato electronic acupuncture treatment instrument (model No. SDZ-V, Suzhou Medical Appliances Co., Ltd, Suzhou, China). The intensity was adjusted to maintain a slight twitching of the local muscles according to individual maximum tolerance, indicating a satisfactory De-Qi phenomenon and thus adequate stimulation. The patients in the control group had the electrodes applied, but received no stimulation.

### Anaesthesia and perioperative management

One surgeon conducted all surgeries according to a standard protocol; surgery commenced between 8:30 and 9:00 a.m. Anaesthesia was induced i.v. with propofol and remifentanil using a target-controlled infusion (TCI) system. After loss of consciousness, vecuronium (0.1 mg  $kg^{-1}$ ) was administered i.v., and patients were orotracheally intubated 5 min later. Anaesthesia was maintained with TCI of propofol and remifentanil. The depth of anaesthesia was monitored using bispectral index (BIS). Effect site concentrations of propofol and remifentanil were adjusted to the haemodynamics and BIS, according to the Marsh and colleagues<sup>13</sup> and Minto and colleagues<sup>14</sup> models. The cumulative dosage of propofol and remifentanil was recorded in TCI pump. The surgeon did not use vasoconstrictors or local anaesthetics in the nose. Patients' lungs were mechanically ventilated in a volume-controlled mode with a tidal volume of 6 ml kg<sup>-1</sup> body weight during the operation. In both groups, remifentanil and propofol infusions were stopped 5 min before the end of surgery. Meanwhile, prophylactic parecoxib (40 mg) and tropisetron (2 mg) were administered for postoperative pain and PONV, respectively. Patients were extubated and transferred to the PACU when extubation criteria had been achieved. 15 Patients who suffered from PONV 24 h after operation were treated with antiemetics.

### Data collection

Heart rate; mean arterial pressure (MAP); leads I–III of the electrocardiogram; end-tidal carbon dioxide pressure; and peripheral oxygen saturation of all patients were recorded before the onset of TEAS (baseline,  $T_0$ ), at the end of TEAS ( $T_1$ ), at the

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