Postoperative analgesia after low-frequency electroacupuncture as adjunctive treatment in inguinal hernia surgery with abdominal wall mesh reconstruction

Maria Dalamagka,1 Christos Mavrommatis,2 Vassilios Grosomanidis,3 Konstantinos Karakoulas,3 Dimitrios Vasilakos3

ABSTRACT

Objective To determine whether an electroacupuncture (EA) technique that was developed for a surgical population under general anaesthesia reduces pain after mesh inguinal hernia open repair.

Methods A total of 54 patients with right or left inguinal hernia were randomised to group I (preoperative, intraoperative, postoperative EA), group II (preoperative, postoperative EA), or a sham control group (group III; preoperative and postoperative placement of needles, but without skin penetration). The Visual Analogue Scale (VAS) (primary outcome) and the State-Trait Anxiety Spielberger Inventory were evaluated preoperatively and at 30 min, 90 min, 10 h and 24 h after surgery. Pain threshold and tolerance were evaluated using an algometer at these same time points and preoperatively before and after EA. Levels of the stress hormones cortisol, corticotrophin and prolactin were determined at 30 min, 90 min and 10 h after surgery and preoperatively before and after EA.

Results The results showed significant differences between the true EA and control groups. The true EA groups (I and II) showed statistically significantly greater improvements in the primary (VAS pain, p<0.05) and secondary outcome measures (Anxiety scale; algometer measurements, p<0.05 and stress hormones, p<0.01) compared to the control group. There were no statistically significant differences between groups I and II.

Conclusions Electroacupuncture reduces postoperative pain after mesh inguinal hernia repair and decreases stress hormone levels and anxiety during the postoperative period.

INTRODUCTION

Postoperative pain after inguinal hernia surgery is attributed to surgical manipulation or placement of the preperitoneal mesh. Trauma to the pudendal, iliohypogastric and ilioinguinal nerves is the most likely cause of pain, with neuropathic components in the femoral and genital regions.1,2 According to Callesen, pain is most pronounced the day after surgery, and one-third of patients have moderate or severe pain after 1 week.3 However, few studies have evaluated the potential contribution of acupuncture to the treatment of postoperative pain.4,5

Acupuncture is mostly widely known for its analgesic effects.6 A meta-analysis of 15 RCTs comparing acupuncture with sham control in the management of postoperative pain showed that acupuncture decreased both pain intensity and opioid consumption up to 72 h after surgery.7 More evidence is provided by two trials8,9 which suggest that the perioperative administration of acupuncture may be a useful adjunct for postoperative analgesia.

The aim of this study was to evaluate the effect of electroacupuncture (EA) on postoperative pain and provide additional information as to whether acupuncture might serve as an important adjunct for pain control. This trial studied the effect of EA in mesh inguinal hernia open repair, using the pain scale VAS (Visual Analogue Scale), the Anxiety Scale, evaluation of pain with an algometer and measurements of stress hormones.
METHODS
Participants
Healthy male American Society of Anesthesiologists (ASA) I–II volunteers undergoing inguinal hernia repair were recruited from 28 December 2008 until 31 December 2010 from the surgical department of the General Hospital of Larissa, Greece. The scientific committee of the General Hospital of Larissa and the ethics committee of the Aristotle University of Thessaloniki approved the trial. Recruitment and flow of patients through the study are shown in figure 1.

The following exclusion criteria were used: bilateral or recurrent hernia; significant cardiovascular, pulmonary, renal, hepatic and neurological disease; psychiatric history; use of opioids in the past month; body mass index >30; treatment with β blockers; >75 years of age; previous experience of acupuncture; known hypersensitivity to opioids; being treated with monoamine oxidase inhibitors and treatment with selective serotonin reuptake inhibitors; wearing a heart pacemaker.

Randomisation
Eligible patients were randomly allocated to one of three treatment groups of 18 patients using computer-generated blocks. The three groups were:

- Group I: preoperative, intraoperative and post-operative EA.
- Group II: preoperative and postoperative EA.
- Group III (control group): preoperative and postoperative placebo EA.

Figure 1 Recruitment and flow of patients through the study.
Anaesthesia protocol

Patients in all three groups received premedication with atropine (0.5 mg) 10 min before the onset of anaesthesia, and food and water was withheld for 8 h. Continuous monitoring of vital functions (Envoy Patient Monitor) included indirect blood pressure, electrocardiography (lead II and V5), pulse oximetry, capnography and Bispectral Index (BIS). Monitor recordings were performed every 5 min until the completion of surgery. The circulating volume was maintained with Ringer’s lactate. Pre-oxygenation of the patient with 100% oxygen was performed for 3 min.

In the induction phase, propofol 3 mg/kg over 30 s, remifentanil 1 μg/kg and rocuronium 0.15 mg/kg were given into a peripheral vein with concomitant oxygen flow 6 L/min. A laryngeal mask (size LMA 4 or 5) was placed after the loss of the ciliary reflex and a BIS≤50. Patients were placed on mechanical ventilation with an anaesthesia machine (Primus Anaesthetic Workstation, Drager). The applied ventilation model was volume control (tidal volume 8 mL/kg body weight) to maintain end tidal respiratory carbon dioxide (EtCO₂) at between 35 and 38 mm Hg. Anaesthesia was maintained with 50% nitrous oxide and 50% oxygen, 4–5% desflurane and remifentanil at an infusion rate of 0.05 μg/kg/min. Furthermore, a ‘bolus’ dose of remifentanil (approximately 25 μg) was available in cases of hypertension and tachycardia, which occur secondary to painful surgical stimuli. Desflurane was titrated appropriately to maintain adequate anaesthesia levels (BIS=45–55). Paracetamol was given at a dose of 1 g intravenously 5 min before awakening the patient for basal pain control in all cases.

All drug administration was discontinued after the completion of surgery. Patients were extubated in the operating room after the recovery of sufficient consciousness. Thereafter, patients were transferred to the recovery room where they were observed for 3 h.

The interaction of the EA device (intraoperatively) with the use of diathermy caused instant inhibition and noise reversion on the ECG monitor. The instant disturbance of heart rhythm was not a particular problem, because the operation was short.

The surgical technique was the Lichtenstein tension-free method. Hernia patients according to the classification of Nyhus were type II or IIIa, which means smaller hernias and less surgical time required. The surgical team and anaesthetist was the same for all procedures.

Postoperative analgesia

Postoperatively, 15 mg intravenous pethidine was administered immediately to all patients. If the pain VAS score (0–10 cm) was ≥3 cm within 90 min of surgery, an intravenous bolus dose of 5 mg pethidine was given and a continuous intravenous infusion pump of pethidine at a rate of 10 mg/h was given for 12 h (total 120 mg). If the levels of analgesia were not satisfactory, rescue treatment was available with parecoxib at a dose of 40 mg. Ondansetron at a dose of 8 mg was given in cases of nausea and vomiting.

Acupuncture protocol

Preoperative EA was given for 40 min before introduction of general anaesthesia, intraoperative EA from the beginning of surgery until its completion, and postoperative EA for 60 min after the patient regained consciousness.

Patients in all three groups, lying supine, were instructed to close their eyes (to reduce the risk of unblinding, although patients selected for the trial were acupuncture naïve) and concentrate on their breathing during the intervention.

The treatment in the control group was identical to that in the true EA groups with the following exceptions. Mild pressure was applied using a plastic tube on the bone near the points to cause a distinct sensation. The needles were secured on the skin with non-transparent adhesive tape, without skin penetration by the needle. The needles were connected to the electrical stimulator in the same way as in true EA. An indicator light was flashing on the same acupuncture electrical stimulation device to create an impression that the machine was working, but no current flowed. Patients were told that they might not feel the electricity owing to its high frequency.

Patients were not aware of the type of acupuncture that they would receive. The words ‘placebo’ or ‘sham’ were not used in the information material or consent forms.

Electroacupuncture points

An acupuncture specialist (certificate from the International Council of Medical Acupuncture and related techniques and Medical Acupuncture Society of Northern Greece) who was an anaesthetist but did not administer the anaesthetic for these patients, selected the acupuncture points. Single-use, sterile, 30 mm long and 0.30 mm diameter acupuncture needles (Ener-Qi, NOVOSAN) were inserted bilaterally into the selected acupoints: SP6, ST36, LI4, PC6, BL60, KI3, and auricular points Thalamus 26a, Shen-Men 55, Lung 101.

A point-detection device was used to confirm these points. Body points (SP6, ST36, LI4, PC6, BL60, KI3) were verified by the de qi sensation (ie, a feeling that indicates effective needling).

Electrical stimulation was performed using an acupuncture electrical stimulation device (Agistim Duo, SEDATELEC), which is a dual electrical stimulator that administers alternating current. The trial used low-frequency (LF) EA of 2 Hz and ‘frequency scanning mode’ (the actual emission frequency oscillates intermittently between 1 Hz and the selected frequency of 2 Hz). Electroacupuncture was applied to
each patient bilaterally to the points in pairs SP6–ST36 and ipsilateral to the hernia to the points in pairs LI4–PC6; Shen-Men 55–Thalamus 26a.

Postoperative assessment
The VAS was used to evaluate pain preoperatively and postoperatively at 30 min, 90 min, 10 h and 24 h after surgery. The Spielberger State-Trait Anxiety Index was used to evaluate anxiety; the Trait Anxiety scale, which evaluates permanent stress, was used only preoperatively to check that the mental health of groups was balanced. The State Anxiety scale, which shows transient stress, was used postoperatively at 30 min, 90 min, 10 h and 24 h after surgery. An independent observer without any previous involvement in the study performed all the evaluations.

Algometry has been used in both experimental pain research and in clinical research for many years. The pressure pain threshold (PPT) is defined as the minimum pressure that produces pain and pain tolerance (PT) as the maximum pressure that was tolerated by the patient. Pressure was applied on the affected side (5 cm from the incision, in the soft tissue of the abdomen) and the healthy side. Pain threshold and tolerance (digital algometer, Wagner) were evaluated preoperatively, before and after EA, and postoperatively at 30 min, 90 min, 10 h and 24 h after surgery.

The frequency of complications of opiates (e.g., sedation, pruritus, nausea, vomiting) was recorded.

Finally, blood levels of stress hormones cortisol, corticotrophin and prolactin were measured at the same time points (excluding 24 h).

Vital signs of patients were monitored postoperatively.

Statistical analysis
Data were processed in SPSS v.17.0. Comparisons between groups were performed with analysis of variance and with Bonferroni post hoc tests for quantitative variables. We chose to report data on the left and right hernia separately, because of anatomical peculiarities. Repeated measures analysis and the Holm’s test were used for differences between various time points. Kruskal–Wallis and Dunn’s test were used for ordered variables. Nominal variables were examined with likelihood ratio test, as frequencies were below five in some cells. Statistical significance was set at p<0.05.

Pain and anxiety levels: power equals 0.95 (Gpower 3.1).
Hormone levels: power equals 0.83 (Gpower 3.1).

RESULTS
The entire study population was male, and the flowchart is shown in figure 1. The age of patients in the three groups, the initial values on the scales VAS, Spielberger’s State-Trait Anxiety Index and measurements of the algometer and stress hormones are shown in table 1. The average time for surgery completion was 15±4 min and the anaesthesia maintenance time was 25±3.5 min.

The pain VAS showed significantly lower scores in group II at 30 min postoperatively compared with the control group (p<0.05), and at 90 min and 10 h postoperatively (p<0.01) (figure 2). Statistically significant differences were also seen between group I and the control group at 30 and 90 min (p<0.01) and 10 h postoperatively (p<0.05). There were no statistically significant differences between groups I and II.

Table 1 Baseline characteristics of the three groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I (N=18)</th>
<th>Group II (N=18)</th>
<th>Group III (N=18)</th>
<th>p Value (ANOVA)</th>
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<tbody>
<tr>
<td>Age (years)</td>
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<td>VAS</td>
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<td>Trait Anxiety</td>
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</tr>
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<td>Algometer values (hernia right)</td>
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<td></td>
</tr>
<tr>
<td>PPT</td>
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<td>2.4±1.12</td>
<td>NS</td>
</tr>
<tr>
<td>PT</td>
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<tr>
<td>Algometer values (hernia left)</td>
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<td></td>
</tr>
<tr>
<td>PPT</td>
<td>2.3±0.55</td>
<td>2.4±0.55</td>
<td>2.4±0.39</td>
<td>NS</td>
</tr>
<tr>
<td>PT</td>
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<td>3.2±0.50</td>
<td>3.5±0.76</td>
<td>NS</td>
</tr>
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<td>Cortisol (µg/dL)</td>
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<td>17.8±6.31</td>
<td>NS</td>
</tr>
<tr>
<td>ACTH (pg/mL)</td>
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<td>41.3±30.33</td>
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</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>6.4±1.76</td>
<td>7.1±1.98</td>
<td>7.1±1.45</td>
<td>NS</td>
</tr>
</tbody>
</table>

All data are presented as the means±SD for the difference between group III and groups I and II.

The entire study group was male.

Group I: EA preoperatively, intraoperatively and postoperatively; group II: EA preoperatively and postoperatively; group III: control group.

Pressure pain threshold is defined as the minimum pressure that produces pain and pain tolerance is the maximum amount of pressure tolerated by the patient.

VAS: pain scaling corresponds to the numerical evaluation of 0–10 cm.

ACTH, adrenocorticotropic hormone; ANOVA, analysis of variance; NS, not significant; PPT, pressure pain threshold; PT, pain tolerance; VAS, Visual Analogue Scale.

Group I: EA preoperatively, intraoperatively and postoperatively; group II: EA preoperatively and postoperatively; group III: control group.

Pain levels: power equals 0.95 (Gpower 3.1).
Hormone levels: power equals 0.83 (Gpower 3.1).

Figure 2 Primary outcomes: Visual Analogue Scale (VAS) scores at 30 min, 90 min, 10 h and 24 h postoperatively.
Postoperative stress measurements with the State Anxiety scale showed significantly reduced anxiety (p<0.05) in groups I and II compared with the control group at 90 min and 10 h postoperatively (figure 3).

Evaluations with the algometer between healthy and affected sides showed a higher threshold and a higher tolerance of pain in groups I and II compared with control group. Patients who had a right inguinal hernia showed statistically significant differences between the control group and groups I and II at 30 min, 90 min, 10 h and 24 h postoperatively (p<0.001); the true EA groups exhibited a higher threshold and higher tolerance of pain than the control group (p<0.001).

In groups I and II (preoperatively after EA), patients who were treated for a left inguinal hernia showed more tolerance to pain than controls (p<0.001) (see online supplementary table S1).

Patients who were surgically treated for a right inguinal hernia demonstrated less deep pain than those with a left inguinal hernia (p<0.001).

There were statistically significant differences between groups I and II and the control group in cortisol, adrenocorticotropic hormone (ACTH) and prolactin measurements after EA preoperatively and at 30 min, 90 min and 10 h postoperatively. More specifically, groups I and II exhibited greater reductions in cortisol and ACTH at 30 min, 90 min and 10 h postoperatively compared with the control group (p<0.001) and preoperatively after EA (p<0.01). In addition, groups I and II exhibited a greater decrease in prolactin preoperatively after EA and 90 min postoperatively compared with the control group (p<0.001). Groups I and II exhibited a greater decrease in prolactin than controls at 30 min and 10 h after surgery (p<0.01) (table 2).

Two patients (11%) in group I received a continuous intravenous infusion pump of pethidine postoperatively, as did four patients (22%) in group II, and 18 patients (100%) in the control group III (p<0.001, likelihood ratio=42.564). The administration of pethidine did not induce tachycardia, probably owing to low-frequency EA and the selected points (PC6, ST36, auricular). Rescue treatment with parecoxib was given to 10 patients in the controls (group III); no patient in groups I or II received parecoxib (p<0.001, likelihood ratio=27.019).

Seven patients in the control group III experienced nausea, but nausea was not reported in the other two groups. Sedation, pruritus and vomiting were not reported.

**DISCUSSION**

The results of this study, which focused on the treatment of acute postoperative pain in mesh inguinal hernia open repair, showed better analgesia for groups I and II compared with the control group, as evaluated both by the VAS scale and by algometer measurements. The stress hormones showed an impressive fall in groups I and II compared with the control group. There were no statistically significant differences between groups I and II.

The use of an algometer and, in particular, the evaluation of PT, as well as measurements of three different stress hormones, reinforce the suggestion that acupuncture may be a useful adjunct tool in the treatment of postoperative pain. On the other hand, the small number of participants is a limitation of this study.

Algometer measurement of PPTs is a crucial aspect of any study on pain in human subjects in experimental laboratory settings. Digital pressure algometry showed high intra-rater reliability for PPT measurements. PPTs detect mechanical hyperalgesia of deep tissues, thus also permitting assessment of heterotopic spread of central sensitisation, and are considered clinically robust and reliable. In our study we used an algometer for the evaluation of PPT and PT, as it is a more objective test of pain assessment.

In group II we used EA intraoperatively. LF electroacupuncture may cause inhibition and noise reversion at high frequencies.

Diathermy can affect the pacing thresholds. The interaction of an EA device with the use of diathermy can be a risk factor for a patient with a pacemaker, and thus for safety reasons, we excluded such patients.

Pelvic splanchnic nerves are parasympathetic nerves that innervate the distal transverse colon, the descending colon and the sigmoid colon. We assume that the arrangement of segmental innervation of different viscera on each side explains why EA was more effective at relieving pain in patients with right inguinal hernia.

In this study, we observed a clear reduction of stress hormones from 30 min to 10 h postoperatively. The effect of EA on corticotrophin-releasing hormone and prolactin have been studied, and there is evidence that it is mediated by β-endorphin. Electroacupuncture regulates levels of these hormones, increasing or...
decreasing them depending on the circumstances. Kotani et al\textsuperscript{19} enrolled 175 patients scheduled for major abdominal surgery who preoperatively randomly received an epidural catheter in combination with acupuncture or non-invasive sham acupuncture. Plasma concentrations of cortisol and adrenaline were lower in the acupuncture group than in the control group. Malizia et al\textsuperscript{20} reported an eightfold rise in plasma ACTH and $\beta$-endorphin in normal volunteers after an EA session of 18 min, with a gradual decline in the values of both in the next 60 min. The statistically significant differences in the hormone values in our study between the control group and groups I, II, provide an objective test that strongly supports the view that acupuncture exerts its action through the neuroendocrine system.

LF EA may activate the endorphinergic system ($\beta$-endorphin) in relieving pain. The effect of LF EA on pain tends to last longer than the stimulation itself. Endomorphin-1, also appears to be involved in 2 Hz EA at a spinal level.\textsuperscript{10} Acupuncture analgesia leads to development of tolerance, when applied continuously.\textsuperscript{21} In this study, we used LF EA of 2 Hz and ‘frequency scanning mode’, in order to avoid accommodation and to achieve longer-lasting analgesia.

The points used in this study have been researched for their specific EA effects\textsuperscript{10} and considered appropriate. Some of these have been used in similar studies\textsuperscript{22–24} including only body points. Several RCTs suggest that auricular acupuncture is at least as effective as benzodiazepines in the treatment of preoperative anxiety but

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**Table 2** Hormone levels during the course of the study

<table>
<thead>
<tr>
<th>Group</th>
<th>Hormone Levels</th>
<th>p Value (ANOVA)</th>
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<tr>
<td>Cortisol ($\mu$g/dL)</td>
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<tr>
<td>Phase 1</td>
<td>19.6±6.79</td>
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<tr>
<td>95% CI (16.22 to 22.97)</td>
<td>95% CI (13.03 to 19.29)</td>
<td>95% CI (15.53 to 22.42)</td>
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<td>Phase 2</td>
<td>11.0±5.73**</td>
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</tr>
<tr>
<td>95% CI (8.11 to 13.81)</td>
<td>95% CI (8.23 to 12.18)</td>
<td>95% CI (14.30 to 19.78)</td>
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<td>Phase 3</td>
<td>24.8±20.62***</td>
<td>22.0±10.79***</td>
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<td>95% CI (46.93 to 94.04)</td>
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<td>95% CI (45.25 to 91.38)</td>
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<td>Phase 5</td>
<td>5.8±5.34***</td>
<td>5.9±4.54***</td>
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<td>ACTH (pg/mL)</td>
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<td>Phase 1</td>
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<td>95% CI (18.93 to 44.91)</td>
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<td>95% CI (26.21 to 62.26)</td>
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<td>52.8±35.26***</td>
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<td>95% CI (84.11 to 154.11)</td>
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<td>26.1±16.77***</td>
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<td>9.3±5.72***</td>
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<td>95% CI (6.50 to 8.12)</td>
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<td>4.4±1.93***</td>
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<td>95% CI (5.77 to 7.28)</td>
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<tr>
<td>Phase 4</td>
<td>14.9±14.43***</td>
<td>17.0±10.52***</td>
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<td>95% CI (7.74 to 22.09)</td>
<td>95% CI (11.77 to 22.23)</td>
<td>95% CI (32.33 to 44.13)</td>
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<tr>
<td>Phase 5</td>
<td>6.9±3.56**</td>
<td>7.4±2.55**</td>
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<tr>
<td>95% CI (5.12 to 8.66)</td>
<td>95% CI (6.11 to 8.64)</td>
<td>95% CI (9.69 to 15.95)</td>
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</table>

All data are presented as the means±SD, 95% CI for the difference between group III and groups I and II. Post hoc results. **p<0.01 vs group III. ***p<0.001 vs group III.

Phase 1: preoperatively before EA; phase 2: after preoperative EA; phase 3: 30 min postoperatively; phase 4: 90 min postoperatively; phase 5: 10 h postoperatively.

Group I: EA preoperatively, intraoperatively and postoperatively; group II: EA preoperatively and postoperatively; group III: control group.

ACTH, adrenocorticotrophic hormone; ANOVA, analysis of variance; NS, not significant.
lacks the side effects of these sedative drugs. Two experimental investigations showed that auricular stimulation can reduce the dose of the volatile anesthetic desflurane required to inhibit the movement of extremities in response to noxious electrical stimulation in healthy volunteers. From the above reports we suspect that it might have been the ear points that were of importance.

Controversial results, dissimilar study designs and diverse modes of acupuncture-point stimulation make it difficult to evaluate the clinical importance of perioperative acupuncture analgesia. General anaesthesia in practice cancels the effect of acupuncture, which affects the nervous system. Gupta et al applied acupuncture for 15 min before surgery while the patient was anaesthetised. There were no significant differences between the acupuncture and control groups. The lack of significant difference between groups I and II (the two timings of EA) suggests that the use of intraoperative EA adds nothing to the perioperative stimulation, confirming the findings of others that acupuncture is ineffective if given during anaesthesia.

There is evidence that placebo analgesia is implicated in the endorphin pathway, which raises doubts about the superiority of EA against placebo acupuncture. In their review, Lee and Ernst state that acupuncture is not better than placebo, and it does not contribute to analgesia when combined with the usual anaesthetics. However, the differences between the groups I, II and the control group in our study were statistically significant for clinical pain assessments made by an independent observer. The true acupuncture showed stronger control of postoperative pain.

CONCLUSION
LF EA for postoperative pain following mesh inguinal hernia repair significantly reduced postoperative pain compared with placebo. Respectively, there were decreases in stress hormones levels and anxiety. Acupuncture could be included in the clinical routine as a complementary method in the perioperative setting.

Summary points
► We investigated electroacupuncture (EA) for postoperative pain.
► We compared EA preoperatively, intraoperatively and postoperatively with EA preoperatively and postoperatively only, and with placebo EA.
► EA significantly reduced pain (and the need for postoperative analgesia, though this was not a primary outcome of the study) compared with placebo.
► EA significantly reduced adrenocorticotropic hormone, cortisol and prolactin levels.
► Addition of intraoperative EA did not increase these effects.

Collaborators
Maria Samara; Christos Saros; George Crommydas.

Contributors
DM: thought the idea, collected the data, electroacupuncture application, analysed the results, drafted and revised the paper. MC: thought the idea, analysed the results, drafted and revised the paper. GV: drafted and revised the paper. KK: thought the idea, analysed the results, drafted and revised the paper. VD: thought the idea, analysed the results, drafted and revised the paper.

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More info
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