Efficacy of Electroacupuncture Combined with Intravenous Patient-controlled Analgesia after Cesarean Section: A Randomized Clinical Trial

Ying JIN MD, Xiaoshuai YU MD, Shen HU MD, Lanying LIU MDPhD, Bin WANG MD, Yuanling FENG MD, Yubo LI PhD, Bing XIONG MD, Liquan WANG MDPhD

PII: S2589-9333(22)00256-7
DOI: https://doi.org/10.1016/j.ajogmf.2022.100826
Reference: AJOGMF 100826


Received date: 15 October 2022
Revised date: 17 November 2022
Accepted date: 28 November 2022

Please cite this article as: Ying JIN MD, Xiaoshuai YU MD, Shen HU MD, Lanying LIU MDPhD, Bin WANG MD, Yuanling FENG MD, Yubo LI PhD, Bing XIONG MD, Liquan WANG MDPhD, Efficacy of Electroacupuncture Combined with Intravenous Patient-controlled Analgesia after Cesarean Section: A Randomized Clinical Trial, American Journal of Obstetrics & Gynecology MFM (2022), doi: https://doi.org/10.1016/j.ajogmf.2022.100826

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Published by Elsevier Inc.
Efficacy of Electroacupuncture Combined with Intravenous Patient-controlled Analgesia after Cesarean Section: A Randomized Clinical Trial

Ying JIN¹,⁴,⁷, MD; Xiaoshuai YU², MD; Shen HU³, MD; Lanying LIU⁴, MD, PhD; Bin WANG⁵, MD; Yuanling FENG³, MD; Yubo LI⁶,⁷, PhD; Bing XIONG¹, MD; Liquan WANG³, MD, PhD

¹Department of Rehabilitation in Traditional Chinese Medicine, The Second Affiliated Hospital of Zhejiang University School of Medicine, No. 88, Jiefang Road, Hangzhou City, Zhejiang Province 310009, China

²The Third School of Clinical Medicine, Zhejiang Chinese Medical University, No. 548 Binwen Road, Hangzhou 310053, Zhejiang, China

³Department of Obstetrics, The Second Affiliated Hospital of Zhejiang University School of Medicine, No 88, Jiefang Road, Hangzhou City, Zhejiang Province 310009, China

⁴Department of Acupuncture and Rehabilitation, Affiliated Hospital of Nanjing University of Chinese Medicine, Jiangsu Province Hospital of Chinese Medicine, 155 Hanzhong Road, Nanjing City 210029, Jiangsu, China
Disclosure: The authors report no conflict of interest.

Funding/Support: This study was funded by Natural Science Foundation of Zhejiang Province (grant no. LQ21H270008 and LY19H040014), Youth Innovative Talents Support Program of Zhejiang Medical and Health Science and Technology Program (grant no. 2022492789), and Key Laboratory of Pulsed Power Translational Medicine of Zhejiang Province (grant no. ZMY-KF-210002). The funding source had no involvement in this research.

Clinical Trial Registration: ClinicalTrials.gov identifier: NCT04879212

Correspondence to: Prof. Bing Xiong (telephone number: 13516803156) and Prof. Liquan Wang (telephone number: 15868448702)

Manuscript Word Count: 2990 words
Abstract Word Count: 364 words

Condensation: Electroacupuncture may improve the efficacy of patient-controlled intravenous analgesia and should be recommended as a complementary therapy for pain control after cesarean section.

Short Title: Electroacupuncture after cesarean section

AJOG MFM at a Glance

Why was this study conducted? We aimed to whether electroacupuncture combined with patient-controlled intravenous analgesia (PCIA) an effective analgesic regimen after cesarean section, and if so, at which frequency and by what mechanism?

What are the key findings? In this randomized clinical trial including 158 female patients, electroacupuncture + PCIA had significantly better clinical efficacy for reducing pain after cesarean section than sham electroacupuncture + PCIA, as shown by reduced number of analgesic pump compressions, reduced pain scores, and decreased fentanyl consumption.

What does this study add to what is already known? Findings from this clinical trial indicate that electroacupuncture may improve the efficacy of PCIA for pain management after cesarean section.
Conflict of Interest: The authors report no conflict of interest.

Keywords: electroacupuncture, patient-controlled intravenous analgesia, cesarean section, fentanyl, analgesic pump compressions, pain scores

Abstract

Background: Electroacupuncture is a non-pharmacological intervention for analgesia that is widely recognized as therapy for pain. However, the clinical efficacy of electroacupuncture combined with patient-controlled intravenous analgesia for postoperative analgesia after cesarean section remains unclear.

Objectives: To assess the efficacy of electroacupuncture + patient-controlled intravenous analgesia for postoperative analgesia after cesarean section, determine the optimal frequency for best analgesic effect, and explore the underlying mechanism of action.

Study Design: This single-center, randomized, single-blinded, sham acupuncture controlled clinical trial was conducted at a tertiary university hospital in China. Female patients who underwent cesarean section and received fentanyl as patient-controlled intravenous analgesia for postoperative analgesia were enrolled. Patients were postoperatively randomized to receive 2 Hz electroacupuncture treatment (n = 53), 20/100 Hz electroacupuncture treatment (n = 53), or sham electroacupuncture treatment (n = 52) (controls). The two electroacupuncture groups
received electroacupuncture treatment at 2 or 20/100 Hz at the ST36 and SP6 points, while in the sham electroacupuncture group, sham electroacupuncture was conducted at non-meridian points with non-energized electroacupuncture instruments. Four electroacupuncture treatments were conducted in all groups, at 6, 12, 24, and 48 h after surgery. The primary outcome was the number of analgesic pump compressions at 48 h postoperatively. Secondary outcomes included number of analgesic pump compressions at 6, 12, and 24 h postoperatively; pain scores at 6, 12, 24, and 48 h postoperatively; fentanyl consumption at 48 h postoperatively; interleukin-6 and procalcitonin levels at 12 and 48 h postoperatively; and time to first exhaust.

Results: In total, 174 primigravida women were included in the intention-to-treat analysis. The number of analgesic pump compressions and pain scores at all four time points, as well as fentanyl consumption at 48 h postoperatively, were significantly lower in the electroacupuncture treatment groups than in the sham electroacupuncture group ($P < 0.001$).

Conclusions: Electroacupuncture + patient-controlled intravenous analgesia had a significantly better analgesic effect than sham electroacupuncture + patient-controlled intravenous analgesia within 48 h postoperatively. Thus, electroacupuncture can be considered safe and effective and may improve the efficacy of patient-controlled intravenous analgesia for pain management after cesarean section. Electroacupuncture can be recommended as a routine complementary therapy for pain control after cesarean section.
Introduction

The overall rates of cesarean section (CS) have been increasing for the past 25 years.¹ Postoperative pain is one of the most common complications of CS, accounting for 54% of problems in postpartum women.²³ Nearly 20% of women undergoing CS experience severe acute pain,⁴ which is not only an important predictor of chronic postoperative pain,⁴⁻⁶ but also increases the probability of postpartum depression and impacts breastfeeding and infant health.³⁻⁹ As post-CS pain can seriously affect the physical and mental health of postpartum women, identification of the best analgesic regimen for its management is imperative; for example, postoperative multimodal analgesia.⁹⁻¹¹

At present, the most commonly used pain management method in clinical practice is patient-controlled epidural or intravenous analgesia (PCEA/PCIA) with local anesthetics (such as ropivacaine) and opioids (such as fentanyl).⁴¹² Local anesthetics block the afferent transmission of nerve impulses in the dorsal root ganglion, while opioids act on opioid receptors in glial cells in the brain or spinal cord.¹³⁻¹⁵ When combined, they block the formation and conduction of pain information and increase the pain threshold to achieve analgesia.¹⁵ Although PCIA with fentanyl can provide an excellent analgesic effect, the side effects of fentanyl, such as tendency to sedate and inhibit respiration, affecting the maternal heart rate and blood pressure, can lead to nausea and vomiting, hypotension, urinary retention, skin

Trial Registration: ClinicalTrials.gov identifier: NCT04879212
itching, and even low saturation.\textsuperscript{4,16,17} Therefore, although it is a conventional analgesic regimen, PCIA may exert potential safety hazards.

Acupuncture is a non-pharmacological intervention for analgesia that has a significant effect on acute and chronic pain.\textsuperscript{18-20} It has the advantages of easy operation, safety, and no toxic side effects and has been widely used in the treatment of postoperative pain in China and Western countries.\textsuperscript{21,22} The early postoperative analgesic effect of acupuncture is the key to successful prevention and reduction of chronic pain and related complications after CS.\textsuperscript{23,24} Some studies have demonstrated that electroacupuncture (EA) alone or combined with conventional analgesic regimens may be more effective than sham acupuncture (simulated acupuncture or acupuncture at non-meridian points) in reducing pain scores and improving efficacy grades.\textsuperscript{25,26} However, a prior study found no significant difference in the clinical efficacy of acupuncture for postoperative analgesia after CS compared with that of placebo or pharmacological analgesia.\textsuperscript{27} The inconsistent findings may be related to differences in interventions, follow-up periods, and study population selection. Nevertheless, the clinical efficacy of EA combined with PCIA, as well as the optimal frequency of EA for analgesic intervention, remains unclear.

Therefore, this study aimed to assess the efficacy of EA combined with PCIA for postoperative analgesia after CS, determine the optimal frequency for best analgesic effect, and explore the underlying mechanisms of action.
Materials and Methods

Study Design and Population

This single-center, randomized, single-blinded, sham acupuncture controlled clinical trial was conducted from January 1, 2021, to December 31, 2021, at the Department of Obstetrics at our hospital. The protocol was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Review Committee of our hospital (permission number: 2021-0373). All participants provided written informed consent before participation. We followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline and the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) guideline for the designing and reporting of this trial. The trial protocol is available in Supplement 1.

Randomization and Blinding

Eligible participants were randomized to receive PCIA + 2 Hz EA, PCIA + 20/100 Hz EA (EA groups), or PCIA + sham EA treatment (sham EA group) with a 1:1:1 ratio after CS (6, 12, 24, and 48 h after surgery). The randomization sequence was generated at our hospital, and participants were randomized using the sealed envelope method. Physicians with experience in acupuncture provided the EA or sham EA intervention. Participants, outcome assessors, data analysts, and statisticians were blinded to treatment allocation, and acupuncturists were not.

Interventions

The acupuncturists who performed the treatment were qualified physicians
with >5 years of experience. To improve maternal compliance, the same physician completed all acupuncture treatments for the same patients. Each patient received four 25 min treatments, at 6, 12, 24, and 48 h postoperatively. Patients were allowed to take anti-inflammatory analgesics as rescue medication for unbearable pain, and their use was recorded in detail.

Jiachen Brand sterile disposable acupuncture needles with 0.30 × 40-mm (Wujiang Jiachen Acupuncture Instrument Co., Ltd., Jiangsu, China) were used in EA groups, while pragmatic placebo needles (with a blunt tip) with 0.25 × 25-mm were used in the sham EA group. All groups used the HuaTuo Electric Acupuncture stimulator (SDZ-IIB, Suzhou Medical Supplies Factory Co., Ltd., Jiangsu, China) with the power indicator lights covered and the battery compartment sealed to assist in blinding and to prevent the patient from adjusting settings other than intensity.

EA groups received acupuncture at bilateral Zusanli (ST36) and Sanyinjiao (SP6) (eFigure 2 in Supplement 1) which were both inserted vertically to a depth of 25 to 30 mm by needles. The acupuncturists twirled the needle handles back and forth to achieve the sensation of heaviness and tightness (known as de qi) at all acupoints. The frequency was set at 2 Hz continuous wave in the 2 Hz group and at 20/100 Hz (EA with alternating administration of 20 Hz and 100 Hz at 3 s intervals) in the 20/100 Hz group, both with an intensity of 0.1–5.0 mA, which was appropriate for patient tolerance.

The sham EA group received sham acupoints (20 mm aside from the ST36 and
SP6 points) (eTable 1, 2 in Supplement 1) using pragmatic placebo needles. Procedures, electrode placements, and other treatment settings were similar to those in the EA groups, but with no skin penetration, electricity output, or needle manipulation for de qi.

**Outcome Measures**

The primary outcome was the change in the NAPC at 48 h postoperatively. Secondary outcomes included: pain scores; fentanyl consumption at 48 h postoperatively; serum levels of interleukin 6 (IL-6) and procalcitonin (PCT) at 12 and 48 h postoperatively; and time to first exhaust.

Any adverse event, such as unfavorable or unintended signs, symptoms, or diseases, related to the acupuncture treatment or the administration of fentanyl was reported by patients and the acupuncturists. Severe adverse events were reported to the principal investigator and the data and safety monitoring board within 24 h after their occurrence.

**Statistical Analysis**

Data analysis was performed from February 4, 2022, to June 13, 2022. Data are expressed as median with interquartile range (IQR) or mean ± standard deviation (SD). The Shapiro–Wilk test combined histogram, P-P plot, and Q-Q plot were performed to confirm whether the data were normally distributed. Normally distributed measurement data are expressed as mean ± SD and were analyzed using the one-way analysis of variance (ANOVA). Skewed variables are expressed as IQR and were
analyzed using the Kruskal–Wallis test. If the overall significance test was significant, pairwise comparisons were performed using the least significant difference (LSD) test when the data were normally distributed; conversely, rank transformed LSD was used when the variables were non-normally distributed. For IL-6 and PCT changes (12 and 48 h after surgery), we planned to use the paired t-test and paired rank sum test for normally and non-normally distributed data, respectively. All data were analyzed using IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$. Post-hoc Bonferroni was used for multiple comparisons, and statistical significance was set at $P < 0.05/k$ (k for number of comparisons).

Results

Patients and Baseline Characteristics

A total of 453 patients were planned scheduled for CS of which 174 eligible patients were enrolled; 250 patients were excluded for different reasons, and 29 were not randomized. The 174 patients were randomized to receive PCIA + 2 Hz EA (n=58), PCIA + 20/100 Hz EA (n=58), or PCIA + sham EA (n=58) treatment (Figure 1). Sixteen patients (9.2%) dropped out of the study owing to time commitment, personal issues, or unsatisfying effects (five in the 2 Hz EA group, five in the 20/100 Hz EA group, and six in the sham EA group). Of the patients who completed the intervention, 53 were in the 2 Hz EA group, 53 in the 20/100 Hz EA group, and 52 in the sham EA group. There were no significant differences in the baseline characteristics of patients among the groups ($P > 0.05$; Table 1).
**Primary Outcome**

Significant differences were observed in the number of analgesic pump compressions (NAPC) among the three groups at 48 h postoperatively (48 h: $H = 63.68, P < 0.001$). After pairwise comparison, a significant difference in the NAPC was observed between the sham EA group and the 2 Hz EA ($P < 0.001$ after adjustment) and 20/100 Hz EA groups ($P < 0.05$ after adjustment), but not between the two EA groups ($P > 0.05$ after adjustment; Table 2).

**Secondary Outcomes**

There were differences in the number of compressions among the three groups at 6 h, 12 h, and 24 h postoperatively (6 h: $H = 25.49, P < 0.001$; 12 h: $H = 40.37, P < 0.001$; 24 h: $H = 64.50, P < 0.001$). After pairwise comparison, a significant difference in the NAPC was observed between the sham EA group and the 2 Hz EA ($P < 0.001$ after adjustment) and 20/100 Hz EA groups ($P < 0.05$ after adjustment), but not between the two EA groups ($P > 0.05$ after adjustment; Table 2).

The effect of EA on the secondary outcomes appeared to persist over the course of the study (Table 3). There was no statistical difference in the pain scores among the three groups at 6 h postoperatively ($P > 0.05$); however, pain scores at 12, 24, and 48 h postoperatively were significantly lower in the two EA groups than in the sham EA group, with little difference between the 2 Hz and 20/100 Hz groups ($P > 0.05$). The decrease in pain scores over time in the sham EA group was significantly smaller than that in the EA groups (Figure 2).
Fentanyl consumption was significantly lower in the two EA groups than in the sham EA group at all time points ($P < 0.05$), with a significant difference between the 2 Hz and 20/100 Hz groups only at 24 h postoperatively (difference 6.41, 95% CI 0.61–12.21, $P = 0.0031$) (Table 3).

Analysis of IL-6 and PCT indicators revealed no significant differences in their levels among the three groups at 12 h and 48 h postoperatively ($P > 0.05$), and paired rank sum test showed that the paired test of IL-6 and PCT changes (12 and 48 h after surgery) levels in the blood of the three groups at 12 h and 48 h postoperatively were statistically significant ($P < 0.05$), suggesting that the improvement of symptoms was related to the changes in IL-6 and PCT content. Regarding the IL-6 index, the paired test of IL-6 levels at 12 h and 48 h after surgery in each group showed a statistically significant difference ($P < 0.05$), and no significant difference was observed between the three groups. In terms of PCT levels, the paired test results of PCT content at 12 h after surgery and 48 h after surgery in the sham EA group and 20/100 Hz group were significantly different ($P < 0.05$), and even the paired test results of PCT content at 12 h after surgery and 48 h after surgery in the 2 Hz group were not significantly different ($P = 0.208$), which required verification using an accurate test with a large sample size (Table 4).

There was no significant difference in the time to first exhaust between the two EA groups and the sham EA group ($P > 0.05$) (Table 3).
**Safety**

Five patients reported adverse events. One patient (1.89%) from the 2 Hz EA group reported skin bruising at ST36, three patients (5.66%) from the 20/100 Hz EA group experienced subcutaneous hematoma at the puncture site, and one patient (1.92%) from the sham EA group developed subcutaneous hematoma in the burrow area. No significant difference in the proportion of patients with adverse events was observed among the groups ($P = 0.10$). No patients had severe adverse events in the trial (eTable 1 in Supplement 2). All patients recovered from the adverse events and were not withdrawn from the trial.

**Discussion**

**Principal Findings**

Our study showed that PCIA + EA had significantly better efficacy than PCIA + sham EA in reducing the NAPC, pain scores, and fentanyl consumption at 12, 24, and 48 h after CS. However, IL-6 and PCT levels at 12 h and 48 h after surgery were not significantly different among the three groups. No patients reported severe adverse events in the trial. These findings indicate that EA may improve the efficacy of PCIA for pain management after CS.

**Results and Clinical Implications**

Compared with the sham EA group, the two EA groups showed significant advantages in various outcome measures at 12, 24, and 48 h postoperatively. However, there was no significant difference in the pain scores among the three groups at 6 h
postoperatively, which may indicate that anesthesia affected pain assessment within 6 h.

According to Duan et al., visceral pain after CS mainly occurs in the early postoperative period; therefore, we speculated that early analgesia after CS may be based on the inhibition of visceral pain. Post-CS visceral pain is mainly due to uterine contraction, leading to ischemia and hypoxia at the uterine base, which together with the noxious stimulation brought about by the surgical incision, jointly stimulates the release of endogenous analgesic substances in the uterine tissue. These endogenous substances, in turn, activate the corresponding receptors, inducing transmission of the stimuli to the dorsal spinal roots at T10–12 and L1 levels through the A and C pain impulse conduction fibers of the pelvic visceral nerves. It has been shown that EA has a unique role in inhibiting the release of endogenous analgesic substances and can effectively inhibit inflammatory mediators, such as 5-hydroxytryptamine, nerve growth factor, tumor necrosis factor alpha, and prostaglandin E2, which can block the transmission of noxious stimuli, increase the pain threshold, and effectively reduce the pain after CS. In addition, acupuncture at ST36 was found to promote glucose metabolism in the dorsal middle pons and midbrain and activate large nuclear neurons in the brainstem raphe, thereby inhibiting nociceptive responses such as pain, while acupuncture at SP6 shows unique superiority in relieving uterine contraction pain by reducing the spasm of uterine smooth musculature, relieving the uterine microcirculation disturbance and local tissue ischemia and hypoxia, and regulating the oxidative stress response of the uterine tissue. Therefore, targeted
selection of EA stimulation at ST36 and SP6 points can effectively block the transmission of pain information, increase the pain threshold, and inhibit pain formation. Wang et al.\textsuperscript{35,36} reported that EA stimulation at SP6 can effectively delay the time to analgesia request after CS and reduce the dose of analgesic drugs used within 24 h. These findings are consistent with the results of our study.

Fentanyl consumption at 24 h postoperatively was significantly lower in the 2 Hz EA group than in the 20/100 Hz EA group, suggesting that 2Hz EA combined with PCIA may exert a more considerable analgesic effect within 24 h after CS. Previous studies have demonstrated that 2Hz EA can stimulate the central nervous system to release endogenous opioid analgesic substances, such as enkephalin and endorphin, which act on μ and δ receptors, respectively, and activate the periaqueductal gray matter of the midbrain, thereby inhibiting the generation of pain perception in the parathalamic nucleus through ascending analgesia, and inhibiting the ascending pain signal transduction pathway along the posterior horn cells, resulting in a slow and long-lasting analgesic effect.\textsuperscript{37,38} Presently, 2 Hz EA is rarely applied for postoperative analgesia after CS, which may be related to the degree of pain in patients; that is, differences in personality.

In our study, EA did not reduce the levels of IL-6 and PCT, which is inconsistent with previous findings\textsuperscript{39-42} that acupuncture is effective in reducing the release of interleukin pain-inducing substances from immune cells. Other studies have also found that the effective application of multimodal analgesic regimens after CS is mostly accompanied by varying degrees of decrease in IL-6 levels.\textsuperscript{43} Additionally, in a
basic experimental study, EA could reduce serum IL-6 levels in rats, thereby inhibiting related neuroinflammation and relieving pain symptoms. Therefore, we still believe that there is a certain correlation between EA and IL-6 levels, which could not be observed in the present study due to the small sample size. Few studies have explored the relationship between PCT and EA for postoperative analgesia after CS. Hence, based on the available evidence and the results of our study, we cannot speculate that the analgesic effect of EA in postoperative analgesia after CS is related to the release of IL-6 and PCT.

**Research Implications**

There are still unanswered questions about the mechanism by which EA combined with PCIA may had a better clinical efficacy after CS. Further randomized controlled trial studies should be needed to determine whether EA combined with PCIA would be associated with reducing the release of interleukin pain-inducing substances from immune cells and other potential mechanisms for improvements in. In addition, whether the results from experimental studies in rats is sufficient to support it.

**Strengths and Limitations**

It was an intention-to-treat analysis on the efficacy of electroacupuncture + patient-controlled intravenous analgesia for postoperative analgesia after cesarean section, determine the optimal frequency for best analgesic effect, and explore the underlying mechanism of action. Data came from a single-center, randomized,
single-blinded, sham acupuncture controlled clinical trial was conducted at a tertiary university hospital in China. Our study design did our success in recruiting a study population and lost very few patients from study.

Our study has some limitations. First, the single-center nature of design which relies on the expertise of the treating clinicians while limiting patient demographic variability. Second, follow-up records after 48 h from CS were insufficient to predict the late analgesic efficacy of EA. Finally, our study could not exclude confounding factors other than treatment, such as mood and sleep. Future prospective large-scale studies are required to address these limitations.

**Blinding**

The blinding assessment results (eTable 2 in Supplement 2) showed that 15 patients (28.8%) in the sham EA group (Bang blinding index, −0.4 [95% CI, −0.6 to −0.3]), 11 (20.8%) in the 2 Hz EA group, and 12 (22.6%) in the 20/100 Hz group made a wrong guess regarding their group assignment. No statistically significant difference in blinding index was observed among the three groups (\( P > 0.05 \)). However, the results indicated a relatively higher degree of blinding in the control group.

**Conclusions**

This study found that EA combined with PCIA had a significantly better clinical efficacy after CS. In view of these results, EA is recommended as a routine complementary therapy for pain control after CS and may improve the efficacy of
PCIA for pain management after CS.

Acknowledgments

Authors' contributions: YJ and LW had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: YJ and LL.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: YJ

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: XY and YL.

Obtained funding: YJ.

Administrative, technical, or material support: YF, SH, and BW.

Supervision: BX and LW.

All the authors read and approved the final manuscript.

Disclosures: The authors report no conflict of interest.

References

1. Slomski A. Pain management video reduces opioid use after cesarean delivery.


37. Wu XL, Li N, Xu C, et al. [Effect of electroacupuncture on pain threshold and expression of pain-related factors cyclooxygenase-2, prostaglandin E2 and


43. Carvalho B, Lemmens HJ, Ting V, Angst MS. Postoperative subcutaneous instillation of low-dose ketorolac but not hydromorphone reduces wound exudate

Table 1. Baseline characteristics of the intention-to-treat analysis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group</th>
<th>F Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCIA + sham EA (n=52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCIA + 2 Hz EA group (n=53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PCIA + 20/100 Hz EA group (n=53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>31.19±3.37</td>
<td>30.83±3.59</td>
<td>30.13±3.31</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.44±5.51</td>
<td>159.87±4.86</td>
<td>159.70±5.38</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.80±9.38</td>
<td>69.37±9.11</td>
<td>71.15±11.37</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.65±3.22</td>
<td>27.16±3.47</td>
<td>27.82±3.54</td>
</tr>
<tr>
<td>Gestational (weeks)</td>
<td>38.19±1.28</td>
<td>37.96±1.64</td>
<td>38.32±1.45</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.

BMI, body mass index; EA, electroacupuncture; PCIA, patient-controlled intravenous analgesia; SD, standard deviation
Table 2. Number of compressions of the analgesic pump after surgery

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>PCIA + sham EA group (n = 52)*</th>
<th>PCIA + 2 Hz EA group (n = 53)*</th>
<th>PCIA + 20/100 Hz EA group (n = 53)*</th>
<th>Statistic</th>
<th>$P$ value difference (95% CI)</th>
<th>$P$ value difference (95% CI)</th>
<th>$P$ value difference (95% CI)</th>
<th>$P$ value difference (95% CI)</th>
<th>$P$ value difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 h after surgery</td>
<td>1.0 (0.0, 2.8)</td>
<td>0.0 (0.0, 0.0)</td>
<td>0.0 (0.0, 1.0)</td>
<td>25.49</td>
<td>&lt;0.001</td>
<td>1.50 (0.73, 2.29)</td>
<td>&lt;0.001</td>
<td>1.20 (0.44, 1.97)</td>
<td>0.001</td>
</tr>
<tr>
<td>12 h after surgery</td>
<td>3.0 (1.0, 6.8)</td>
<td>0.0 (0.0, 1.0)</td>
<td>0.0 (0.0, 1.0)</td>
<td>40.33</td>
<td>&lt;0.001</td>
<td>3.58 (2.28, 4.87)</td>
<td>&lt;0.001</td>
<td>3.48 (2.41, 4.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24 h after surgery</td>
<td>5.5 (3.0, 10.0)</td>
<td>0.0 (0.0, 2.0)</td>
<td>0.0 (0.0, 2.0)</td>
<td>64.50</td>
<td>&lt;0.001</td>
<td>5.72 (4.10, 7.34)</td>
<td>&lt;0.001</td>
<td>5.57 (3.98, 7.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>48 h after surgery*</td>
<td>9.0 (4.3, 12.0)</td>
<td>1.0 (0.0, 3.0)</td>
<td>1.0 (0.0, 4.5)</td>
<td>63.68</td>
<td>&lt;0.001</td>
<td>7.91 (5.81, 10.00)</td>
<td>&lt;0.001</td>
<td>7.04 (4.84, 9.24)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Presented as median (P25, P75) or median (IQR)

Abbreviations: CI, confidence interval; EA, electroacupuncture; PCIA, patient-controlled intravenous analgesia; NA, not applicable; *, Primary Outcome; SD, standard deviation
Table 3. Pain score, fentanyl consumption, and the time of the first exhaust after surgery

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>PCIA + sham EA group (n = 52)</th>
<th>PCIA + 2 Hz EA group (n = 53)</th>
<th>PCIA + 20/100 Hz EA group (n = 53)</th>
<th>PCIA + sham EA vs PCIA + 2 Hz EA</th>
<th>PCIA + sham EA vs PCIA + 20/100 Hz EA</th>
<th>PCIA + 2 Hz EA vs PCIA + 20/100 Hz EA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statistic</td>
<td><em>P</em> value</td>
<td><em>P</em> value (95% CI)</td>
<td><em>P</em> value (95% CI)</td>
<td><em>P</em> value (95% CI)</td>
<td><em>P</em> value (95% CI)</td>
</tr>
<tr>
<td>Pain score 6 h after surgery</td>
<td>7.23 ± 1.13</td>
<td>6.87 ± 1.32</td>
<td>6.17 ± 1.21</td>
<td>0.266</td>
<td>0.798</td>
<td>0.36 (0.11, 0.63)</td>
</tr>
<tr>
<td>Pain score 12 h after surgery</td>
<td>2.62 ± 0.84</td>
<td>2.42 ± 0.77</td>
<td>118.98</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.21 (0.12, 0.31)</td>
</tr>
<tr>
<td>Pain score 24 h after surgery</td>
<td>4.71 ± 0.92</td>
<td>2.42 ± 0.77</td>
<td>118.98</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.21 (0.12, 0.31)</td>
</tr>
<tr>
<td>Pain score 48 h after surgery</td>
<td>2.62 ± 0.84</td>
<td>2.42 ± 0.77</td>
<td>118.98</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.21 (0.12, 0.31)</td>
</tr>
</tbody>
</table>

*P Value based on Kruskal-Wallis analysis among the three groups (adjusted value).

*P Value based on ANOVA (analysis of variance) and LSD analysis among the three groups.
<table>
<thead>
<tr>
<th>Time after Surgery</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 h after surgery</td>
<td>14.61 ± 6.55</td>
<td>9.37</td>
<td>&lt;0.001</td>
<td>4.45 (2.37, 6.53)</td>
<td>&lt;0.001</td>
<td>3.12 (1.04, 5.20)</td>
<td>0.004</td>
</tr>
<tr>
<td>12 h after surgery</td>
<td>30.29 ± 10.47</td>
<td>17.50</td>
<td>&lt;0.001</td>
<td>8.20 (4.65, 11.75)</td>
<td>&lt;0.001</td>
<td>10.83 (5.00, 16.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>24 h after surgery</td>
<td>56.54 ± 12.50</td>
<td>17.38</td>
<td>&lt;0.001</td>
<td>17.24 (11.40, 23.07)</td>
<td>&lt;0.001</td>
<td>10.83 (5.00, 16.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>48 h after surgery</td>
<td>94.88 ± 9.91</td>
<td>8.45</td>
<td>&lt;0.001</td>
<td>12.47 (5.90, 19.04)</td>
<td>&lt;0.001</td>
<td>11.12 (4.55, 17.69)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The time of the first exhaust after surgery, Mean±SD, No.:

<table>
<thead>
<tr>
<th>Time after Surgery</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 h after surgery</td>
<td>32.19 ± 12.93</td>
<td>8.00</td>
<td>0.40</td>
<td>0.675</td>
<td>1.41 (3.75, 6.58)</td>
<td>0.589</td>
<td>2.30 (2.86, 7.46)</td>
</tr>
</tbody>
</table>

Fentanyl consumption 6 h, 12 h, 24 h, and 48 h after surgery, Mean±SD, No.

<table>
<thead>
<tr>
<th>Time after Surgery</th>
<th>Mean ± SD</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
<th>Median</th>
<th>P-value</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 h after surgery</td>
<td>14.61 ± 6.55</td>
<td>9.37</td>
<td>&lt;0.001</td>
<td>4.45 (2.37, 6.53)</td>
<td>&lt;0.001</td>
<td>3.12 (1.04, 5.20)</td>
<td>0.004</td>
</tr>
<tr>
<td>12 h after surgery</td>
<td>30.29 ± 10.47</td>
<td>17.50</td>
<td>&lt;0.001</td>
<td>8.20 (4.65, 11.75)</td>
<td>&lt;0.001</td>
<td>10.83 (5.00, 16.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>24 h after surgery</td>
<td>56.54 ± 12.50</td>
<td>17.38</td>
<td>&lt;0.001</td>
<td>17.24 (11.40, 23.07)</td>
<td>&lt;0.001</td>
<td>10.83 (5.00, 16.66)</td>
<td>0.001</td>
</tr>
<tr>
<td>48 h after surgery</td>
<td>94.88 ± 9.91</td>
<td>8.45</td>
<td>&lt;0.001</td>
<td>12.47 (5.90, 19.04)</td>
<td>&lt;0.001</td>
<td>11.12 (4.55, 17.69)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
after surgery (hour)

*Bonferroni method corrected, the P value less than 0.0167 indicated it was statistically significant different.

Abbreviations: CI, confidence interval; EA, electroacupuncture; PCIA, patient-controlled intravenous analgesia; NA, not applicable; *, Primary Outcome; SD, standard deviation

a P Value based on Kruskal-Wallis analysis among the three groups (adjusted value).

b P Value based on ANOVA (analysis of variance) and LSD analysis among the three groups.
Table 4. Changes in IL-6 and PCT levels after surgery in the three groups

<table>
<thead>
<tr>
<th>Index</th>
<th>Outcomes</th>
<th>PCIA + sham EA group (n = 52)</th>
<th>PCIA + 2 Hz EA group (n = 53)</th>
<th>PCIA + 20/100 Hz EA group (n = 53)</th>
<th>Statistic</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 content</td>
<td>12 h after surgery</td>
<td>60.69 (48.96, 80.24)</td>
<td>68.41 (49.42, 83.52)</td>
<td>58.18 (44.70, 86.04)</td>
<td>1.07</td>
<td>0.587</td>
</tr>
<tr>
<td></td>
<td>48 h after surgery</td>
<td>17.19 (12.65, 23.90)</td>
<td>15.92 (9.84, 20.05)</td>
<td>15.16 (12.61, 21.90)</td>
<td>3.21</td>
<td>0.201</td>
</tr>
<tr>
<td>Z value&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>-6.21</td>
<td>-6.33</td>
<td>-6.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT content</td>
<td>12 h after surgery</td>
<td>0.11 (0.08, 0.18)</td>
<td>0.11 (0.08, 0.17)</td>
<td>0.11 (0.08, 0.18)</td>
<td>0.48</td>
<td>0.201</td>
</tr>
<tr>
<td></td>
<td>48 h after surgery</td>
<td>0.08 (0.06, 0.13)</td>
<td>0.09 (0.05, 0.20)</td>
<td>0.07 (0.05, 0.12)</td>
<td>2.75</td>
<td>0.253</td>
</tr>
<tr>
<td>Z value&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td>-3.25</td>
<td>-1.26</td>
<td>-4.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value&lt;sup&gt;f&lt;/sup&gt;</td>
<td></td>
<td>0.001</td>
<td>0.208</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EA, electroacupuncture; IL-6, interleukin 6; PCIA, patient-controlled intravenous analgesia; PCT, procalcitonin

<sup>c</sup>P Value based on Kruskal-Wallis analysis among the three groups (adjusted value).

<sup>d</sup>P and <sup>d</sup>Z Values based on Wilcoxon signed-rank test of IL-6 and PCT at 12 h and 48 h after surgery in the three groups.

<sup>e</sup>P and <sup>e</sup>Z Values based on Wilcoxon signed-rank test of IL-6 at 12 h and 48 h after surgery in each group.

<sup>f</sup>P and <sup>f</sup>Z Values based on Wilcoxon signed-rank test of PCT at 12 h and 48 h after surgery in each group.
Figure Legends

Figure 1. Study flowchart

EA, electroacupuncture; ITT, intention to treat; PCIA, patient-controlled intravenous analgesia

Figure 2. Pain score curves at 6 h, 12 h, 24 h, and 48 h after surgery

EA, electroacupuncture; PCIA, patient-controlled intravenous analgesia
The graph illustrates the pain scores over time (in hours) for different treatment groups: PCIA + sham EA, PCIA + 2 Hz EA, and PCIA + 20/100 Hz EA. The pain scores are shown at 6, 12, 24, and 48 hours. The treatments are indicated by different colors: blue for PCIA + sham EA, red for PCIA + 2 Hz EA, and green for PCIA + 20/100 Hz EA. The error bars indicate the variability in the data. The graph shows a decrease in pain scores over time for all groups, with the PCIA + 20/100 Hz EA group having the lowest pain scores.