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Original Article

Electro-Acupuncture in Relieving Labor Pain

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To study the efficacy of electro-acupuncture for the relief of labor pain, and to build a better understanding of how electro-acupuncture might influence the neuroendocrine system, 36 primiparas were randomly divided into an electro-acupuncture group and a control group. Assessments of pain intensity and degree of relaxation during labor were analyzed. The differences between the electro-acupuncture group and the control group on the concentration of β-endorphin (β-EP) and 5-hydroxytryptamine (5-HT) in the peripheral blood were compared. The electro-acupuncture group was found to exhibit a lower pain intensity and a better degree of relaxation than the control group ($p = 0.018$; $p = 0.031$). There existed a significant difference in the concentration of β-EP and 5-HT in the peripheral blood between the two groups at the end of the first stage ($p = 0.037$; $p = 0.030$). Electro-acupuncture was found to be an effective alternative or complementary therapy in the relief of pain during labor. The benefit of electro-acupuncture for relieving labor pain may be based on the mechanism of producing a synergism of the central nervous system (CNS) with a direct impact on the uterus through increasing the release of β-EP and 5-HT into the peripheral blood.

Keywords: electro-acupuncture – labor pain – β-endorphin (β-EP) – 5-hydroxytryptamine(5-HT)

Background

Pain relief during labor is an essential aspect of obstetrical care. Presently, there is no standard method available that delivers excellent pain control without having adverse side effects on the mother or the fetus. Labor pain may cause anxiety and exhaustion to mothers in labor and can have a negative influence on the progress of labor. If more oxygen is administered then a high level of catecholamines may be observed in the placenta.

In recent years, there has been an increasing demand among parturients, especially with primiparas, for non-pharmacological analgesia during childbirth and many have expressed a willingness to receive electro-acupuncture treatment during childbirth. Although numerous positive descriptive and retrospective reports on acupuncture for reducing pain and suffering during labor have been published over the previous decades[1,2], it was not until 2002[3,4] and 2003[5] that the first 3 randomized controlled trials of acupuncture for pain relief in labor were published. The aim of this study was to investigate how electro-acupuncture affected labor pain and determine its possible mechanisms. That is, does electro-acupuncture affect labor pain and produce any mechanism of synergism within the central nervous system (CNS) through the increase of the release of β-endorphin (β-EP) and 5-hydroxytryptamine (5-HT) into the peripheral blood [6]. In addition, does electro-acupuncture have a direct impact on the uterus?

Subjects and Methods

Subjects

The study was carried out during a 10-month period, between August 2004 and May 2005, in the first affiliated hospital of Heilongjiang University of Chinese Medicine. This auxiliary hospital has an average of 300 deliveries per year, although the main system has many-fold more. Ethical approval and permission to conduct the study were obtained from the Local Ethical Committee and the administration based on international guidelines. The aim and methodology of the study were

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explained to the patients. Voluntary participation was requested and informed consent was obtained. The inclusion criteria were a normal single pregnancy with a spontaneous onset of labor, cephalic presentation, a cervical dilatation <6 cm at admission, and gestational age ranging from 37–42 completed weeks. Exclusion criteria were diagnoses of diabetes, pre-eclampsia, hypertension, kidney disease, thrombocytopenia, psychological distress or anorexia, infectious blood disease, atopic eczema or psoriasis. Group selection of individual cases was randomized based on protocol assignments being given to the electro-acupuncture group or to the control group through a simplified numerical probability from manual selection. Cases were randomized and neither the doctors, midwives, nor the primiparas could predict the group allocation. The study was completed after 39 women were asked and all those asked were recruited. In the statistical analysis, 36 women were included. Three subjects were considered as missing cases, due to the inclusion criteria not being fulfilled, e.g. not spontaneous onset of labor, and no assessment made of pain intensity or degree of relaxation (Fig. 1).

Group and administration

1. Electro-acupuncture group: The acupuncture points used were Hegu (LI-4) and Sanyinjiao (SP-6) bilaterally. Treatment was started at the beginning of the active phase in the first stage of labor. Stainless steel filiform needles (gauge: 0.25mm diameter by 50mm long) were inserted into the acupoints to depth of 15 mm (Hegu), and 20 mm (Sanyinjiao). When the patients underwent a sore and distending sensation, the needles were retained for 2 mins. Then, the handles of the needles were respectively connected to the electro-acupuncture stimulation apparatus (Model G6805, Shanghai Medical Electronic Apparatus Co, China) at a frequency of 2–100 Hz and electric current of 14–30 mA (tolerable strength) with a dense-and-disperse wave form. The stimulation strength was increased gradually. The needles were removed after 20 minutes. When 7 cms to 8 cms of cervical dilatation was present, the procedure above was performed again.

2. Control group: The patients in the group were under natural vaginal delivery without pain-relief intervention.

A protocol was constructed to assess pain intensity and degree of relaxation throughout the labor. The assessments were consistently obtained every hour. The assessment was numerically based on an 11-point scale. Painless and well relaxed experiences were defined as 0, worst pain imaginable and very tense states were defined as 10. All data were collected and recorded by the midwife in charge of the delivery. At the beginning of the active phase and the end of the first stage, 3ml of blood was removed from the vena cubiti. After 30 minutes static rest, the blood samples were centrifuged at 3000 RPM for 10 minutes, and the resultant sera were kept under −80°C condition.

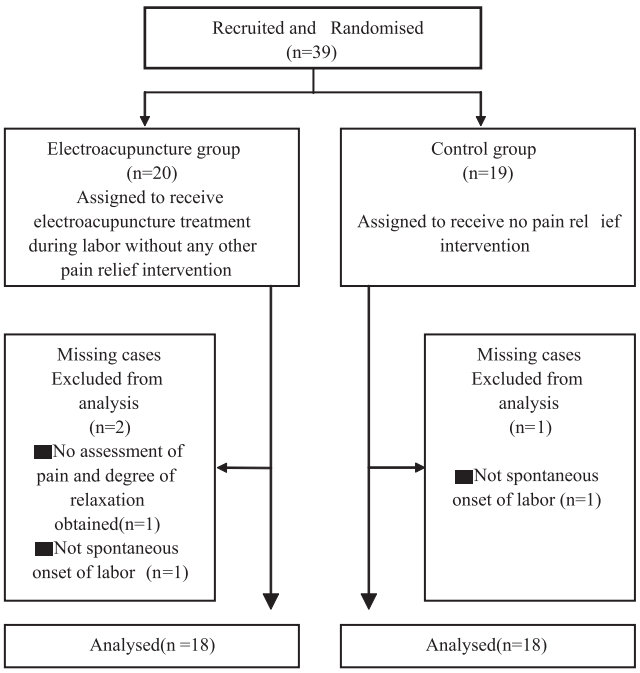

Figure 1. Study design.

Detection index and method

A radioimmunoassay (RIA) method was used to detect 5-HT and β-EP. 5-HT and β-EP reagents were provided by Haikerui Biological Technology Company (Beijing, China) and Lianxing Biological Technology Company (Tianjin, China).

Data analysis

Results were analyzed by an independent university-based statistician. Data were analyzed using the computer software, Statistical Package for Social Sciences (SPSS 10.0 for Windows). To compare the differences of pain and relaxation score between electro-acupuncture group and control group, Mann-Whitney Test, (a kind of Two-Independent-Samples Tests of Nonparametric Test) was used. Comparison of serum β-EP and 5-HT in the peripheral blood were calculated with Student's t test. For all hypothesis tests a 5% significance level ($p < 0.05$) and two-tailed tests were used. Ninety-five percent (95%) Mann-Whitney confidence intervals (CI) for the median difference between electro-acupuncture group and control group were determined.

Results

Patient characteristics

The Patient characteristics prior to any intervention are listed in Table 1 and 2. No significant difference existed in the patient characteristics between the two groups prior to any

Table 1. Characteristics of the primiparas participating in the study

Item	Electro-acupuncture group (n = 18)	Control group (n = 18)	*p*
Maternal age (year)	28.7 ± 3.1	28.9 ± 2.9	0.436
Weight (Kg)	78.2 ± 9.4	77.9 ± 9.6	0.940
Gestational age (weeks)	39.6 ± 1.1	39.9 ± 0.9	0.261
Cervical dilation at admission (cm)	3.5 ± 0.8	3.4 ± 1.1	0.398

Table 2. Ranks:Pain assessment and degree of relaxation at admission (prior to any intervention)

Item	Group	n	Mean Rank	Sum of Ranks	*p*
Pain	Electroacupuncture group	18	17.97	323.50	0.767
Score	Control group	18	19.03	342.50	
(0–10)*	Total	36			
Relaxation	Electroacupuncture group	18	18.00	324.00	0.791
Score	Control group	18	19.00	342.00	
(0–10)*	Total	36			

Note:*0 defined as no pain / quite relaxed; 10 defined as worst pain imaginable/extremely tensed.

Table 3. Ranks: Rating of in-labor pain and relaxation in the two groups

Item	Group	n	Mean Rank	Sum of Ranks	*p*
Pain	Electro-acupuncture group	18	14.33	258.00	**0.018**
Score	Control group	18	22.67	408.00	
(0–10)*	Total	36			
Relaxation	Electro-acupuncture group	18	14.72	265.00	**0.031**
Score	Control group	18	22.28	401.00	
(0–10)*	Total	36			

Note: :*0 defined as no pain/quite relaxed; 10 defined as worst pain imaginable/extremely tensed.
Bolded items show statistically significant results.

intervention. The degree of the pain/relaxed is from 0–10.0 defined as no pain/quite relaxed; 10 defined as worst pain imaginable/extremely tensed. The randomization in the study was successful due to the similarity of the sample data ($p = 0.767$; $p = 0.791$).

Ratings of in-labor pain and relaxation

Ratings of in-labor pain and relaxation in the two groups are shown in Table 3. During labour, the electro-acupuncture group assessed a lower pain intensity and a better degree of relaxation than the control group as there existed significant difference between them ($p = 0.018$; $p = 0.031$).

Table 4. Group Comparison: β-EP (ng/ml)

	Electro-acupuncture group (n = 18)	Control group (n = 18)	*p*
At the beginning of the active phase	1119.61 ± 381.29	1061.46 ± 421.23	0.695
At the end of the first stage	1597.90 ± 275.69	1313.45 ± 521.01	**0.037**

Note: Bolded items show statistically significant results.

Table 5. Group Comparison: 5-HT (ng/ml)

	Electro-acupuncture group (n = 18)	Control group (n = 18)	*p*
At the beginning of the active phase	1917.01 ± 510.97	2068.72 ± 568.71	0.474
At the end of the first stage	2501.32 ± 890.16	2099.19 ± 675.41	**0.030**

Note: Bolded items show statistically significant results.

Serum β-EP

Comparison of serum β-EP between the two groups is shown in Table 4. No significant difference was found between electro-acupuncture group and control group in β-EP concentration in the peripheral blood at the beginning of the active phase ($p = 0.695$). However, at the end of the first stage, there existed significant difference in the concentration of β-EP in the peripheral blood between the two groups ($p = 0.037$).

Serum 5-HT

Comparison of serum 5-HT between the two groups is shown in Table 5. No significant difference was found between electro-acupuncture group and control group in 5-HT concentration in the peripheral blood at the beginning of the active phase ($p = 0.474$). However, at the end of the first stage there existed significant difference in the concentration of 5-HT in the peripheral blood between the two groups ($p = 0.030$).

DISCUSSION

Pain during labor is usually defined as an unpleasant sensory and emotional experience. Electro-acupuncture is a method which now is increasingly being used in China and some other countries. No undesirable side-effect has been observed and it is thought that electro-acupuncture could be an alternative to other methods of pain relief during labor.

Selection of acupoints

In ancient acupuncture practice, Hegu (LI-4) and Sanyinjiao (SP-6) were listed as forbidden acupoints for pregnant women due to their oxytocic effects[7]. The forbidden acupoints for pregnant women were indicated even in the most ancient extant book on acupuncture[7], the *Su Wen (Essential Questions)* of the *Huang Di Nei Jing (The Yellow emperor's*

Internal Medicine) in which an entire chapter is devoted to this topic. Huang Fu Mi's *Zhen Jiu Jia Yi Jing (The systematic Canon of Acupuncture and Moxibustion)*, 3rd century AD lists 24 points of forbidden to acupuncture and moxibustion, and Yang Ji-Zhou's *Zhen Jiu Da Chen (The Great Compendium of Acupuncture and moxibustion)* [7] was published in 1602 AD. Yang Ji-Zhou summarized the forbidden points in two odes[7]. *:Jin Jiu Xue Ge (Ode to the Forbidden Points for Moxibustion)* which lists 45 points, and *Jin Zhen Xue Ge (Ode to the Forbidden Points for Needling)* which lists 32 points. Modern experiments[8-10] have shown that Hegu (LI-4) has a dual effect on the uterine smooth muscle through the regulation of the CNS. Acupuncture on Sanyinjiao (SP-6) which lies within the innervation of L4, can excite the spinal central nerves by stimulating the somatic sensory nerve fibers and by exciting the pelvic neuroplex through sympathetic nerves, resulting in contraction of uterus [9,10]. The pain during labor is mainly caused by uterine contractions. Both Hegu (LI-4) and Sanyinjiao (SP-6) have an effect on the contraction of uterus. Needling the two points can produce the rhythmic coordination of the uterus muscles during the oxytocic process and neuroendocrine alteration[9–15].

Optimal conditions for eliciting maximal electro-acupuncture analgesia with dense-and- disperse wave form

According to the thousand years of experience in acupuncture practice, it is known that different manners of needle manipulation may produce different therapeutic effects, though the scientific mechanisms remain unknown [7]. Some studies[16–25] have indicated that analgesia produced by electro-acupuncture of different frequencies are mediated by different varieties of opioids in the spinal cord: low frequency (2Hz) electro-acupuncture analgesia is mediated by enkephalin and high frequency (100Hz) electro-acupuncture analgesia by dynorphin. Enkephalin and β-EP were mixed μ and δ opioid receptor agonists as the endomorphin was considered as the pure μ opioid receptor agonist [17] and dynorphin the relatively pure κ opioid agonist [18]. Study [19] has suggested that the analgesia induced by 2 Hz electro-acupuncture was mediated by the μ receptor and that of 100 Hz electro-acupuncture by κ opioid receptors. This conclusion was verified later by the use of subtype specific opioid receptor antagonists[20]. The direct evidence [21]was obtained by measuring the neuropeptide release in the CNS triggered by electro-acupuncture of different frequencies. Results have shown that 2 Hz electro-acupuncture produced a 7 fold increase in enkephalin but not dynorphin. In contrast, 100 Hz electro-acupuncture produced a 2 fold increase in the release of dynorphin but not enkephalin. Further studies have shown that β-EP [22] and endomorphin [23] share similar characteristics of a stimulation-induced release profile as enkephalin, i.e. preferable to 2 Hz stimulation, leaving dynorphin as the only opioid peptide responsive to high-frequency stimulation and there was a general consensus that μ and κ opioid receptor agonists possess an analgesic effect [24,25]. These results were primarily obtained in animals and recently verified in humans. One could thus anticipate that if low-frequency stimulation appears alternately with high-frequency stimulation, both enkephalin and dynorphin will be released successively or simultaneously to produce a more potent analgesic effect via a synergistic interaction between the opioid peptides.

β-EP, 5-HT and the mechanism of electroacupuncture for relieving labour pain

β-EP and 5-HT are both neurotransmitters of CNS, which interact with each other and have relationship with the transmission of peripheral pain and contraction of the uterus. Selection of them is based on observed indexes.

β-EP is derived from proopiocortin, in the anterior pituitary gland and is released into the circulation under conditions of pain and stress. The concentration of this increases during unmedicated labor. Abboud *et al*. [26] measured concentrations of β-EP in non-pregnant healthy women, and among two groups of women in established labor: one prior to and after epidural analgesia, and the other before and after saline. β-EP concentration decreased by 50% in those who received epidural analgesia whereas there was no significant change in those who received saline. The finding suggests that labor pain is an important factor in causing β-EP release during labor. Thomas [27] et al also found that serum β-EP concentration increased during labor and the increase was significantly greater among women who received nitrous oxide than those who received intramuscular pethidine or epidural analgesia.

Studies have demonstrated that acupuncture-mediated analgesia is modulated through a central mechanism involving neurohumoral pathways. The stimulation of the acupuncture point by needling, selectively activates myelinated nerve fibers [28–30]. This subsequently results in the activation of certain neurons in the spinal cord and supraspinal regions, including neurons in the deep layers of spinal dorsal horn, [31-33] the nucleus raphe magnus in the brain stem,[34] and the hypothalamus and thalamus [35,36]. These neurons modulate pain by inhibiting neurons located at the superficial layer of the dorsal horn and small unmyelinated fibers [31,33,37] as well as releasing neurotransmitters, such as β-EP and 5-HT [38-48].

Opioid peptides bind to their receptors on central neurons and produce analgesic effects [49]. However, whether, and to what extent, the peripheral release of opioids plays a role in acupuncture analgesia has not been investigated. Two lines of evidence suggest that acupuncture-induced peripheral opioid release is possible. First, acupuncture has been shown to modulate immunological activities,[50–58] and immune cells are a key component of the peripheral opioid system. Second, central opioid mechanisms do not explain why needling an acupuncture point adjacent to a painful area, a common clinical practice, is generally more effective in relieving pain

than needling remote areas, a phenomenon that is consonant with the presence of a localized analgesic mechanism. Endogenous morphine release has been described as a possible mechanism of acupuncture-mediated analgesia [59]. This is confirmed by our data.

Electro-acupuncture relieves pain through regulation of CNS and contraction of the uterus

Clinical research has shown that after electro-acupuncture, the release of β-EP into the peripheral blood improved and patients' labor pain was alleviated. The release of β-EP represents a natural mechanism for the modulation of stress. β-EP can antagonize and coordinate contraction of uterus caused by oxytocin. The increased release of β-EP into the peripheral blood after electro-acupuncture, which is greater than natural vaginal delivery, activates an endogenous analgesia system and lessens the afferent sign of labor pain and increases the tolerance to labor pain. One might then believe that increasing the release of β-EP into the peripheral blood is one mechanism of the electro-acupuncture in relieving labor pain. It is through regulating the CNS and the contraction of uterus that β-EP plays a significant role in relieving labor pain with electro-acupuncture.

5-HT functions through the CNS to relieve labor pain with electro-acupuncture

Prior to the discovery of endogenous opioids, Han [60] focused on various candidate neurotransmitters including monoamines, and found that 5-HT was most important among classical neurotransmitters for the mediation of acupuncture analgesia. 5-HT is released from platelets due to tissue damage or ischemia and participates in pain mediation via the 5-HT_3 receptor. A previous study [61] has shown that high levels of 5-HT in the masseter muscle was associated with pain and allodynia/hyperalgesia in patients with chronic myalgia. It also seems that circulating 5-HT may be involved in determining the mechanical pain threshold over healthy muscles, since a high level of 5-HT was associated with a low pressure pain threshold (PPT) in healthy subjects [62]. Electro-acupuncture can increase the concentration of 5-HT in peripheral blood and the CNS, as electro-acupuncture can improve the concentration of tryptophane in blood which is a necessary precursor to combine 5-HT. As a consequence, this improves the permeability of blood-brain barrier [63]. The study has shown that it is through the CNS that 5-HT functions in relieving labor pain with electro-acupuncture.

Conclusions

The electro-acupuncture group was found to exhibit a lower pain intensity and a better degree of relaxation than the control group and electro-acupuncture can improve the concentration of β-EP and 5-HT in the peripheral blood. The effect of electro-acupuncture for relieving labor pain may be produced by the synergism of CNS through increasing the release of β-EP and 5-HT into the peripheral blood, and that there is a direct impact of electro-acupuncture on the uterus.

Electro-acupuncture may provide an effective alternative to pharmacological as well as non- pharmacological labor pain relief. It may be useful for those women who want to avoid or delay pain medications or in settings where pain medications are not available or cost prohibitive.

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