Ideal Parameters for Electroacupuncture Analgesia: A Review of Neurophysiological and Clinical Evidence

Zhen Zheng (B Med), Chinese Medicine Unit, RMIT University, Bundoora, Vic 3085

Abstract

Electroacupuncture (EA) is getting more attention as a method of producing analgesia. However, parameters used in EA vary greatly among studies. In the present paper, neurophysiological and clinical studies on ES analgesia were reviewed in order to provide a set of ideal parameters for EA analgesia. The release of endogenous opioid peptides depends on the frequency of EA. Alternating frequency (2/15 Hz or 2/100 Hz) may enhance the analgesic effect and reduce the risk of opioid tolerance. Given a certain frequency, intensity is the most important parameter. EA at strong but tolerable levels induces strong and long analgesia. Depth of stimulation appears to be important in the depth of analgesia. For relieving pain at deep muscle or viscera, EA with needles should be used. Traditional acupoints may offer extra analgesic effects, however, studies are needed to clarify the role of acupoints.

Introduction

Acupuncture has been practised in China for more than 3,000 years, and has been used in conjunction with Chinese herbal medicine in controlling or relieving many medical problems, such as various types of pain, stroke rehabilitation, muscle weakness, insomnia, common cold, asthma, indigestion, urination infection, irregular menstruation and so on. The traditional form of acupuncture involves selecting acupoints according to Chinese medicine principles, inserting fine needles into acupoints and manipulating needles with certain techniques, such as twisting and lifting, to achieve “De Qi” (arrival of Qi) sensation, which includes heaviness, numbness, distension or warmth. “Qi” is one of the essential concepts in Chinese medicine, and is considered to be the metaphysical understanding of human body and body functions (Ulett et al. 1998). According to traditional Chinese medicine (TCM), Qi sustains human life and the movement of Qi enables physiological and psychological functions. Normal functions depend on the fluent movement of Qi. Acupoints are the loci where Qi is in and out of the body to connect with the nature. Acupoints are also the place where Qi of body can be regulated by administering treatment, such as acupuncture, moxibustion and massage, onto such loci. TCM books record 365 loci over a human body. Each point is said to have its specific functions.

With the introduction of modern technology and neurophysiological studies into acupuncture, some practices of acupuncture have been challenged and modified. Electroacupuncture (EA) is a typical example and was first practised in Japan and France between 1800s and (Ulett and Nichols 1996). Instead of using needles or manually manipulating the needles, practitioners apply electrodes onto the acupoints directly or attach the outlet of an electrical device to the handle of a needle, thereby allowing electrical current to pass through acupoint (s).

Obviously, there are several advantages in using EA. Firstly, unlike the manual manipulation, electrical stimulation can be easily controlled and reliably repeated. Secondly, an electrical current has a set of parameters that can be manipulated. Different sets of parameters may produce different physiological effects, therefore treatment may be more specific. For instance, EA of different frequencies (2, 15, and 200 Hz) has been shown to increase the release of three types of opioid peptides, respectively (Han 1989; Han et al. 1991). In clinical practice, it is recommended to use alternating frequencies, such as 2/15 Hz, or 2/100 Hz to reduce opioid tolerance and enhance analgesia (Han 1989). Finally, it has been reported that EA produces better analgesic effect than manual acupuncture (Wang et al. 1992). Nowadays EA is so widely practised that the term “acupuncture” in many papers often means EA (Carlsson and Sjölund 1994; Chapman et al. 1983b; Dawidson et al. 1998; Gerschman and Wikström 1984; Kho et al. 1991; Price et al. 1984).

EA may be conducted in several forms: with needles or without needles, stimulating traditional acupoints or acupoints that have neural backgrounds, such as trigger points or tender points. The form of EA may also vary according to electrical parameters, such as frequency, intensity, pulse duration and size of
electrodes. Among the literature, there is no consistent understanding of the ideal parameters of EA. Thus, the aims of the paper were to review the role of each parameter in EA and to provide background for searching for the ideal set of parameters. Because the neurophysiology studies have been focused on EA analgesic effect, this paper would discuss the ideal parameter within the limit of analgesia.

**Frequency-dependent release of endogenous opioids peptides**

Endogenous opioid peptides are an essential part of pain modulation systems. Increased release of opioids is understood to be the underlying neural mechanism for analgesic effect induced by acupuncture, certain modes of transcutaneous electrical nerve stimulation (TENS) and exercises (Thorén et al. 1990, for review). The endogenous opioids can be divided into endorphins, enkephalins and dynorphins. These three types of opioids have different levels of affinity to three types of receptors, i.e., µ, δ and κ (Table 1). Exogenous opioid substances have their preferential binding to different types of opioid receptors. Morphine is known to have high affinity to µ receptors while benzomorphan opiates bind to κ receptors (Nestler 1997).

EA can increase the release of all three types of endogenous opioids, however, the type of the opioid peptide released depends on the frequency of electrical stimulation (Table 1). In rats, analgesia induced by EA of 2 Hz on ST 6 and SP 6 points is abolished by naloxone of 1 mg/kg, but analgesia induced by 100 Hz can only be abolished by 10 to 20 times the dose of naloxone. Moreover, there is no cross-tolerance between EA of 2 Hz and of 100 Hz, indicating different types of opioids peptides are involved. Studies with radioimmunoassay have shown that immunoreactive met-enkephalin (ir ME) increased in rats after 2 Hz EA, and ir dynorphin increased after 100 Hz EA. β-endorphin is also involved in analgesic effect induced by 2 and 15 Hz EA, but not by 100 Hz EA (Han 1989). The frequency-dependent opioid release is also confirmed in humans. The level of ir ME and ir dynorphin A in the cerebrospinal fluid is enhanced by 367% and 49%, respectively after 2 Hz and 100 Hz TENS on acupoints (Han et al. 1991).

A recent study examined the frequency of EA on clinic-like pain. Subcutaneous injection of formalin into forepaws of rats induces two phases of responses: an early-phase response resulting from direct stimulation of nociceptors, which lasts for 5 mins and an late-phase inflammatory response which happens 20 mins after an injection and lasts for 20-30 mins. Stimulating sciatic nerve with 2 or 15 Hz produces anti-nociception on both early and late-phases responses. In contrast, stimulation with 100 Hz produced a strong anti-nociception effect on the late phase only. The results of the study confirm that frequency-dependent analgesic effect of electrical stimulation (ES) also applies to clinic-like pain. Furthermore, compared to post treatment, pre-treatment with 2 Hz produces stronger analgesic effect on late-phase response (Hsieh et al. 2000).

**Table 1** A summary of endogenous opioids and their relationship with the frequency of EA.

<table>
<thead>
<tr>
<th>Peptide</th>
<th>Site</th>
<th>Opioid receptor</th>
<th>F (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-endorphin</td>
<td>Brain, not in SC</td>
<td>µ, blocked by LD NAL</td>
<td>2 &amp; 15</td>
</tr>
<tr>
<td>Enkephalins</td>
<td>Brain &amp; SC</td>
<td>δ; blocked by HD NAL</td>
<td>2</td>
</tr>
<tr>
<td>Dynorphins</td>
<td>SC (DH), not brain</td>
<td>κ; blocked by HD NAL</td>
<td>100</td>
</tr>
</tbody>
</table>

NAL - naloxone; SC - spinal card; DH - dorsal horn; LD - low dose (1 mg/kg); HD - high dose (10-20 mg/kg).

So far, no evidence is available on which frequency should be used under what condition. However, the studies described above have several implications for clinical practice.

1) Alternating the frequency of EA between 2/15 Hz or 2/100 Hz can reduce risk for developing tolerance to endogenous opioid and achieve better analgesia (Han 1989);

2) Both morphine and β-endorphin bind to µ receptors. Cross-tolerance between low frequency EA and morphine has been shown (Han 1989). Thus, when treating patients who are under morphine treatment, one should avoid using 2/15 Hz EA only, instead 2/100 Hz is recommenced to reduce the risk of cross-tolerance.
The role of pulse duration

Pulse duration is another parameter that may affect EA analgesia. A recent study by Romita and colleagues examined the effects of EA parameter on tail withdrawal reflex to noxious radiant heat in rats (Romita and Henry 1997). Withdrawal latency is considered to be the pain threshold, with an increased latency indicating analgesia. Given a certain frequency (4 Hz) and intensity (20 times threshold, 20T), ES with 0.2, 2 and 5 ms shortened the latency, however, only ES with 2 or 5 ms produced up to one hour antinociception effect.

The underlying neural mechanisms for pulse duration-related analgesia may depend on different afferent fibres activated. ES with 2-50 µs pulse duration mainly evokes sensation, but not pain (sensory-level); ES over 0.15 ms may evoke muscle contraction, and further activate Aδ afferent fibres in the muscles (motor-level); and ES with over 1.0 ms activates C fibres and produces painful sensation (noxious-level) (Howson 1978; Snyder-Mackler 1989). Of course, the intensity of ES is also important in the three levels of stimulation, and this issue will be discussed in the next section. The induced analgesia effect by the sensory-level stimulation does not outlast ES stimulation, while analgesia induced by motor or noxious stimulation lasts hours. Thus, in Romita et al (1997), ES with 2 or 5 ms most likely excites C afferent fibres, and further activates endogenous pain inhibition systems and produces the persistent analgesia effect. In contrast, ES with 0.2 ms may activate Aδ fibres. However, the authors did not report whether this type of stimulation evoked muscle contraction. In addition, the stimulation only lasted for 20 minutes, much shorter than required stimulation time, 30-45 minutes for motor-level stimulation. Thus, the transient analgesia may be induced via segmental pain control.

Intensity-related analgesic effect

Intensity may be the most important parameter in EA analgesia (Chakour 1998; Romita and Henry 1997; Wang et al. 1997). ES of high intensity that induces “strong but tolerable” or “strong but comfortable” sensation produces more satisfactory analgesia than ES of low intensity. This is true no matter if needles are used or not, or if the ES is at low frequency (Romita and Henry 1997), high frequency (Chakour 1998) or an alternating frequency (Wang et al. 1997).

In rats, ES with 4 Hz at 10 times the threshold to induce muscle twitch (10T) induces only a brief increase in tail withdrawal latency while ES at 20T provokes both a brief and a persistent antinociception up to one hour (Romita and Henry 1997). When EA is used for assisting patient-controlled analgesia (PCA) to manage postoperative pain, EA with high intensity (9-12 mA) reduced both PCA hydromorphine requirement and opioid-related side effect after surgery. In contrast, the effect of PCA and EA with low intensity (4-5 mA) was not statistically significant from that induced by PAC and sham EA (Wang et al. 1997).

Size of electrodes

When EA with needles is practised, an electrical device is connected to the handle of needles, and therefore, there is no issue about size of electrodes. However, there is a tendency to avoid the use of needles and to replace needles with electrodes to conduct TENS over acupoints (Gadsby et al. 1997; Hyodo et al. 1980; Shirakabe et al.; Wang et al. 1997). Thus, the size or the shape of electrodes may be a factor in EA analgesia.

In the practise of electrotherapy, the selection of electrode size or shape usually depends on the area of stimulation. The smaller the size of electrode, the higher the current density is under the electrode. A smaller electrode size also requires less amount of current to stimulate certain tissue (Myklebust and Robinson 1989).

A recent study examined three type of TENS electrodes: a cone-shape metal electrode with a diameter of 13 mm, a rubber electrode with 13-mm in diameter and a gelatinous electrode with 50 * 150 mm in size (Ishimaru et al. 1995). Electrical pain threshold was tested before and after a 30-min treatment in humans. TENS (100 Hz and intensity at just below pain tolerance) with two smaller electrodes increased skin and fascia pain threshold, while TENS with a soft, large electrode increased skin pain threshold only. The shape of electrode might not be important, however, a small electrode may produce analgesia in relatively deep tissue.

Depth of stimulation - the role of needles

The advantages of using transcutaneous electrical stimulation are obvious. This practise is non-invasive, not having the side-effect of needles, such as infection and slow healing,
easy to be accepted, and easy to apply. It has also been claimed that EA without needles is as effective as with needles (Wang et al. 1997). However, needles insertion have its own advantage, that is depth of stimulation.

Ishimaru and colleagues (1995) examined the analgesic effect of TENS and EA with needles on pain in four layers, skin, fascia, muscle and periosteum. Acupuncture needles were inserted to a depth of 30 mm and were connected to a electrical device (100 Hz, 1 ms, intensity at below pain tolerance), TENS increased pain threshold at skin and fascia, and EA with insulated needles increased pain threshold in muscle and periosteum. A TENS study on post-caesarean pain confirms that TENS is effective in reducing cutaneous pain, but not visceral pain (Smith et al. 1986). These results suggest that the depth of stimulation is related to the depth of analgesic effect. Deep muscle pain, pain in the joint or visceral pain may be more effectively managed with EA with needles than EA without needles.

It has been suggested that Acupuncture produces local as well as general analgesic effect. However, only pain threshold at the EA or TENS treatment area was measured in the study Ishimaru et al (1995). It would be of great interest to assess pain threshold at different depths on remote parts of the body. The result may provide evidence for the relationship between the depth of stimulation and the degree of general analgesia.

The role of acupoints
Acupoints are considered to be the essential part of acupuncture. However, the concept of acupoints has been challenged. It has been pointed out that acupoints are highly correlated with trigger points (Melzack et al. 1977) and motor points (Ulett and Nichols 1996). Some has gone further and claimed “acupuncture points, in the traditional sense, do not exist” (Mann 2000, p. 3). Indeed, so far no physiological evidence is available for the existence of acupoints, except for lower skin resistance to electrical current. The reduced skin resistance is also true to motor or trigger points, and provides ideal condition for electrical stimulation.

The crucial issue about acupoints is not about where the acupoints are or whether they are correlated with trigger or motor points, but whether the underlying theory about Qi, about Yin and Yang balance is true and whether acupuncture treatment produces the effect as the theory claims. Argument about TCM theory is beyond the scope of the current paper. There is, however, limited evidence to show that transcutaneous electrical stimulation over acupoints produces better pain relief in chronic low back pain patients than TENS with a criss-cross electrode placement at lumbar area (Aquilante and Snyder-Mackler 1986).

To better answer the question of whether acupoints should be included as a factor in EA analgesia requires systematic studies of several issues: 1) a comparison of analgesia induced by acupoints selected according to TCM theory versus those selected according to neural anatomy; 2) a comparison of analgesia induced by traditional acupoints, but not trigger or motor points versus those acupoints that are also trigger and motor points; 3) a comparison of analgesia induced by acupoints versus conventional TENS. Results of these studies will provide a clearer picture of whether EA analgesia is purely due to the co-occurrence of acupoints and motor or trigger points. Last, let us not forget that the correlation between acupoints and motor or trigger points was generated from acupuncture analgesia studies. Acupoints may have specific effects in relation to other physiological functions that are regulated by acupuncture, such as blood pressure, breath, sleep pattern etc.

The ideal parameter of EA analgesia
In practise, EA analgesia may be applied in the following conditions:

1) patients who suffer from pain and would like to have acupuncture;
2) patients who need analgesia for a small operation or dental surgery but cannot have conventional analgesics. It has been reported that EA successfully induced analgesia for a dental surgery in a patient who had multiple allergies (Gerschman and Wikström 1984);
3) patients who want or need to reduce the side effects that are associated with narcotics. A study has shown that using EA in conjunction with narcotics can reduce the dose of analgesics and eliminate the side effects that are brought by such drugs (Kho et al. 1991; Wang et al. 1997; Wang et al. 1997).

In conclusion, the ideal parameter of EA may vary according to the patient condition. Alternating frequency can increase the release of various types of endogenous opioids and reduce the risk of opioid tolerance that is often
seen in pain management with narcotics. EA of 2 Hz before a surgery may assist the management of post-operative pain. Intensity of stimulation is recommended to be kept at strong but tolerant level in order to achieve better and longer analgesia. Smaller electrodes may be helpful in treating a relatively deep pain. For relieving pain at the deep muscle or viscera, EA with needles should be used. Traditional acupoints may offer extra analgesic effect, however, this needs further studies.

References


Howson, D.C., Peripheral neural excitability - implication for transcutaneous nerve stimulation, Physical Therapy, 58 (1978) 1467-1473.


Hyodo, H., Kataoka, K., Miyazaki, T., Inamori, K. and Hyodo, M., Combination application of SSP anesthetics with general anesthesia or conduction anesthesia, Easter Medicine and Pain Clinic, 10 (1980) 1-6.


Shirakabe, T., Shirakabe, Y. and Hyodo, M., Acupuncture (SSP therapy) practical use for anesthetic & plastic surgery (pain - sedation & swelling). In: T. Kitade (Ed.), Recent
Wang, J.Q., Mao, L. and Han, J.S., Comparison of the antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat, International Journal of Neuroscience, 65 (1992) 117-129.