

Acupuncture and Chronic Pain Management

T L Lee,**FAMS, M Med (Anaes), FANZCA*

Abstract

Introduction: Although acupuncture has been widely used to treat a variety of pain conditions, convincing scientific evidence for its efficacy is lacking. Earlier randomised controlled trials attempted to follow a double-blind, placebo-controlled model. This approach has encountered many problems such as the virtual impossibility of blinding the acupuncturist and the uncertainties inherent in choosing control acupuncture points. The objective of this review is to assess if acupuncture is an effective treatment for chronic pain. In addition, a number of key methodological issues that arise in the controlled evaluation of acupuncture will be discussed. **Methods:** This review is based on the result of previous reviews, meta-analyses and consensus conference. The search was performed with MEDLINE (from 1966), EMBASE (from 1980) and Cochrane library (1999, volume 1). Only randomised trials of acupuncture (involved needling) for subjects with chronic pain published in English were included. **Results:** Basic science research has demonstrated convincingly that at least in the context of acute pain, acupuncture's effects are related to the release of a variety of natural opioids. Acupuncture has been shown to be effective for postoperative dental pain. There are reasonable studies showing relief of pain with acupuncture on diverse pain conditions such as menstrual cramps, tennis elbow, low back pain and fibromyalgia. This suggests that acupuncture may have a more general effect on pain. However, there are also studies which provide equivocal results because of design, sample size and other factors. The issue is further complicated by inherent difficulties in the use of appropriate controls, such as placebo and sham acupuncture groups. **Conclusion:** As most of the studies were of poor methodological quality, there is a need for further high quality randomised controlled trials. Future studies should also have larger sample sizes, use a valid acupuncture treatment, and have both a short-term and long-term follow-up.

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Introduction

Acupuncture is a component of the health care system of China that can be traced back for at least 2500 years. The general theory of acupuncture is based on the premise that there are patterns of energy flow (Qi) through the body that are essential for health. Disruption of this flow is believed to be responsible for disease. The acupuncturists can correct imbalances of flow at identifiable points close to the skin. Acupuncture describes a family of procedures involving stimulation of anatomical locations on the skin by a variety of techniques. The most studied mechanism of stimulation of acupuncture points employs penetration of the skin by thin, solid, metallic needles, which are manipulated manually or by electrical stimulation. The comments in this review are based on data that arises from such studies.

During the past 20 years or so, a growing database of clinical trials has produced a clearer picture of how effective acupuncture can be for treatment of a variety of pain conditions. While researchers have attempted to follow a double-blind, placebo-controlled model when testing

acupuncture, this approach has encountered many problems and has left many questions unanswered. Two of the difficulties encountered were the virtual impossibility of blinding the acupuncturist and the uncertainties inherent in choosing control acupuncture points. Inadequate solutions to these methodological problems have often resulted in clinical trials of questionable quality. Thus, when reviewing an acupuncture efficacy trial with a reported negative outcome, it is crucial to determine the extent to which the outcome was due to poor study design rather than to an actual failure of acupuncture to ameliorate the condition.¹

This article will address a number of key methodological issues that arises in the controlled evaluation of acupuncture for the treatment of chronic pain; offer some suggestions as to how these issues may be addressed.

Sources of Bias in Acupuncture Controlled Clinical Trial (CCT)

This subject was reviewed recently by Lewith and Vincent.² Firstly, trials of acupuncture have to be single blind. Inevitably the clinician giving the acupuncture

* Senior Consultant

Department of Anaesthesia, National University Hospital

Address for Reprints: Dr Lee Tat-Leang, Department of Anaesthesia, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074.

E-mail: analeetl@nus.edu.sg

TABLE I: ACUPUNCTURE CONTROL CONDITIONS AND THEIR PURPOSES [adapted from Lewith and Vincent² and Hammerschlag¹⁰]

Control Condition	Description	Question addressed	Comments
No treatment	Monitoring of waiting list or no treatment group	Are observed changes simply due to the passage of time?	Possible to show that effects not due simply to passage of time; no information about placebo effects or comparison with other treatments
Sham (mock) acupuncture	As true acupuncture except with altered point location; needles approximately half inch from usual location; depth and stimulation the same	Is point location an important determinant or effect of acupuncture?	Mistakenly used in many trials involving chronic pain as placebo equivalent, with consequent misinterpretation of results; huge subject numbers needed to detect difference to true acupuncture
Minimal acupuncture	Acupuncture away from usual locations, very shallow needling, and very slight stimulation	Is acupuncture more effective than placebo? (Strictly speaking, more effective than a near-placebo)	Advantage: almost exact semblance of true acupuncture; disadvantage: may have slight effect
Placebo acupuncture needle ¹¹	Specially designed needle with a blunt tip. The needle is not fixed inside the handle, the needle moves inside the handle when it touches the skin and appears to be shortened.	Is acupuncture more effective than placebo?	Advantage: exact resemblance of true acupuncture with no skin penetration. Not tested in clinical trial yet
Mock TENS (placebo controls)	Transcutaneous nerve stimulation (TENS) with surface electrodes, but no current passing; may be enhanced with additional monitors, etc.	Is acupuncture more effective than placebo?	First attempt to address problems associated with sham acupuncture; advantage: completely inert, hence excellent placebo; disadvantage: may be perceived differently from acupuncture by trial subjects
Alternative treatment (standard care comparisons)	Usually comparison with standard treatment (e.g. physiotherapy, medication or medical device)	Does acupuncture have any advantage/disadvantage over standard treatment in terms of efficacy, adverse effects, cost?	Valuable for assessing direct clinical consequences of different treatment policies
Adjunctive care comparisons	Assess the efficacy of acupuncture plus standard care relative to standard care alone	Is acupuncture plus best standard treatment more effective than standard treatment alone?	All patients received standard care. The non-specific effects of acupuncture are not addressed

treatment is aware of which is the true treatment and which is the control.

Secondly, there is difficulty with the control procedure, particularly if it is of a different form from the true treatment (which is neither a drug nor a surgical intervention). This itself may have a different psychological impact. A bewildering variety of control procedures have been used in acupuncture trials. In the most commonly used control treatment, needling is carried out at incorrect, theoretically irrelevant sites. Usually this simply means carrying out a procedure similar to the real treatment at nearby, non-classical locations. Depth of insertion and stimulation are the same; only location differs. This procedure, which is termed “sham” or “mock” acupuncture, has been used as a placebo in many studies.³⁻⁵ Sham acupuncture was initially assumed by most investigators to be ineffective and, therefore, ideal as a placebo. However, Lewith and Machin⁶ had shown that sham acupuncture appeared to have an analgesic effect in 40% to 50% of patients compared with

60% to 75% for real acupuncture and 30% to 35% for placebo (control). There is doubt whether acupuncture points and non-points can be reliably distinguished.⁷ Even if they can, there is evidence that acupuncture at non-classical locations may have analgesic effects.^{8,9} A sham acupuncture control condition really only offers information about the most effective sites of needling, not about the specific effect of acupuncture. A summary of questions addressed in clinical acupuncture research regarding the appropriate control group is shown in Table I.^{2,10,11}

Efficacy of Acupuncture for Pain Based on Results of CCT

Although the status of acupuncture as a treatment for chronic pain has been extensively assessed, according to contemporary research standard, there is paucity of high quality research assessing efficacy of acupuncture compared with placebo or sham acupuncture. The majority of papers studying acupuncture in the biomedical literature consist

of case reports, case series, or intervention studies with designs inadequate to assess efficacy. Richardson and Vincent¹² reviewed controlled trials of acupuncture versus placebo (minimal acupuncture or mock TENS) published in English language before 1986. There are only 12 studies that involved treatment of a variety of pain disorders. Of these, only 5 showed a significant advantage of acupuncture over placebo, though several others showed a non-significant advantage. However, these trials were very small, with 4 involving fewer than 20 subjects. It is doubtful if many of them have sufficient power to conclude that a non-significant result definitely shows acupuncture to be equivalent to placebo. The probability of a Type II error—failing to detect an actual difference—is high. The results of these trials suggest that acupuncture is ineffective in post herpetic neuralgia and angina, that acupuncture may well be helpful for low back pain, and that its efficacy for migraine remains to be solved. The results need cautious interpretation because of these limitations.

Two meta-analyses of the literature on chronic pain have been reported. The purposes of such a procedure include increasing overall statistical power, resolving uncertainty between conflicting reports and improving estimates of the size of the effect being investigated. However, it should be emphasised that although these techniques have the potential for resolving questions about the efficacy of acupuncture, they cannot compensate for the poor quality of studies they set out to combine. In other words, if the placebo control is unsatisfactory in the original studies, then biased estimates will be reproduced in the final meta-analysis. Patel and colleagues¹³ reviewed all randomised controlled trials of acupuncture for chronic pain that measured outcome in terms of the number of patients who improved. Because of the difficulties in finding studies similar enough to pool, only 14 trials of various chronic pain problems were included. The authors concluded that “results favourable to acupuncture (for chronic pain) were obtained significantly more often than chance alone would allow”. A more comprehensive meta-analysis, and the most recent review available, was produced by Ter Riet et al.¹⁴ They decided not to attempt a statistical pooling of results, arguing that the studies were on the whole too poor and too disparate to allow their results to be combined. Their report is therefore perhaps best considered a critical review on the issue of study design in acupuncture clinical trials. Because their analysis revealed that few studies were methodologically sound, they concluded that (as of 1989), “the efficacy of acupuncture in the treatment of chronic pain remains doubtful”. This conclusion was criticised by Morris¹⁵ on the ground that treatment plan and outcome were assumed to be independent variables. He pointed out that their methodological criteria for scoring studies did not include adequacy of treatment (only the adequacy of the description

of the treatment was scored). Thus, an individual study may receive a good score overall but have a poorly designed (though adequately described) treatment plan which undertreats the patients, leading to a negative result.

In another analysis of clinical trial design, Birch et al¹ evaluated the quality and adequacy of the acupuncture treatments in 29 head, neck and back pain studies. Their first major finding was that acupuncture employed as the test treatment was often inadequate. The more adequate the treatment, the more likely the study will reveal positive outcome. The converse also held. Further, after sorting the studies on the basis of control treatment employed, they found that the clinical trials comparing acupuncture to standard therapy (TENS, medication, or physiotherapy) had a higher proportion of positive results (acupuncture performed at least as well as standard therapy) than did trials comparing acupuncture to some form of “control” needling. Thus, similar to the findings of Lewith and Machin,⁶ a reported lack of significant difference between test and control groups could mean that the control needling might also have induced positive effects (see *vide infra* on endorphins mechanism and diffuse noxious inhibitory control). This may also suggest that point location might be an important variable in the treatment of chronic pain.

An important recent event was the Consensus Development Conference held by the United States National Institutes of Health (NIH) in November 1997.¹⁶ The consensus panel evaluated existing clinical research and weighed the strength of the data supporting acupuncture for the treatment of various clinical conditions. The panel, after hearing presentations from experts in various areas, concluded that there is evidence that needle acupuncture treatment is effective for postoperative dental pain (among other conditions). In addition, acupuncture may be effective as an adjunct therapy, as an acceptable alternative, or as part of a comprehensive treatment programme for headaches, menstrual cramps, tennis elbow, fibromyalgia and low back pain.

The studies reviewed so far were clinically very heterogeneous, there was a large variety of the types, locations and duration of disorders, the interventions (types of acupuncture) and the outcomes measured. Furthermore, the outcomes were poorly presented in many studies to the extent that pooling was not possible. Further larger scale, high quality clinical studies focusing specifically on the effectiveness of acupuncture for specific type of chronic pain (e.g. low back pain, headache, osteoarthritis) are warranted.

Mechanism of Acupuncture Analgesia

While it is still unclear what exact mechanism underlying the action of acupuncture, Western scientific research has

proposed mechanisms for the effect of acupuncture on pain relief. It has been suggested that acupuncture might act by principles of the gate control theory of pain.¹⁷ One type of sensory input (backache) could be inhibited in the central nervous system (CNS) by another type of input (needling).^{18,19} The same needling sensation has also been suggested to activate two descending neuronal mechanisms. The first of this is serotonergic and the second noradrenergic.^{18,19} Another theory, the diffuse noxious inhibitory control (DNIC) implies that noxious stimulation of heterotopic body areas modulates the pain sensation originating in areas where a subject feels pain.^{20,21} There is convincing evidence that acupuncture stimulates the production of endorphins, serotonin and acetylcholine within the CNS thus enhancing analgesia.²²⁻²⁹ All these proposed mechanisms may explain why “sham acupuncture” can produce some analgesic effect. In addition, there is evidence to show that placebo effect appears to evoke responses by increasing endogenous opioids.³⁰ A recent systematic review has confirmed that the placebo effect is mediated via endogenous opioids.³¹ Therefore, it may be difficult to delineate the placebo effect from the acupuncture effect, as both treatments seem to share common pathways in analgesia.

Future Direction

With the recent development of positron emission tomography (PET) and functional magnetic resonance (MR) imaging technology, many secrets of brain functions are being revealed but they still remain qualitative rather than quantitative. Nevertheless, these technologies are useful to examine the effect of body acupuncture on brain physiology. Wu et al³² characterised the CNS pathway for acupuncture stimulation in the human brain using functional MR imaging. They demonstrated that acupuncture performed at LI.4 (*Hegu* acupoint) and ST.36 (*Zusanli* acupoint) (both acupoints are known to cause analgesia) activates structures of descending antinociceptive pathway (hypothalamus and nucleus accumbens), and deactivates multiple limbic areas subserving pain association. Control stimulations did not result in such activations and deactivations. Such studies will be very useful for future investigations of endogenous pain modulation circuits in the human brain. Cho et al³³ also demonstrated that both the static and dynamic activation of the visual cortex by acupoints (specific for the treatment of eye disorders) are consistent with visual light stimulation previously observed by functional MR imaging.

Conclusion

For the past 25 years, studies have demonstrated the physiological and neurobiological basis of analgesic effect of acupuncture. These studies demonstrate convincingly

that acupuncture's effects are related to the release of a variety of natural opioids (and other monoamines). However, these findings are supported almost exclusively by evaluating acupuncture in the context of acute pain within an animal model and sometimes on humans. It is quite probable that chronic pain has different underlying mechanisms to that involved in acute experimental pain in animals and humans.

Although the status of acupuncture as a treatment for chronic pain has been extensively assessed, the evidence is at best equivocal. Many of the trials are methodologically flawed (including trials which do not show a positive outcome). To meet the increasing demand for evidence-based complementary medicine, the validity and credibility of acupuncture can only be established by using research designs that embody the highest standards for demonstration of efficacy: randomised controlled trials, taking into account the unique considerations that acupuncture has when it comes to blinded prospective studies and controlled conditions. In many acupuncture trials, patients in the acupuncture group received a fixed protocol treatment (same acupoints, same number and duration of sessions) that was based on biomedical diagnostic criteria. In contrast, the clinical practice of acupuncture involves individualised acupoint selection, based on patient-specific systemic imbalances informed by Oriental medical diagnostic procedures. Serious consideration should thus be given to the argument that most clinical trials of acupuncture have undervalued its efficacy.¹⁰

An increasing number of research grants have been given in the past few years. The NIH has funded a US\$1 million grant for a 3-year trial of acupuncture for knee osteoarthritis. Three additional grants were awarded recently for back pain, dental pain and depression. In the UK, the NHS Health and Technology Assessment Research and Development Programme awarded the Research Council for Complementary Medicine a 2½-year grant to evaluate acupuncture for the management of headache.³⁴ A Cochrane Complementary Medicine Field has been established within the Cochrane Collaboration since 1996 to produce, maintain and disseminate systematic reviews on topics pertaining to complementary medicine. Three systematic reviews on acupuncture for low back pain, headache and osteoarthritis are currently in progress.³⁵ These systematic reviews, supported by high quality studies with sufficient number of patients and appropriate control, will provide evidence-based answers to the role of acupuncture in various chronic pain conditions in the near future.

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