

원저

## Review of Pragmatic Clinical Trials on Acupuncture

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### Abstract

**Background** : Over the last thirty years, majority of researches on clinical effectiveness of acupuncture have been explanatory (or experimental) randomized controlled trial. The benefits of acupuncture in clinical trials are still controversial and most studies concluded that further control studies were required. Standardized combinations of acupuncture points for all the experimental subjects in various past studies have been criticized because such treatments do not reflect current routine clinical treatment.

**Objective** : This paper aims to review pragmatic clinical trials on the effect of acupuncture treatment and to develop the ideal clinical research methodology of acupuncture study.

**Method** : Clinical studies of acupuncture relevant with pragmatic or individualized trials were searched mainly in Pubmed and Science direct databases. All articles were fully reviewed by researchers, and data were evaluated by usage of a standardized form.

**Results & Suggestion** : Pragmatic acupuncture researches were tried for various symptoms (eg. low back pain, hypertension, depression during pregnancy, sleep quality in HIV disease, chronic poststroke leg spasticity, headache, etc). Individualized acupuncture treatments based on oriental disease pattern diagnosis reflexes practical treatments which is

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more effective than unified and fixed acupuncture treatments without any theoretical basis of oriental medical philosophy.

**Conclusion** : To overcome the controversies and limitations of past explanatory acupuncture trials, more individualized and tailored acupuncture trials with the theoretical basis of oriental medical diagnosis is highly recommended. Also clear definition and categorization of pattern identification should be established for further active clinical researches and applications of acupuncture.

## I. Introduction

Over the last thirty years, various clinical trials were executed in order to prove the effectiveness of acupuncture<sup>1)</sup>. The effectiveness of acupuncture treatment for postoperative nausea/vomiting and dental pain is consistently being reported<sup>2)</sup>. Acupuncture also shows promising possibility for migraine<sup>3)</sup> and osteoarthritis of the knee<sup>4)</sup>. However, the evidence of effectiveness for many other conditions often treated by acupuncture, including chronic pain, smoking addiction, fibromyalgia, are either insufficient or controversial<sup>1)</sup>. These outcomes are far from the real outcomes of practice where many patients and doctors actually experience the effectiveness of acupuncture. One of the main reasons of this diversity between the experimental results and practical effects is the standardized combinations of acupuncture points for all the experimental subjects. Therefore, in order to overcome the gap between the results of standardized clinical trials and the real practice, new pragmatic studies have been tried to establish reliable evidence of clinical practice. For example, the United Kingdom's National Health Service decided to fund pragmatic trials evaluating acupuncture effects on migraine and chronic

low back pain patients in normal clinical practice<sup>5)</sup>.

This paper aims to review pragmatic clinical trials on the effect of acupuncture treatment and to develop the ideal clinical research methodology of acupuncture study.

## II. Methods

Clinical studies of acupuncture relevant with pragmatic or individualized trials during recent five years (1999-2004) were searched mainly in Pubmed and Science direct databases. Finally eight full text articles were selected and fully reviewed by researchers, and data were evaluated by a standardized form (design type, sample size, inclusion/exclusion criteria, intervention, assessment tool, end point measurement, data integration, etc).

## III. Review of Pragmatic Trials

### 1. Low Back Pain

1) Acupuncture for low back pain: traditional diagnosis and treatment of 148 patients in a clinical trial<sup>6)</sup>

To assess patterns of diagnosis, concordance, and treatment, a pragmatic randomized controlled clinical trial was performed on 148 low back pain patients.

Standardized diagnosis and individualized acupuncture was practiced by six practitioners. Diagnostic inter-rater reliability was assessed in terms of percentage congruent classifications and Cohen's Kappa. Diagnostic concordance among practitioners was reasonable, and clear themes emerged for treatment.

2) How traditional Chinese medicine acupuncturists would diagnose and treat chronic low back pain: results of a survey of licensed acupuncturists in Washington State<sup>7)</sup>

To learn how TCM acupuncturists diagnose and treat chronic low back pain patients and to develop a standardized treatment for a clinical trial, practitioner surveys were proceeded, concerning the acupuncture styles, diagnosis patterns, and frequency of specific acupuncture points or specific meridians applied by 56 licensed acupuncturists in Washington State. The use of practitioner surveys can enhance the systematic development of acupuncture study protocols and should become an essential process in future clinical trials of common conditions.

3) Variation in diagnosis and treatment of chronic low back pain by traditional Chinese medicine acupuncturists<sup>8)</sup>

To assess inter-rater reliability of TCM diagnosis and treatment of chronic low back pain, six TCM acupuncturists evaluated the same six patients on the same day under a Latin square design. Short questionnaire was composed of the symptoms compiled from nine

acupuncture texts, and used for diagnosis of participants. TCM diagnoses and treatment recommendations for specific clinical trials using an individualized treatment arm may be difficult to replicate or evaluate because of low concordance among acupuncturists. Comparison of individualized treatment with a thoughtfully developed standardized approach is warranted to determine which, if either, is superior.

## 2. Headache

1) Acupuncture for migraine and headache in primary care: a protocol for a pragmatic randomized trial<sup>9)</sup>

To determine the effects of a policy of 'use acupuncture' on headache and migraine compared to a policy of 'avoid acupuncture', protocol for pragmatic randomised controlled clinical trial was presented. Subjects will be treated by qualified physiotherapist with individualized acupuncture, based on the TCM/Trigger points/Formula acupuncture which will be chosen by practitioner. Outcome will be assessed by headache diary, medication diary and SF36 at 3 months and 1 year. Resource use and days off sick will be assessed by quarterly questionnaire. Adverse events will be monitored by self report. The primary outcome measure will be the change in mean daily headache score between baseline and the 1 year follow-up. An economic evaluation will be undertaken.

## 3. Hypertension

1) Stop hypertension with the acupuncture research program (SHARP): clinical trial design and screening results<sup>10)</sup>

To gather preliminary data regarding the

efficacy of acupuncture for essential hypertension control, a pilot randomized clinical trial was performed on 192 patients included in the eligibility criteria for the SHARP trial. Patients were allocated to the each group treated with individualized, standardized or control acupuncture according to principles of TCM, and assessed with SF-36, self-report questionnaire for functional health status as the end point measurement. The adherence to strict methodological techniques and the maintenance of traditional acupuncture precepts are combined to provide a model for future evaluations of CAM therapies.

#### 4. Other Conditions

##### 1) Acupuncture: a promising treatment for depression during pregnancy<sup>11)</sup>

To determine whether or not acupuncture is a promising treatment for depression during pregnancy, randomized controlled pilot study was performed on 61 pregnant women with major depressive disorder. The assessment, treatment design, needle insertion, and needle stimulation were all standardized, but individually tailored. Acupuncture holds promise for the treatment of depression during pregnancy. Generalization is limited due to the small sample size and its relative homogeneity of the subjects.

##### 2) Needle acupuncture in chronic poststroke leg spasticity<sup>12)</sup>

To determine whether or not needle acupuncture reduces leg spasticity in a chronic state, single-blind, randomized, placebo-controlled trial was performed on 25 patients with chronic poststroke leg spasticity with pes equinovarus deformity.

Participants were randomly assigned to placebo treatment by using a specially

designed placebo needling procedure, or verum treatment. The results indicate that needle acupuncture may not be helpful to patient with chronic poststroke spasticity. However, there was neurophysiologic evidence for specific acupuncture effects on a spinal level involving nociceptive reflex mechanisms.

##### 3) Effects of individualized acupuncture on sleep quality in HIV disease<sup>13)</sup>

To test the effectiveness of acupuncture on improving sleep quality in HIV, clinical trial was performed on 21 HIV-infected men and women between the ages of 29 and 59. Acupuncture was individualized to address insomnia and other symptoms claimed by the participants, and the treatment was modified over the course of study to accommodate the individual's changing sleep pattern, pain, or other health issues. Sleep activity and sleep quality significantly improved after 5 weeks of individualized acupuncture treatment delivered in a group setting.

## IV. Discussion

Traditional medicine was empirically tested and survived throughout the history, and now is more popular than ever. Although randomized controlled trials are "golden standards" for proving scientific evidence, researches on traditional medicine such as acupuncture in Asia require a different approach from general explanatory process of new medication development. More efforts should be taken to find out meaningful evidence about overall routine care, and then specific factors out of the total effects should

be analysed<sup>14)</sup>. Recently new pragmatic studies have been tried to establish reliable evidence of clinical practice in order to overcome the gap between the results of standardized clinical trials and the real practice. This paper aims to review and evaluate the pragmatic clinical trials for recent 5 years and to suggest a ideal clinical research methodology of acupuncture study.

MacPherson et al<sup>6)</sup> reported their trial of assessing patterns of diagnosis, its concordance, and acupuncture points recommended in the setting of a pragmatic randomized controlled clinical trial. Prior to commencement of the trial, three low back pain syndrome with key features was established after a series of meetings held between the six practitioners and two researchers. The trials was executed according to the diagnosis in the pre-defined syndromes, and the concordance on key syndromes between practitioner-researcher was measured. In spite of the description of the list of the acupuncture points used, the acupuncture prescription including the oriental medical basis of the prescription was not mentioned. No result about the assessment of the treatment outcome was described, neither.

In the report of Vickers et al<sup>9)</sup>, protocol for a pragmatic randomized clinical trial was presented. In that paper, key steps in conducting a pragmatic trial<sup>14)</sup> were well described, such as objectives, patient recruitment and inclusion/exclusion criteria, adequate sample size calculated, informed consent, treatment allocation, and outcome assessment. But some part of protocol such as acupuncture prescription, quality of practitioner, and the establishment of treatment arm was not clearly described. The proficiency of the physiotherapist who had minimum post-graduate training in acupuncture was not

defined adequately. And in the establishment of treatment arm, in the group of 'use acupuncture', patients would be free to receive any further care that their general practitioner feels appropriate. In addition to the problem of the protocol, general practitioners who referred patients took the initiative in the progress of the trial so that they could decide whether patients would continue acupuncture.

Kalish et al<sup>10)</sup> reported a clinical trial design for Stop Hypertension with the Acupuncture Research Program (SHARP) and their screening results without treatment. In the paper, it was well documented on the study organization, treatment group, treatment comparisons, endpoints, eligibility of participants, randomization, acupuncture treatment, blood pressure measurement, antihypertensive medications, adverse events monitoring, assessment masking, functional health status measurement, and statistical consideration. According to the protocol, treatment will be accomplished in two session. In the first session, a diagnosing acupuncturist would diagnosis, prescribe an individualized set of corporeal needling points, and order stimulation method for each acupuncture point of specific treatment arm based on the consensus of the research team in consultation with a group of senior TCM acupuncturists and colleagues and the scientific literature and standard TCM textbooks. After the first session, the treating acupuncturist just followed the prescription of the diagnosing acupuncturist. All the acupuncturists had received acupuncture training at colleges in the Peoples' Republic of China, and licensed to practice in Massachusetts.

The pilot study on individualized acupuncture treatment for the depression during pregnancy<sup>11)</sup> was armed in three ways as active acupuncture, active control

acupuncture, and massage group. Although standardized acupuncture tailored individually, there was no description on the method of the standardization including acupuncture point prescription, needle insertion, and needle stimulation. And additional treatment including massage which is the main treatment of the massage group was not controlled adequately.

In a study of needle acupuncture in chronic poststroke leg spasticity<sup>12)</sup>, participants were randomly assigned to placebo treatment by using a specially designed non-invasive placebo needling procedure, or verum treatment which used predefined acupuncture points selected by practitioner. No mention about the theoretical basis of the selection of specific acupuncture point and the quality of the practitioner was described.

There was a case report of pretest, post-test, pre-experimental design on the effects of individualized acupuncture on sleep quality in HIV disease<sup>13)</sup>. Subjects neither were randomly allocated, nor blinded by proper method. Diagnosis and acupuncture treatment were not standardized. And acupuncture points used individually were not clearly documented.

In 1997, NIH also emphasized that acupuncture studies should be planned on theoretical basis of eastern medical systems and designed to allow divergent approaches as in clinical practice and to compare these systems with treatment using fixed acupuncture points<sup>2)</sup>.

In order to develop protocols for the pragmatic randomized controlled trials, some obstacles such as the pattern identification, selection of acupuncture points, period of time to retain needles, number of needles practiced, elicitation of de qi, depth of insertion, types of needle manipulation must be overcome in rigorous way. However, doctors of Korean Medicine or Oriental Medicine treat patients

not in uniform way but in taxonomical way called pattern diagnosis. Because there can be several different discriminative diagnosis and acupuncture prescription for the same western medical diagnosis, the reproducibility and generalizability of a single treatment prescription would be low.

In previous studies, Sherman et al<sup>7)</sup> and Hogeboom et al<sup>8)</sup>, undertook the practitioner surveys were proceeded, concerning the acupuncture styles, diagnosis patterns, key symptoms, influencing factors in the way of pattern diagnosis, frequency of specific acupuncture points or specific meridians was performed on licensed acupuncture practitioners, and the inter-rater reliability in the diagnosis of the same patients between practitioners. Because the standardization of the pattern diagnosis and treatment prescription may be one of the most important steps to the pragmatic randomized clinical trials, it would be pessimistic that consistency across acupuncturists regarding diagnostic details and other acupuncture points were poor. But in these two reports, the number of the practitioner and patients was too small to conclude adequately. Besides, the practitioner was not authorized as the expert in the field of the disease carried in the studies. In order to overcome various problems of standardizing pattern diagnosis, thorough preliminary analysis on specific diseases must be accomplished by a large number of qualified experts.

Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) was recommended in 2001 to lead more rigorous trial design, more robust conclusions and better data to determine future policy and practice<sup>15)</sup>. At first, STRICTA and pragmatic trials might seem to be totally opposite. But, we suggest a specified protocol adopting

advantages of both methods can be established. Although practitioners can use complex and individual approaches for different patients, pragmatic trial does not mean spontaneous applications of any interventions without any standards. Clear definition about what variations in treatment are permitted in the protocol should be set up in advance. That means a range of options, from a very open protocol allowing a wide flexibility within a defined framework, to a tightly specified protocol determined by consensus of experts. Pragmatic trials also can be replicated and generalized by other researchers<sup>14)</sup>.

## V. Conclusion

To overcome the controversies and limitations of past explanatory acupuncture trials, more individualized and tailored acupuncture trial based on oriental medical diagnosis is highly recommended. Also clear definition and categorization of pattern identification should be established for active clinical research and application of acupuncture.

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