Review of controlled clinical trials on acupuncture versus sham acupuncture in Germany

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Abstract

OBJECTIVE: To examine German controlled clinical trials on the therapeutic effects of acupuncture vs sham acupuncture, and to find whether there are problems with the conclusion that sham acupuncture has no significant deviation from acupuncture.

METHODS: We focused on literature from the last ten years (2002-2011) included in PubMed about controlled clinical trials on acupuncture vs sham acupuncture carried out in Germany. The methods applied in sham acupuncture are summarized, and the difference between the acupuncture and sham groups were analyzed. We measured effects based on the following criteria: acupuncture is effective and superior to sham, acupuncture is effective but similar to sham, both of them have uncertainty regarding treatment effect, or no significant effect. Finally, we reviewed the hypotheses of different scholars on sham acupuncture and analyzed their results.

RESULTS: Four types of controlled clinical trials including sham acupuncture on non-Traditional Chinese Medicine acupoints, minimal acupuncture on non-acupoints, placebo needle and sham laser acupuncture had varying results in the 57 articles analyzed. Some showed that acupuncture had a better effect than sham, while some suggest acupuncture and sham had similar effects. In all studies using sham acupuncture on non-therapeutic points, sham electrodes, and sham electro-acupuncture, the therapeutic effect was better than sham. Of the trials, 37 demonstrated that acupuncture had a better effect than sham acupuncture. Only nine trials found no significant difference between acupuncture and sham. Two controlled trials for the same condition (neck pain) conducted by two different German research institutes used the same control method, but reached contradictory conclusions.

CONCLUSION: We found problems in conclusions based on results of controlled clinical trials of sham acupuncture in Germany. Therefore, there is still not enough evidence to support the statements that "acupuncture and sham acupuncture have no difference in treatment effect" and "acupuncture is just a placebo effect." The control methods of sham acupuncture used in Germany may not be standardized and may not be suitable for acupuncture clinical trial research. We suggest that research on the methodology of sham acupuncture should be given priority in the design of acupuncture trials in the future.

Key words: Acupuncture therapy; Placebos; Con-
INTRODUCTION

In 2006, German researchers reported a controlled randomized clinical trial of sham acupuncture. In this trial, 1007 patients with chronic pain were randomly assigned to an acupuncture group, a sham acupuncture group (acupuncture at non-acupoints), or a conventional drug treatment group. 320 Western Medicine doctors from 315 clinics were involved in the trial. The results demonstrated that the effective rates of the two acupuncture groups were higher than the conventional drug treatment group. However, there was no significant difference between the two acupuncture groups.5 This trial was one of the first large-scale controlled clinical trials of acupuncture in the world. The results suggested that there was no difference between acupoints and non-acupoints, and some insurance companies in Germany stopped reimbursement for acupuncture treatment. The trial’s conclusion has had a negative impact on acupuncture and moxibustion in the international community.

In this study, we comprehensively searched the literature for controlled trials of sham acupuncture in Germany from the past ten years (2002-2011) (retrieval date: June 2012). We analyzed the relationship between control methods and treatment effects, and provided measures and suggestions for future trials. We also focused on research that reported differences or no difference between acupuncture and sham acupuncture.1

OVERVIEW ON SHAM ACUPUNCTURE METHODS

Sixty-one controlled clinical trials using sham acupuncture were carried out in Germany (57 full-text). According to a classification method from the Chinese University of Hong Kong (CUHK),7 seven methods were used in the sham acupuncture trials, including sham acupuncture on non-Traditional Chinese Medicine acupoints, acupuncture on non-therapeutic points, minimal acupuncture on non-acupoints, placebo needles, sham acupuncture on non-acupoints, sham electrodes or sham electroacupuncture (EA), and sham laser acupuncture.

Sham acupuncture on non-Traditional Chinese Medicine acupoints

Some clinical acupuncture research used non-Traditional Chinese Medicine acupoints as the placebo control. These points were often 0.5-5 cm lateral to the traditional acupoints or were selected between two meridians. Acupuncture for migraine prevention and its relationship with autonomic regulation was studied with 30 patients randomly divided into an acupuncture group and a sham acupuncture group.5 Acupoints selected for the acupuncture group were Baihui (GV 20), Fengchi (GB 20), Taiyang (EX-HN5), Sizhukong (SJ 23), Wai-guan (SJ 5), Tai-chong (LR 3), and Zulingqi (GB 41). For the sham acupuncture group, the non-Traditional Chinese Medicine acupoints included one point on the deltoid muscle, one point on the upper arm, and three points on the thighs. The trial suggested that both acupuncture and sham acupuncture had positive effects on the autonomic nervous system of migraine patients. However, acupuncture had a more significant effect by high-frequency power (P=0.03).

Acupuncture for chemotherapy-induced nausea and vomiting was studied with 28 patients divided randomly into an acupuncture group and a sham acupuncture group.1 For patients in the sham acupuncture group, stimulation was applied to non-acupoints close to Neiguan (PC 6). In this experiment, no significant difference was found between the effects of acupuncture on Neiguan (PC 6) and non-acupoints (P=0.96).

Acupuncture on non-therapeutic points

The effect of acupuncture on the pregnancy rate in patients treated with intracytoplasmic sperm injection (ICSI) and in vitro fertilization (IVF) was studied with 225 subjects randomly divided into an acupuncture group and a sham acupuncture group.5 Acupoints selected for the acupuncture group were Guanyuan (CV 4), Qihai (CV 6), Guilai (ST 29), Neiguan (PC 6), Xuehai (SP 10), and Diji (SP 8). Acupoints selected for the sham acupuncture group were not directly related to the illness, and included Sidu (SJ 9), Xiaolu (SJ 12), Fengshi (GB 31), Zhongdu (GB 32), and Yanglingquan (GB 34). The results of the trial showed that, compared with sham acupuncture, acupuncture could improve the pregnancy rate of patients treated with ICSI and IVF (P<0.01).

Minimal acupuncture on non-acupoints

Acupuncture for exercise-induced delayed-onset muscle soreness was studied with 22 healthy subjects randomly assigned to an acupuncture group, a sham group, or a control group.6 The acupuncture group needled at Yanglingquan (GB 34), Tianfu (LU 3), Chize (LU 5), Quchi (LI 11), Xuehai (SP 10), and tender points. The sham group had superficial needling at non-acupoints 2 inches across from acupoints. The trial suggested that acupuncture could reduce exercise-induced muscle soreness (P<0.05).

In another study of acupuncture for chronic lower back pain, 1162 patients were randomly divided into 3 groups: an acupuncture group, a sham acupuncture group (superficial needling at non-acupoints), and a conventional therapy group (a combination of drugs, physical therapy, and exercise).7 The study found that both acupuncture and sham acupuncture had better effects on chronic lower back pain than conventional therapy. However, the difference between acupuncture and sham acupuncture was not significant (P=0.39).
In a study of acupuncture for male infertility, 57 patients were randomly divided into an acupuncture group and a sham acupuncture group which used non-penetrating acupuncture. The same acupoints were selected for the two groups: Zusanli (ST 36), Sanyinjiao (SP 6), Taixi (KI 3), Taichong (LR 3), Shenshu (BL 23), Ciliao (BL 32), Guanyuan (CV 4), and Baihui (GV 20). The trial found that, compared with sham, acupuncture had a better effect on the percentage of motile sperm, though no significant effect was found on sperm concentration \((P=0.035)\).

Acupuncture for irritable bowel syndrome was studied with 43 patients randomly assigned to an acupuncture group and a sham acupuncture group using Streitberger needles. The study found no difference in symptom improvement between patients treated with acupuncture and sham acupuncture \((P=0.022)\).

Sham acupuncture on non-acupoints

Twenty-five patients were randomly assigned to an acupuncture group and a sham acupuncture group (needle at the non-acupoints by using blunts) to study acupuncture’s effect on post-stroke leg spasticity. The study found that both groups had no significant effect on the symptoms of patients with chronic post-stroke spasticity. However, acupuncture had effects on spinal (segmental) level involving nociceptive reflex mechanisms \((P<0.05)\).

Sham electrode or sham EA

Acupuncture for nausea and vomiting after surgery was studied using a sham electrode. 229 patients undergoing laparoscopic cholecystectomy were divided into four groups: a pre-anesthesia acupuncture group, a post-anesthesia acupuncture group, a pre-anesthesia sham group and a post-anesthesia sham group. In this trial, all four groups of patients received real and sham acu-stimulation at Neiguan (PC 6) by using Relief Bands, an electric current stimulation tool (worn on the wrist, it emits electric current). The study found that acupuncture could better decrease nausea and vomiting in patients undergoing laparoscopic cholecystectomy compared to sham acupuncture \((P=0.043)\).

In one study for EA on pain, 16 volunteers were divided into an electro-acupuncture group and a sham electro-acupuncture group, and received stimulation to produce pain. The results demonstrated that the rate of pain episodes in the acupuncture group was much lower than before \((P<0.05)\) and that the sham acupuncture group had no effect.

Sham laser acupuncture

Two separate studies used sham laser acupuncture on the cervical function of patients with chronic neck pain, but their conclusions were divergent.

In one trial, 36 patients were randomly divided into 3 groups: acupuncture plus remote point selection, acupuncture at local tender points, and sham laser acupuncture. The study found that for improving activity, acupuncture at remote points had an effect \((P=0.014)\) and acupuncture at local tender points also had an effect \((P=0.028)\). However, sham acupuncture had no effect.

In another trial, 177 patients were randomly divided into an acupuncture group, a massage group, and a sham laser acupuncture group. The study indicated that acupuncture had a better effect on the recovery of cervical vertebra function than massage \((P=0.03)\). However, there was no significant difference between acupuncture and sham acupuncture \((P=0.38)\).

**Table 1 Articles on treatment effects concerning to sham acupuncture and acupuncture methods**

<table>
<thead>
<tr>
<th>Sham acupuncture methods</th>
<th>Effective and superior to sham acupuncture</th>
<th>Uncertainty over treatment effect</th>
<th>No significant effect</th>
<th>Effective but similar to sham acupuncture</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sham acupuncture on non-Traditional Chinese Medicine acupoints</td>
<td>14</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Acupuncture on non-therapeutic points</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Minimal acupuncture on non-acupoints</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Placebo needle</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Sham acupuncture on non-acupoints</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sham electrode/ sham EA</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Sham laser acupuncture</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>5</td>
<td>6</td>
<td>9</td>
<td>57</td>
</tr>
</tbody>
</table>

RESULTS

Fifty-seven sham acupuncture controlled trials were carried out in Germany. All trials were randomized and controlled, and all types of results are presented in Table 1. In relevant research on acupuncture, four different types of controlled clinical trials had varying re-
sults. Some studies found that acupuncture had better effects than sham acupuncture, but some suggest acupuncture and sham acupuncture had similar effects. In all studies using sham acupuncture on non-therapeutic points, sham electrodes, and sham EA, the effect of acupuncture was better than sham acupuncture. Only one article studied sham acupuncture on non-acupoints, and its results demonstrated that neither acupuncture nor sham acupuncture had any clinical effect.

**DISCUSSION**

The effect caused by sham acupuncture belongs to a placebo effect, which is composed of a variety of non-specific factors associated with the treatment. However, the specific treatment effect should exclude, for example, routine medical care, the relationship between patients and doctors, and the medical environment. These methods can be used as the control factors to evaluate whether a treatment has only a non-specific placebo effect instead of the expected therapeutic effect. Therefore, in clinical trials, the control method of sham/placebo acupuncture is supposed to create a placebo effect on patients that is similar to the effect of acupuncture. However, it should be stressed that the placebo effect is not supposed to have therapeutic effects. Therefore, the control methods of sham/placebo acupuncture used in Germany might not fit the above-mentioned requirement. In the present study, among German controlled clinical trials of sham acupuncture, 37 demonstrated that acupuncture had a better effect than sham acupuncture. Only nine trials found no significant difference between acupuncture and sham. Therefore, there is still not enough evidence to reject the use of clinical acupuncture. Two controlled trials for the same disease (neck pain) conducted by two different German research institutes used the same control method, but reached contradictory conclusions. Therefore, the control methods of sham acupuncture used in Germany may not be standardized and may not be suitable for clinical trial research on acupuncture.

Different scholars hold different views regarding the scientific level and rationality of the control methods of sham acupuncture. An "Acupuncture Research Report" released by the National Institutes of Health of the United States in 1997 discussed the method of sham acupuncture. The report defined sham acupuncture as a commonly used control method and its purpose was not to stimulate the well-known acupoints. However, there was debate over the correct position of the needle. Especially in the study of pain, the effect of sham acupuncture seemed to be at a position between the placebo effect and the real acupuncture effect. However, acupuncture and moxibustion at any point will induce a biological reaction. Therefore, it is complicated to analyze the effect of sham acupuncture. Chinese scholars believe that the sham acupuncture method used in Germany was just the superficial needling method used in ancient China. With this method, the regulation system of the human body is activated, achieving the effect of real acupuncture. Placebo-controlled trials have been widely used overseas, aiming to minimize the influence of psychological factors. However, the ideal design of sham/placebo acupuncture has not yet emerged. Many acupuncture clinical trials did not conform to the standards of conventional clinical trials. A clearer understanding of the placebo effect in acupuncture and the difference between pharmacological studies is key to solving this problem.

Even if acupuncture only has a placebo effect on the treatment of certain diseases, it does not mean that acupuncture has no clinical value. If there is no well-accepted effective treatment for a pathology, and if placebo treatment can improve the patient’s condition, then the placebo treatment should be considered as an effective treatment method. Because the placebo effect of acupuncture cannot be replaced, it could be an effective treatment for some conditions.

In addition, because a large number of clinics were involved in these clinical trials, it was difficult to ensure that all doctors conducted sham acupuncture according to the unified scheme. Moreover, the effect of acupuncture could be affected by the different skills of doctors. Thus, the difference between the effects of acupuncture and sham acupuncture might not be correctly reflected.

Currently, because control methods are yet to be clearly defined, and there is not sufficient evidence or solid experimental basis, we cannot conclude that the control method of sham acupuncture is not scientific. It is necessary to research the standardization of sham acupuncture. Moreover, Chinese scholars should not rely on foreign scholars who may lack an understanding of Traditional Chinese Medicine to design the standards of acupuncture and sham acupuncture in clinical trials. Most current acupuncture research, both in China and abroad, focus on the study of efficacy. However, the methods used in trials are a critical problem. As multi-center and large randomized controlled trials are carried out, the standardization of control methods becomes an important problem that needs to be solved, especially the controversial sham acupuncture. Future clinical studies face at least two problems. One problem is the requirement of skilled clinical doctors. The effect of acupuncture should be maximized in treatment according to the ancient theory of diagnosis and treatment. Moreover, the differences between the effect of acupuncture and the placebo effect of sham acupuncture should be demonstrated, instead of just focusing on the non-specific acupuncture effect. The other problem is the standardization and assessment of the control methods of sham acupuncture. An objective control method of sham acupuncture should be de-
signed that can be used in controlled acupuncture trials and can be evaluated in terms of scientific level and feasibility. The ultimate goal is to establish an international standard of sham acupuncture. We will further research the standardization of the control methods of sham acupuncture based on literature review, clinical trials, and evidence-based medicine. We will also put forward several possible control methods based on literature studies, and through clinical trials and evidence-based medicine. Eventually, a standard of the control methods of sham acupuncture for acupuncture clinical trials can be formulated. However, it will take many years to perform a full literature study, including clinical trials and the verification of evidence-based medicine to come to a conclusion.

REFERENCES