J. Acupunct. Tuina. Sci. 2011, 9 (4): 199-203
DOI: 10.1007/s11726-011-0511-7

Critical Review

Assessments of Different Kinds of Sham Acupuncture Applied in Randomized Controlled Trials

随机对照试验研究中各种假针刺的评价

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【**Abstract**】**Objective**: Different kinds of sham acupuncture are widely applied in randomized controlled trials (RCTs) to explore whether acupuncture has intrinsic therapeutic effects beyond the placebo effects for certain indication. To make conclusions of trials more comparable and convincing, it is of great necessity to unify the sham acupuncture procedure. **Methods**: RCTs of acupuncture with high quality in the recent 14 years were reviewed, and the appropriateness of the sham acupuncture procedures was assessed. **Results**: The sham acupuncture procedures were mainly classified into five kinds according to their administered sites, penetrating, and intervention apparatus. **Conclusion**: Among the sham acupuncture procedures, needling near the selected acupoints, needling at a distant non-acupoints, and non-penetrating sham acupuncture are most commonly used. Sham acupuncture performed at distant site belongs to non-meridian and non-acupoint may be an ideal control for the study of the intrinsic therapeutic effects of acupuncture. Besides, the selection of controls must focus on the design and aim of RCTs, such as non-inferiority, equivalence and superiority trials.

【**Key Words**】Acupuncture Therapy; Placebo Effect; Randomized Controlled Trial

【**摘要**】**目的**：在随机对照试验（Randomized Controlled Trials，RCTs）研究中，不同的假针刺方法广泛地用于评价针刺对某种病症除安慰效应外是否具有内在的治疗作用。为使试验结果可信和更有可比性，有必要对假针刺方法做个统一的规范。**方法**：回顾了最近 14 年高质量的针刺RCT研究，评价其中的各种假针刺方法的恰当与否。**结果**：根据进针部位、破皮方式、所用仪器的不同，这些假针刺方法主要可以分为 5 类。**结论**：最常用的假针刺方法有穴位旁开针刺、远部非穴部位针刺和不破皮假针刺 3 种，其中远部非经非穴部位针刺可能是比较理想的假针刺对照。另外，对照的设立应结合考虑RCT研究的目的和设计，如非劣效性、等效性、优效性试验。

【**关键词**】针刺疗法；安慰治疗效应；随机对照试验
【**中图分类号**】R245-3　　【**文献标志码**】A

The placebo is an important element for evaluating curative efficacy. It is generally defined as an inactive substance or procedure designed to satisfy or "please" patients, which has no intrinsic therapeutic value. Successful placebo control should be indistinguishable and physiologically inert. In the context of the randomized controlled trials (RCTs) of acupuncture, it is important to assess whether acupuncture has specific effects beyond placebo effects. Since acupuncture is a manual treatment involving an invasive element, it is difficult to design a placebo procedure which fully mimics real acupuncture yet does not produce any physiological effects[1]. Sham acupuncture is preferred to placebo acupuncture under this circumstance.

Nevertheless, many researchers are confused as to what the "active" ingredient of acupuncture is. Is it acupoint related, the penetration of the skin, manipulation of the needles, or pressure exerted over the acupoint? Thus, it is not surprising that a variety of sham acupuncture procedures have been used in RCTs. This makes conclusions of trials not comparable. In addition, some conclusions are not

Fund Items: National Natural Science Foundation of China (No. 30873299, 90409014, 81001548, 30701123); Shanghai Leading Academic Discipline Project (S30304)
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convincing since the sham acupuncture procedures are obviously inappropriate. It is of great necessity to access the appropriateness of different kinds of sham acupuncture to improve and unify their designs in future RCTs. In the paper, the sham acupuncture procedures were classified into five kinds according to their administered sites, penetration, and intervention apparatus; and then discussed.

1 Sham Acupuncture at Selected Acupoints

One of the sham acupuncture control procedures is to insert needles superficially without manipulations at the same selected acupoints in the experimental group[2, 3]. Needling the same acupoints superficially is a control for the influence of needling depth; however, it is unsuitable to serve as a control to evaluate the efficacy of acupuncture. First, needling superficially is actually one kind of the acupuncture techniques commonly used in clinical practice. Superficial insertion is applicable to syndromes with shallow pathological conditions, such as facial palsy, for which deep insertion may produce less therapeutic effects, even resulting in adverse effects. Second, the depth of needling insertion also depends on the physical status of patients. Superficial insertion should be applied to patients as infants, the elderly, or people with a delicate constitution. Third, the depth of needling insertion is also determined by the location of the acupoint. Superficial insertion is commonly performed at the acupoints of head, face, and chest. Thus it is not surprising that superficial insertion exerts better therapeutic effects than deep insertion for certain indications. Sham acupuncture in this way may actually be equivalent to comparing the two needling techniques of acupuncture treatment, but not proper for assessing whether acupuncture has specific effects beyond placebo effects.

2 Sham Acupuncture at Non-acupoints

Lots of RCTs performed sham acupuncture at non-acupoins. How these non-acupoints were localized differed considerably. They might be 1-3 cm away from the selected acupoints in some trials or in the same neural segment but non-acupoints in others and some trials choose non-acupoints in distant areas. Here we discussed the two commonly used sham acupuncture of needing near the selected acupoints and at distant non-acupoints.

2.1 Needling near the selected acupoints

Needling near the selected acupoints is commonly applied to serve as sham acupuncture in RCTs[4-9]. Researchers who use sham acupuncture this way may consider that acupoints are the fixed points on the skin, and thus sites near the acupoints can be used for control. As a matter of fact, it is not the case neither in the theory of meridian and acupoint nor in clinical practice. First, acupoints are the sites where Qi from the viscera and meridians "effuse and infuse" as well as "run out and in"[10]. These sites are not single points on the skin, but possess certain area and consist of multiple layers of tissues. Nobody, until now, has successfully defined how large an acupoint should be. Distinguishing acupoints and non-acupoints by a short distance (like 1-3 cm) shows a lack of validity in the theory. Second, sites near the selected acupoints may belong to other nearby acupoints, while nearby acupoints always have similar therapeutic effects due to the fact they all have proximal therapeutic effects, or that they possess similar distant therapeutic effects if these nearby acupoints below the knee and elbow[11]. Third, in clinical practice, in order to get needling sensation which is important to acupuncture therapy, acupuncturists sometimes may needle again somewhere near the first insertion position in the site of acupoint where it fails to get needling sensation. Acupoints, to some extent, are certain functional sites rather than the fixed points on the skin. Furthermore, sometimes, the so called "needling near acupoints" may be the real acupuncture for the next time since it is difficult for acupuncturists to needle a second time precisely in the same position as needling the first time. Thus, needling near acupoints is vague and misleading both in the theory and clinical practice, and may produce similar therapeutic effects, consequently leading to the conclusion that acupuncture is of no specific effects beyond placebo effects. It is unreasonable to serve needling near acupoints as a sham control to evaluate the efficacy of acupuncture.

2.2 Needling at distant non-acupoints

Needling at distant non-acupoints with superficial insertion is another commonly applied sham

acupuncture procedure[12-18]. Two trials on acupuncture for intractable epilepsy provided examples of this kind of sham control[19, 20]. Acupoints Taichong (LR 3), Hegu (LI 4) and Baihui (GV 20) were selected in the real acupuncture group, while three non-acupoints as 2.5 cun to the side of the umbilicus, 3 cun above the midpoint of the patella, and 1 cun below the midpoint between Jianyu (LI 15) and Jianliao (TE 14) were selected in the sham acupuncture group with superficial needling. The three non-acupoints are far from the selected acupoints. In addition, acupoints near the three non-acupoints are not appropriate for treating epilepsy. Thus, the possibility that sham acupuncture may produce similar therapeutic effects to the real acupuncture is, at least theoretically, excluded. And superficial needling makes this sham procedure indistinguishable since the subjects believe that they receive acupuncture treatment. Needling at distant non-acupoints with superficial insertion is a reasonable way for sham acupuncture in RCTs.

3 Needling at Inappropriate Acupoints

Needling at inappropriate acupoints that are inactive for the indication is another form of sham acupuncture in RCTs[21, 22]. It is a way to test acupoint specificity, but not reasonable for assess the efficacy of acupuncture for certain indication. Since acupoints have their own therapeutic action, sham acupuncture in inappropriate acupoints is actually a real acupuncture for another indication. The sham procedure in this way is not physiologically inactive.

4 Non-penetrating Sham Acupuncture

Non-penetrating sham acupuncture refers to tapping a blunt needle[23-25] or guide tube[26] to the dermal surface without skin penetration on the selected acupoints, or non-acupoints. In 1998, Streitberger designed a "placebo needle" device[27]. Using this device, the blunt needle retracts inside the handle when the needle touches the skin, giving an appearance of puncturing the skin. Streitberger needles were commonly used as sham acupuncture in the late RCTs[28-31]. The advantage of non-penetrating sham acupuncture is that it avoids the possible therapeutic effects caused by penetrating the skin. However, it has a risk of failing to produce real "placebo effects". For patients who never receive acupuncture treatment, it may be a good placebo control. While for patients who experienced acupuncture treatment, they will easily perceive the difference between non-penetrating sham acupuncture and real acupuncture. In addition, when on the selected acupoints, it might be an effective acupressure which may produce therapeutic effects. It seems not sensible to take non-penetrating sham acupuncture in RCT, especially in China.

5 Pseudo-interventions

Acupuncture has also been compared with other "placebo" interventions such as mock transcutaneous nerve stimulation[32], or inactivated laser apparatus[33, 34]. These "placebo" interventions clearly differ from acupuncture, like the way performed, and the sensation received by the subjects. Thus, unless they are demonstrated to have the same total psychological influence as acupuncture, it is inappropriate to directly compare acupuncture with these pseudo-interventions. Any differences between the effects of acupuncture and these controls could be due to the different manipulations and stimulations[35]. Acupuncture is sometimes compared with electro-acupuncture. They are both real acupuncture, and can not serve as sham acupuncture for each other, which we should also pay attention to. Thus, these pseudo-interventions can not convincingly testify the efficacy of acupuncture for certain indications.

In summary, the control procedure is determined by the research questions. If the question is whether acupuncture is better than doing nothing, the control can be waiting list. If the question is whether acupuncture is better than commonly applied treatment for certain indications, then the control can be the standard treatment. If the question is whether acupuncture has any efficacy besides placebo effects for certain indication, then the control can be some procedure that is indistinguishable from the true acupuncture and physiologically inactive.

For the purpose of distinguishing the intrinsic therapeutic effects of acupuncture from placebo effects; many kinds of sham acupuncture procedures are designed. Among them, needling near the selected acupoints, needling at distant non-acupoints, and

non-penetrating sham acupuncture are most commonly used. Sham acupuncture performed at distant sites belonging to non-meridian and non-acupoint may be an ideal control for the study of the intrinsic therapeutic effects of acupuncture as discussed above. Besides, the selection of controls must be considered with the design and aim of RCT, such as non-inferiority, equivalence and superiority trials.

6 Conflicts of Interest and Informed Consent

There are no conflicts of interest. All the authors have reviewed the final version of the manuscript and approved its submission.

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Received Date: March 15, 2011