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REVIEW ARTICLE

Types of Control in Acupuncture Clinical Trials Might Affect the Conclusion of the Trials: A Review of Acupuncture on Pain Management

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Abstract
Analgesic effects of acupuncture have been extensively studied in various clinical trials. However, the conclusion remains controversial, even among large scale randomized controlled trials. This study aimed to evaluate the association between the conclusion of the trials and the types of control used in those trials via systematic review. Published randomized controlled trials of acupuncture for pain were retrieved from electronic databases (Medline, AMED, Cochrane libraries, EMBASE, PsycINFO, Clinicaltrials.gov, and CAB Abstracts) using a prespecified search strategy. One hundred and thirty-nine studies leading to 166 pairs of acupuncture-control treatment effect comparisons (26 studies comprised of 53 intervention-control pairs) were analyzed based on the proportion of positive conclusions in different control designs. We found that treatment effects of acupuncture compared with nontreatment controls had the highest tendency to yield a positive conclusion (84.3%), compared with nonneedle-insertion controls (53.3%).

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Whereas with needle-insertion controls, the lowest tendency of positive conclusions was observed (37.8%). Consistently, in studies reporting successful blinding, a higher tendency of positive findings on the treatment effect of acupuncture was found in the noninsertion sham controls compared with that in the insertion sham controls. We conclude that the type of control is likely to affect the conclusion in acupuncture analgesic trials. Appropriate control should be chosen according to the aims of studies.

1. Introduction

The number of randomized controlled trials (RCTs) conducted on acupuncture have dramatically increased over the past decade. The efficacy of acupuncture for pain is one of the most interesting outcomes in studies. Although many basic science studies have revealed the analgesia mechanisms of acupuncture [1,2], the efficacy of acupuncture remains controversial in clinical trials, e.g., in knee osteoarthritis (KOA) [3–8]. The diverse mechanisms and complicated manual procedures involved in acupuncture treatment have contributed to the challenges of evaluating acupuncture trials [9]. For example, acupuncture produces a specific physiological effect and nonspecific needling effect (e.g., diffuse noxious inhibitory control) during the treatment [10]. Patient expectations, acupuncturist experience, number and specificity of acupoints, depth of needling, and dosage of acupuncture (duration, frequency, and time) also affect the efficacy of acupuncture analgesia in RCTs [11]. The benefits during the treatment are usually explained by: (1) treatment effects; (2) nonspecific effects; or (3) spontaneous remissions [12,13]. A proper control or controls, e.g., waitlist, noninsertion sham acupuncture, and insertion sham acupuncture, are utilized to evaluate the true effects in RCTs [9].

Arguments have been raised on the efficacy of acupuncture controls [14–16]. Meng et al [17] reviewed acupuncture RCTs on pain published in 2006–2007 and found that trials using noninsertion shams yielded more positive outcomes (6 of 7 trials) than those using insertion shams (2 of 8 trials). Madsen et al [18] found that the type of placebo acupuncture was not associated with the estimated analgesic effect of acupuncture. In this study, we aimed to examine whether positive conclusion is correlated with the type of controls in RCTs of acupuncture for pain. We systematically reviewed clinical trials of acupuncture for pain from 2004 to 2014. The association between the type of controls used in these studies and conclusion of acupuncture efficacy were further analyzed.

2. Materials and methods

2.1. Database

A systematic search of RCTs with acupuncture was conducted to evaluate the proportion of positive conclusions in the different controls in RCTs. The search strategy was defined as below. Databases searched included Medline, AMED, Cochrane libraries, EMBASE, PsycINFO, Clinicaltrials.gov, and CAB Abstracts.

2.2. Search strategy

The search keywords were as follows: "acupuncture*", "acupoint*", "acupress*", "meridian*", "needle*", "sham acupuncture", "placebo acupuncture", "control acupuncture", "acupuncture control", and "pain". Studies were limited to RCTs and journals in Science Citation Index (SCI). The search was conducted in March 2015.

2.3. Screening

The retrieved studies were imported into Endnote and any duplicates were removed. The abstracts of the studies were screened, followed by full-text screening according to the selection criteria below. The screening was performed by two individuals. Discrepancies were resolved by discussion with a third reviewer. Information on the type of controls and acupuncture efficacy conclusion from eligible studies were extracted according to the definition of outcomes.

2.4. Selection criteria

2.4.1. Inclusion criteria

Studies: (1) were RCTs; (2) used pain score as an outcome; (3) used needling acupuncture (traditional acupuncture, electro-acupuncture, and medical acupuncture) as the major intervention (not restricted to auricular acupuncture and scalp acupuncture as the secondary intervention); and (4) were published from 2004 to 2014.

2.4.2. Exclusion criteria

Studies: (1) used bee venom acupuncture as the intervention; (2) used acupoint injection as the intervention; (3) of poor quality design (unclear randomization method, incorrect concealment, and individual assessment), with low risk items less than five of seven (according to risk bias assessment tool in Cochrane review handbook); and (4) used active treatment of any acupuncture modalities (e.g., active acupuncture, auricular acupuncture, etc.) as control(s).

2.5. Outcomes

2.5.1. Type of acupuncture controls

We classified acupuncture controls into several types according to the purpose of controls: (1) "nontreatment" control: patients usually received nontreatment, delayed treatment (waiting list), usual care, or/and rescue medication in consideration of medical ethics; (2) noninsertion sham: these do not penetrate the skin, but usually use the

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