Acupuncture Clinical Trials on Knee Osteoarthritis

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Abstract

The outcomes of eight acupuncture clinical trials on knee osteoarthritis were published in well-regarded English-language mainstream medical journals between 1975 and 2022. Reported trial results were equally balanced between positive and negative outcomes, thus producing an overall impression of ambiguity in regard to the efficacy of acupuncture in the treatment of knee osteoarthritis. This paper reviews these trials, analyzes the factors taken into account in each trial, and has posited two reasons for the continuing lack of consensus in regard to the medical effectiveness of acupuncture: the difficulty of designing scientifically consistent clinical-trial studies; and an institutional bias toward ambiguity on the part of scientific and medical journals.

Keywords
- knee osteoarthritis
- acupuncture
- clinical trials
- sham control
- medical journals
- institutional bias

Introduction

Acupuncture application to knee osteoarthritis has been the subject of numerous clinical trials over the last 50 years, but the ambiguity of the published results has been a consistent factor. Eight of these trials were published in high-profile medical journals including *New England Journal of Medicine, The Journal of American Medical Association (JAMA), Lancet, British Medical Journal, Annals of Internal Medicine*, and *Arthritis and Rheumatology*. In 2017, the author of this article examined the positive/negative balance of acupuncture/Chinese medicine clinical trials published in *JAMA*[1–11] and observed that there seemed to be a "calculated politics" of inclusion which mandated that the publication of a positive-result acupuncture study must be balanced by a negative-outcome clinical trial, and *vice versa*. The same principle, calculated or not, is evident in the eight studies of acupuncture and knee osteoarthritis which are the subject of this article.[8,10,12–17] These clinical trials were organized along scientific principles. Generally, the end result of conducting numerous studies on a specific subject is the establishment of a preponderance of evidence for or against the subject or theory being tested. But in Western medical journals, the end result of acupuncture research is a perfect yin/yang balance of positive and negative.

Why is this so? Is it a matter of reconciling the vocabulary of acupuncture theory with the vocabulary of standard scientific practice? Is the undeniable presence of a placebo effect too difficult to account for? Many observers believe that the main problem is the number of variables inherent in acupuncture treatment. In itself, acupuncture is a relatively simple procedure, but many factors have to be taken into account when setting up a research study: sham/control design; patient selection and randomization; outcome measurement; point selection/prescription; and penetration depth, intensity and duration of needling, etc.

However, one question begs to be answered: what is the actual proportion of positive-to-negative study results which are submitted to, and selected for publication by, the medical journals in question? Are the total number of submitted studies indeed evenly balanced between positive and negative results or are the medical journals actively selecting an equal number of positive and negative studies in order to present a "fair and balanced" image?

Eight Studies on Knee Osteoarthritis

The first acupuncture clinical trial ever conducted was on knee osteoarthritis, published in the *New England Journal of Medicine* in 1975.[12] It enrolled 40 patients who had chronic pain associated with osteoarthritis. The acupuncture treatment group received standard acupuncture treatments and the control group received treatments on placebo points. The

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measurement of outcome was the reduction of pain associated with osteoarthritis. The results showed a significant improvement in tenderness and subjective report of pain in both groups, but response to treatment between the real-acupuncture and placebo-acupuncture groups showed no significant difference. This small-sample study produced obviously ambiguous results on acupuncture's effectiveness and initiated the claims that acupuncture was not "more effective than placebo" or simply that "acupuncture is theatrical placebo."[18,19]

In 2004, a study by Berman et al[13] firmly responded that acupuncture for knee osteoarthritis is more effective than placebo. The study was conducted as a randomized, controlled trial at two outpatient clinics (an integrative medicine facility and a rheumatology facility) to determine whether acupuncture provided greater pain relief and improved function compared with either sham acupuncture or education for knee osteoarthritis patients. The true-acupuncture group received 23 acupuncture sessions over 26 weeks. The control group received six two-hour sessions over 12 weeks or 23 sham acupuncture sessions over 26 weeks. The study demonstrated that the true-acupuncture group experienced greater functional improvement than the sham-acupuncture group at 8 weeks but did not improve in their pain scores or in the patient global assessment. At 26 weeks, the true-acupuncture group experienced a significantly greater improvement in function, pain relief, and patient global assessment than the sham group.

At the turn of the new millennium, Germans were debating whether to provide national health insurance coverage for acupuncture. Two studies were conducted on acupuncture application to knee osteoarthritis, one by the German Acupuncture Trials and the other by the Acupuncture Randomized Trials group.[14,15] These two studies produced different outcomes.

In the trial of Witt et al, conducted by specialized physicians in 28 outpatient centers, 294 patients with chronic osteoarthritis of the knee were provided with true acupuncture, minimal acupuncture (superficial needling at nonacupuncture points), or no acupuncture.[14] After 8 weeks of treatment, pain and joint function were improved more with acupuncture than with minimal acupuncture or no acupuncture in patients with osteoarthritis of the knee. The improvements remained at 26 weeks. However, after 52 weeks, the difference between the true-acupuncture and minimal-acupuncture groups was no longer significant.

In the trial of Scharf et al,[15] conducted at 315 primary-care practices, 1,007 patients who had had chronic pain for at least 6 months due to osteoarthritis of the knee were randomly assigned to traditional Chinese acupuncture, sham acupuncture (needling at defined nonacupuncture points), or conservative therapy. The conservative-therapy group was offered up to six physiotherapy sessions and as-needed anti-inflammatory drugs. The traditional-Chinese-acupuncture group was offered conservative therapy plus 10 sessions of traditional Chinese acupuncture. The sham acupuncture group was offered conservative therapy plus 10 sessions of sham acupuncture or 10 physician visits within 6 weeks. Patients could be offered up to five additional sessions or visits if the initial treatment was viewed as being partially successful.

Scharf et al[15] demonstrated that compared with physiotherapy and as-needed anti-inflammatory drugs, the addition of either traditional Chinese acupuncture or sham acupuncture led to greater improvement in an osteoarthritis index including pain, stiffness, and physical functioning of the joints at 26 weeks. There was no statistically significant difference observed between traditional Chinese acupuncture and sham acupuncture. The authors conjectured that the observed differences could be due to the following reasons: a placebo effect; differences in intensity of the provider contact; a physiologic effect of needling regardless of whether or not it was done according to traditional Chinese acupuncture principles.

In the first decade of the new century, two studies published by the *British Medical Journal* again showed very different interesting results.[16,17]

In a study by Vas et al,[16] researchers assessed the effect of adding acupuncture to the nonsteroidal anti-inflammatory drugs diclofenac for the treatment of osteoarthritis of the knee. Researchers measured pain relief, reduction of stiffness, and increased physical function during treatment; modifications in the consumption of diclofenac during treatment; and changes in the patient's quality of life. This randomized, controlled, single blind trial was conducted in a public primary care center in southern Spain over a period of 2 years. Ninety-seven outpatients with osteoarthritis of the knee participated in the study. The experimental group received acupuncture plus diclofenac. The control group received placebo acupuncture plus diclofenac. The results showed that the intervention group presented a greater reduction of pain and stiffness than the control group and an even greater reduction in the subscale of functional activity. The study also showed that acupuncture treatment produced significant changes in physical capability and psychological functioning.

A study by Foster et al[17] assessed adding acupuncture to physiotherapy for pain reduction in patients with osteoarthritis of the knee. This multicenter, randomized controlled trial was conducted in 37 physiotherapy centers accepting primary care patients referred from general practitioners in the Midlands area of the United Kingdom. In total, 352 adults aged 50 years or more with a clinical diagnosis of knee osteoarthritis joined the study and were randomly assigned into one of three groups: an advice-and-exercise group; an advice-and-exercise plus true-acupuncture group; and an advice-and-exercise plus nonpenetrating acupuncture group. The result showed that the addition of acupuncture to a course of advice and exercise for osteoarthritis of the knee delivered by physiotherapists provided no additional improvement in pain scores.

In 2014, the *Journal of the American Medical Association* published a study by Hinman et al[10] that rocked the professional acupuncture community. The conclusion of the researchers was that acupuncture was not recommended for patients over the age of 50. Hinman's team conducted a Zelen-design clinical trial in Victoria, Australia, in which patient randomization occurred before informed consent. Participants included 282 patients who were 50 years or older, with chronic knee pain, who were community volunteers treated by family physician

acupuncturists. The patients were randomly assigned to one of four groups: a needle-acupuncture group; a laser-acupuncture group; a sham-laser-acupuncture group; and a control group. The needle-acupuncture group is inferred by the current authors to have been set up as a positive control in the original study. The sham-laser-acupuncture group acted as the negative control for the laser acupuncture intervention. The control group received conventional care, but no acupuncture or laser treatments. All patients received treatments for 12 weeks. Participants and acupuncturists were blinded in regard to whether laser or sham-laser acupuncture was being administered. Control-group participants were unaware of the trial.

Hinman's study showed that neither needle nor laser acupuncture significantly improved pain or function compared with sham-laser at 12 weeks.[10] Compared with the control group, needle and laser acupuncture demonstrated modest improvements in pain at 12 weeks, but not at 1 year. Needle acupuncture resulted in modest improvement in function compared with the control group at 12 weeks but was not significantly different from sham treatment and was not maintained at 1 year. The authors concluded that neither laser nor needle acupuncture conferred benefit over sham treatment for pain or function in patients older than 50 years with moderate to severe chronic knee pain. Therefore, the study did not support acupuncture for these patients.

Hinman's study aroused strong responses from the acupuncture community[20,21] but also planted the expectation that a subsequent study would affirm the thousand-year clinical experience of acupuncture effectively treating knee osteoarthritis. With weak evidence of acupuncture benefit to knee arthritis patients from systematic reviews and meta-analysis, more rigorous clinical trials were demanded.[22] In 2020, a multicenter, randomized, sham-controlled trial, was conducted by Tu et al[23] which randomly assigned 480 patients with knee osteoarthritis to receive electroacupuncture, manual acupuncture, or sham acupuncture three times a week for 8 weeks. The researchers demonstrated a positive patient response rate, which they defined as the proportion of participants who simultaneously achieved minimal clinically important improvement in pain and function by week 8.

Analysis

The clinical experience of acupuncture practitioners is that acupuncture is definitely effective in the treatment of knee osteoarthritis. Clinical trials which produce negative results or which ascribe positive patient response solely to the placebo effect are counterintuitive to acupuncturists' daily experience. Numerous case studies, classical texts, historical documentation and everyday practice testify to the need for acupuncture to be validated by scientific methodology and clinical research. The positive results cited in the studies by Berman et al,[13] Witt et al,[14] and Tu et al[23] corroborate the therapeutic efficacy of acupuncture but are not unqualified proof. For acupuncture to be accepted as an effective medical modality by the medical community, the positive evidence provided must be consistent and convincing.

Fan et al[21] re-analyzed the data produced by Hinman's knee osteoarthritis study[10] and identified problems with the randomization of patients and high heterogeneity among groups. Their reanalysis of the data resulted in the conclusion that acupuncture had been effective for the patients in Hinman's study in terms of overall pain and function and concluded that acupuncture treatment was moderately effective for chronic knee pain in patients aged 50 years and older compared with conventional care.

A common issue in acupuncture clinical trials including Gaw et al[12] and Scharf et al[15] is the selection of sham acupuncture points. What criteria are used to define what a sham point is and where it is located? In classical TCM texts, acupuncture points are well-defined, fixed sites along clearly-diagrammed meridians. Using this frame of reference, any acupoint that is not a defined point is by definition a non-acupuncture point and can be used as a sham point. However, even in classical acupuncture theory, ashi points (or tender points) are defined as acupuncture points. In the last half-century, many microacupuncture systems, such as ear acupuncture, head acupuncture, hand acupuncture, ankle acupuncture, knee acupuncture, wrist acupuncture, have been developed and have won popularity in clinical practice. The recent therapeutic application of "dry needling" is based solely on the use of trigger points as acupuncture needling sites.

In an attempt to rationalize acupuncture theory, scientists have attempted to identify special anatomical structures underlying each acupuncture point. So far, identifiable anatomical structures underlying the classical points have yet to be identified. However, an original study published by Li[24] in 2019 correlates acupuncture point distribution, including points in the microacupuncture system, with the distribution of subcutaneous mast cells. Li's study establishes a strong association between mast cell distribution, density, and physiology and recognized acupuncture points. The dynamic properties of mast cells and their close association with the neuro-immuno-endocrine system make them a strong candidate to be the "missing link" between classical acupuncture and modern science. Many other efforts have been made in redefining the acupuncture points, such as Zhu's sensitization points.[25]

This article has posited two reasons for the continuing lack of consensus in regard to the medical effectiveness of acupuncture: the difficulty of designing scientifically consistent clinical-trial studies; and an institutional bias toward ambiguity on the part of scientific and medical journals. Although the eight studies on knee osteoarthritis described in this article were published in six different medical journals, the positive/negative ratio was 4:4. As cited above, *JAMA*'s publication of acupuncture-related clinical trials over the years has also maintained an equal balance between positive- and negative-result trials. In the case of an individual journal such as *JAMA*, it is entirely possible that a consistent editorial policy is being applied in favor of equally balanced study outcomes. It is harder to impute a consistent editorial "ambiguity bias" when six different journals are involved.

Acupuncture studies continue to pour into medical journals for publication. The studies continue to construct their

outcome measurements around variable factors such as sham points, sham needling, penetration versus nonpenetration, disparate combinations of acupuncture with other therapeutic modalities, etc. The studies by Vas et al[16] and Foster et al[17] which were published in the *British Medical Journal* illustrate this point: the study which paired acupuncture with diclofenac produced positive results; the study which paired acupuncture with physiotherapy produced negative results. While each study in itself may be scientifically valid, the lack of consistent methods of comparison across studies, and the continuing presence of ambiguous or negative study results may be a sufficient explanation of the apparent institutional bias toward ambiguity. Medical journals may easily justify their "balanced" editorial policy by saying: these studies are interesting enough to publish, but do they actually prove or disprove the efficacy of acupuncture on an overall basis? We cannot be seen to be favoring one side's viewpoint in the absence of conclusive evidence.

Conclusion

At this stage, acupuncture remains on the margins of the medical establishment: a promising curiosity. There seems to be a consensus that acupuncture does work or can work under certain circumstances, but naysayers are quick to point to the placebo effect as an insurmountable barrier to conclusive proof. Even a thousand-year experience of successful clinical application of acupuncture to knee osteoarthritis has not constituted evidence of efficacy in the eyes of modern science. Going forward, the acupuncture community should be mindful of the ambiguity problem and the reasons for its persistence. Acupuncture researchers around the world are well-advised to construct their studies within a consistent, universal framework, including a systematization of the variables which are inherent in the practice of acupuncture. It has been said that medicine is the most conservative of the sciences in regard to accepting and integrating new theories and practices. Ultimately, it is possible that the clinical success of acupuncture in treating a multiplicity of chronic and functional health conditions will prevail in the court of public opinion and render the cautious, ambiguous approach of mainstream medical journals irrelevant.

CRediT Authorship Contribution Statement

C.G. is responsible for writing—original draft, investigation, conceptualization, writing-review and editing.

Conflict of Interest

The author declare no conflict of interest.

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