

Current Research and Clinical Applications

Response to: Madsen MV, Gøtzsche PC, Hróbjartsson A. Acupuncture Treatment for Pain: Systematic Review of Randomised Clinical Trials with Acupuncture, Placebo acupuncture, and No Acupuncture Groups.

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This January, BMJ published a systematic review of acupuncture clinical trials for pain conditions. The authors were from Nordic Cochrane Centre in Denmark. They have been researching the placebo effect in medical interventions for a number of years.

The results of this paper were publicised in many newspapers, radio and online media, and caused a world wide discussion on whether acupuncture was effective. I believe most of you would have read the news or heard of the review. At the time of publication, I was busy working on three Human Research Ethics applications for a clinical trial we planned to conduct in Melbourne and paid little attention to the review. I said to myself it was just another such paper, failing to recognise its wide impact. Then two Human Research Ethics Committees questioned me about the implication of the review on our clinical trial. The committees wanted to know, given there was little difference between real and sham acupuncture as shown by the Madsen review, how we could justify the clinical trial we proposed and if we should consider adopting Madsen's recommendations? A couple of weeks

later, a potential patient told me that from his reading there was little evidence supporting the use of acupuncture for pain relief, and asked me what my opinions about acupuncture for pain management were. These incidents highlight the wide and strong impact of research on, not only further studies in the area, but also clinical practice.

ABOUT THE REVIEW

So what is the review about and what are the recommendations? Madsen and colleagues wanted to know if real acupuncture was better than fake/sham acupuncture or no acupuncture for pain relief. To answer the questions, they conducted a comprehensive literature search and utilized a set of selection criteria. Briefly, they selected randomised controlled studies; (1) using invasive acupuncture as the real procedure; and (2) reporting pain intensity measured on a Visual Analogues Scale (VAS) or ranking scale. Thirteen studies with a total of 3025 patients were selected. The study conditions included post-operative pain, scar pain, tension-type headache, migraine, fibromyalgia, osteoarthritis and low back pain. They found that

although there was a statistically significant difference between real and sham acupuncture in pain relief [Standard Mean Difference (SMD) -0.17], the effect was small, about 4 mm on a 100 mm VAS, and clinically insignificant. The difference between real and no acupuncture groups was moderate (SMD -0.42). Furthermore, and contrary to the common view, the authors did not find any difference in pain relief between sham acupuncture using invasive methods and non-invasive methods. The authors concluded that the analgesic effect of acupuncture was clinically irrelevant and the psychological effect of acupuncture needs to be studied.

The authors went further to recommend:

- (1) '...having the needling done by acupuncture naïve clinicians blinded to the hypothesis of the trial'; and
- (2) '...try to separate the effects involved: the physiological effect of needling at acupuncture sites or at other sites and psychological effect of the treatment...'

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ANALYSIS OF THE REVIEW

The authors attempted to answer an important question: the difference between real and sham acupuncture for treating painful conditions. Overall the review was executed with well-accepted methods and adequate statistical analysis. The two weaknesses of the review are the main threats to the validity of the study. Firstly, the review did not distinguish between chronic and acute pain in the analysis. Secondly it failed to assess the quality of acupuncture treatment.

Chronic pain differs from acute pain in its pathology and management approaches. Chronic pain is considered not just a symptom, but a disease in itself,¹ whereas acute pain is often self-limiting and disappears as tissue heals. Furthermore, chronic pain affects one's physical function, cognition and emotion. Due to the complexity of chronic pain, the International Association for the Study of Pain (IASP), the main organisation that promotes pain research, education and practice, advocates multidisciplinary pain management. 'The Initiative on Methods, Measurement, and Pain Assessment on Clinical Trials (IMMPACT)²' states that pain intensity is only one aspect of any pain condition. When assessing the efficacy of an intervention, one has to consider not only reduction in pain, but also improvement in physical function, quality of life and psychological status. Using pain intensity alone to judge the clinical use of a therapy is not adequate. Thus, using limited data, a single type of outcome assessment, or a single modality to judge the efficacy of acupuncture for pain, is also inadequate.

Even within chronic pain, there are various types. For instance, fibromyalgia (FM), a type of wide-spread pain, is quite different from commonly seen localised musculoskeletal conditions, such as knee pain. One study showed that both real and sham acupuncture increased the blood flow in the muscle of FM patients; whereas in the healthy humans, only real

acupuncture had this effect.³ The results indicated that both types of acupuncture could be similarly effective in FM patients, possibly due to physiological, rather than psychological factors. Experienced acupuncturists would know that only shallow needling, similar to that used in sham acupuncture, should be used in FM patients at the early stages of treatment because patients are often extremely sensitive to needling.

Acupuncture is a complex intervention; even in its technique, it is more than just *deqi* and acupuncture points. Two questions students often ask about *deqi* and yet we do not have the answer are how long *deqi* sensation should be maintained and whether we need to produce *deqi* in all acupuncture points used in the treatment. These questions imply the fine techniques involved in needling. Let me illustrate the importance of this question with an example. In recent years, two clinical trials of acupuncture for tension-type headache were conducted in Germany.^{4,5} Both compared real with sham acupuncture, selected similar acupuncture points, and the treatment was delivered by physicians who had similar qualifications. The results were, however, different. For headache days, Melchart's study showed no difference between real and sham acupuncture whereas Endres's study found that real acupuncture reduced headaches by 2.3 headache-days more than sham acupuncture did. Fortunately the authors of the two studies published their research methods and conduct of the trials in great detail,^{6,7} which allowed in-depth comparison of the two trials. It became apparent that the administration of acupuncture and the adherence to protocol differed in the two trials. In the Melchart study, one of the eight main centres delivered 214 out of 1507 sessions of treatment, and did not use two of the three mandatory points for 80% of their patients. '*Deqi* was achieved if possible'. In contrast, in the Endres study, mandatory points had to be needled in every patient and in every

session, '*Deqi* ... had to be elicited at all points', and needles were manipulated 2 to 3 times during the treatment to achieve consistent *deqi*. Independent clinical monitors visited the trial centres repeatedly to ensure the quality of the intervention. The differences between the two trials highlights that the effect of acupuncture is beyond a simple reporting of *deqi* and the acupuncture points selected.

It is not surprising that the recent CONSORT statement on trials assessing non-pharmacological treatments⁸ expanded the 'Intervention' section from one item in the previous statement⁹ to three items. The recent statement also emphasises the inclusion of experienced therapists. For instance, trial surgeons must be experienced in and comfortable with the studied surgical procedure.

WHAT DO I THINK ABOUT THE RECOMMENDATIONS?

The authors of the Madsen review should have discussed the above-mentioned confounding factors before concluding that acupuncture has only a small analgesic effect that is of little clinical relevance. The suggestion of using 'naïve clinicians' so as to ensure the blinding of therapists is not scientifically sound and clearly against the CONSORT statement as outlined above. Such a suggestion will only introduce more variances. The suggestion is also unethical, being against the International Conference on Harmonization Guideline for Good Clinical Practice (ICH-GCP) E6 (1996). Item 4 states that in order to protect trial subjects, the investigators should meet 'all the qualifications specified by the applicable regulatory requirement(s)' and their qualifications should be up-to-date. What would a subject in an acupuncture trial think when he or she is told that the trial therapist is a 'naïve' acupuncturist? I think any Human Research Ethics Board or Committee that approves such practice in acupuncture trials would be

deemed to be unethical.

The second recommendation is reasonable given the complexity of acupuncture. As practitioners, we ought to be mindful that the procedure of acupuncture enhances its therapeutic effect.¹⁰ As researchers, we ought to find if it is possible to separate the physiological and psychological effects of acupuncture and how.

CONCLUSION

Overall, the Madsen review provokes more questions than it provides answers. Future systematic reviews need to take the quality of treatment administration and adherence to protocol into account. These factors of acupuncture treatment need to be further studied in relation to their impact on the outcomes. In addition, before we understand the underlying mechanisms of fibromyalgia, systematic reviews of pain should not confuse wide-spread musculoskeletal pain with other types of pain.

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