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Research Paper Review

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Acupuncture for Chronic Pain: Individual Patient Data Meta-Analysis

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ABSTRACT

Background

Although acupuncture is widely used for chronic pain, there remains considerable controversy as to its value. We aimed to determine the effect size of acupuncture for 4 chronic pain conditions: back and neck pain, osteoarthritis, chronic headache, and shoulder pain.

Methods

We conducted a systematic review to identify randomized controlled trials (RCTs) of acupuncture for chronic pain in which allocation concealment was determined unambiguously to be adequate. Individual patient data meta-analyses were conducted using data from 29 of 31 eligible RCTs, with a total of 17 922 patients analyzed.

Results

In the primary analysis, including all eligible RCTs, acupuncture was superior to both sham and no-acupuncture control for each pain condition ($P < .001$ for all comparisons). After exclusion of an outlying set of RCTs that strongly favored acupuncture, the effect sizes were similar across pain conditions. Patients receiving acupuncture had less pain, with scores that were 0.23 (95% CI, 0.13-0.33), 0.16 (95% CI, 0.07-0.25), and 0.15 (95% CI, 0.07-0.24) SDs lower than sham controls for back and neck pain, osteoarthritis, and chronic headache, respectively; the effect sizes in comparison to no-acupuncture controls were 0.55 (95% CI, 0.51-0.58), 0.57 (95% CI, 0.50-0.64), and 0.42 (95% CI, 0.37-0.46) SDs. These results were robust to a variety of sensitivity analyses, including those related to publication bias.

Conclusions

Acupuncture is effective for the treatment of chronic pain and is therefore a reasonable referral option. Significant differences between true and sham acupuncture indicate that acupuncture is more than a placebo. However, these differences are relatively modest, suggesting that factors in addition to the specific effects of needling are important contributors to the therapeutic effects of acupuncture.

ANALYSIS

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Background Information

Acupuncture is a popular treatment employed by many manual medicine providers. Insertion and stimulation of acupuncture needles at certain locations on the body is done to facilitate pain reduction, improve circulation or induce other beneficial health effects. Originally developed as a component of Traditional Chinese Medicine, many clinicians successfully utilize acupuncture in a contemporary, physiological/anatomical fashion, with little or no reference to acupuncture's pre-modern concepts.

One of the most common reasons patients seek acupuncture treatment is for chronic pain. Although known to produce physiological effects that are related to analgesia, no consensus exists on the exact mechanism(s) involved in acupuncture. A large number of randomized controlled trials (RCTs) have investigated the effects of acupuncture on chronic pain. Unfortunately, most of them are of low methodologic quality, making meta-analyses of this literature of questionable interpretability and value.

The authors of this study attempted to improve on this by presenting an individual patient data meta-analysis of RCTs on acupuncture for chronic pain, including only high-quality studies. Individual patient data meta-analyses are superior to the use of summary data (which is the customary method) because they enhance data quality, enable different forms of outcomes to be combined, and allow use of statistical techniques that can increase precision of the results.

SYSTEMATIC REVIEW RESULTS

Studies Included

- 82 studies were identified, of which 31 were deemed eligible for inclusion in this review.
- 11 of the studies employed a sham control, 10 used a no acupuncture group, and 10 were 3-armed studies – using both a sham and a no acupuncture group.

Clinical Heterogeneity in Control Groups

In the 11 sham RCTs, the sham treatment included acupuncture needles inserted superficially, sham devices featuring needles that retract into the handle rather than penetrate the skin, and non-needle approaches, such as deactivated electrical stimulation or detuned laser. Co-interventions also varied, with no additional treatment other than analgesics in some RCTs, whereas in other studies, acupuncture and sham groups received a course of additional treatment (like exercise). Similarly, the no-acupuncture control groups varied – including 'usual care', mere advice to "avoid acupuncture", attention controls (such as group education sessions), and "guidelined" care (advice as to specific drugs and doses).

Results

- Raw patient data was obtained from 29 of the 31 studies – including a total of 17922 patients
- Patients in all RCTs had access to analgesics and other standard treatments for pain
- Acupuncture was statistically superior to sham acupuncture and no treatment in all analyses ($P < 0.001$)
- Effect sizes were larger when comparing acupuncture to no treatment, versus comparing acupuncture to sham acupuncture – (0.37, 0.26, and 0.15 in comparison with sham vs. 0.55, 0.57, and 0.42 in comparison with no-acupuncture control for musculoskeletal pain, osteoarthritis, and chronic headache, respectively)
- In RCTs comparing acupuncture to no acupuncture, the effect size did vary, which seems at least partly explicable in terms of the type of control employed. To illustrate, as might be expected, acupuncture had a smaller benefit in patients who received a program of ancillary care (such as physical therapist-led exercise) than patients who received usual care
- The authors repeated their meta-analysis excluding studies with fewer than 100 participants – this had essentially no effect on the results

CLINICAL APPLICATION & CONCLUSIONS

After reviewing data from almost 18000 patients, this study provides the most robust evidence to date that acupuncture is effective for the treatment of chronic pain. Even after excluding a set of outlying studies, the meta-analytic results remained consistent across pain conditions. The authors demonstrated a significant difference between acupuncture and sham control that can be distinguished from bias, indicating that acupuncture is more than a placebo, as many detractors consistently imply. However, these differences were relatively modest, suggesting specific effects of needling may be enhanced by other factors that contribute to the therapeutic effects of acupuncture.

Demonstrating even a modest difference between sham and true acupuncture advances beyond prior literature, making this study both clinically and scientifically relevant. The total effects of acupuncture, as experienced by a patient in routine clinical practice, are clinically relevant, but an important part of these total effects is not due to issues considered crucial by many acupuncturists, including precise location of points and depth of needling.

Several have suggested that acupuncture (whether real or sham) is associated with more potent placebo or context effects than other interventions. This makes many clinicians, not to mention insurance companies and third-party payers, uncomfortable. Is it reasonable to withhold a potentially beneficial treatment because we are unsure of, or uncomfortable with, its mechanism? When the mechanism of benefit is unknown, we often label it “non-specific”, or more damningly, “placebo”. Acupuncture is an intervention that causes activation of the endogenous opioid system, modulating the processing of cortical pain signals, thus attenuating the perception of pain (1). Should we abandon this because we don’t fully understand it?

The finding here that acupuncture has effects over and above those of sham acupuncture is therefore very important for clinical practice. Even though these effects are small (on average), the clinical

decision made by clinicians and patients is not between true and sham acupuncture, but between whether or not acupuncture treatment will be implemented directly or via referral.

Study Methods:

The authors systematically searched MEDLINE, the Cochrane Collaboration Central Register of Controlled Trials, and the citation lists of systematic reviews. No language restrictions were employed. There were 2 searches - the initial search, current to November 2008, identified studies for the individual patient data meta-analysis, while the second was conducted in December 2010 for summary data to use in a sensitivity analysis.

Inclusion Criteria

- Randomized controlled trials including at least 1 group receiving acupuncture and 1 group receiving a sham/placebo/no acupuncture control treatment
- Patients had to have 1 of 4 conditions – non-specific back or neck pain, shoulder pain, chronic headache, or osteoarthritis – with the additional criterion that the current episode of pain must be of at least 4 weeks duration for musculoskeletal disorders
- There was no restriction on the type of outcome measure, but it was specified that the primary end point must be measured > 1 month after the initial acupuncture treatment
- Only studies where allocation concealment was deemed adequate were included to remove a common source of potential bias

Assessment of Study Quality

The authors contacted the primary investigators of each included RCT to obtain raw data. The RCTs were graded as having a low likelihood of bias if:

- The adequacy of blinding was checked by direct questioning of patients; and
- No important differences were found between groups, or the blinding method had previously been validated as able to maintain blinding.

Randomized controlled trials with a high likelihood of bias from un-blinding were excluded from the meta-analysis. The sensitivity analysis included only RCTs with a low risk of bias.

Data Synthesis & Analysis

Sometimes it's best to let the authors describe this: "Each RCT was reanalyzed by analysis of covariance with the standardized principal end point (scores divided by pooled standard deviation) as the dependent variable, and the baseline measure of the principal end point and variables used to stratify randomization as covariates. This approach has been shown to have the greatest statistical power for RCTs with baseline and follow-up measures. The effect size for acupuncture from each RCT was then entered into a meta-analysis using the metan command in Stata software (version 11; Stata Corp)." (pg. 1445).

STUDY STRENGTHS / WEAKNESSES

Strengths

- The authors employed an exhaustive search strategy, established clear, justifiable and specific inclusion criteria (prior systematic review inclusion criteria were quite broad [2]), and assessed included studies for relevant sources of bias
- They also validated study eligibility, used appropriate statistical techniques and conducted a wide range of sensitivity analyses
- Most important, by establishing a wide-ranging collaboration, the authors obtained raw data from 29 of 31 eligible trials, allowing data to be pooled and analyzed at the individual level

Weaknesses/Critique

- Because the comparisons between acupuncture and no-acupuncture cannot be blinded, both performance and response bias are possible
- The meta-analyses combined different end points, such as pain and function, measured at different times. The authors did address this, and the results did not change when the analysis was restricted to pain end points measured at a specific follow-up time, 2 to 3 months after randomization.
- Another potential criticism of this paper is that the authors relied on fixed effects models that are less conservative than random-effects models, more likely to yield statistical significance, and less appropriate when the goal is to generalize beyond included studies (but, they did conduct the analysis with both methods and found few differences).

Additional References

1. Benedetti F, Mayberg HS,Wager TD, Stohler CS, Zubieta J-K. Neurobiological mechanisms of the placebo effect. J Neurosci. 2005; 25(45):10390-10402.
2. Furlan AD, van Tulder MW, Cherkin DC et al. Acupuncture and dry-needling for low back pain. Cochrane Database Syst Rev. 2005; (1): CD001351.