The effectiveness and safety of acupuncture therapy in depressive disorders: systematic review and meta-analysis

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CRD summary
This review concluded that acupuncture therapy appeared safe and effective for major depressive disorders and post-stroke depression, but evidence for other depressive disorders was lacking. The authors' findings did not reflect the evidence presented and limitations in study numbers, sample sizes and study pooling, particularly in some subgroup analyses, suggested that the conclusions are not reliable.

Authors' objectives
To determine the safety and effectiveness of acupuncture for the treatment of depressive disorders.

Searching
PubMed including MEDLINE (1950 onwards), Cochrane Central Register of Controlled Trials (CENTRAL), China Journals Full-text Database (1915 onwards), China Master and Doctor Theses Full-text Database (1999 onwards) and China Proceedings of Conference Full-text Database (1999 onwards) were searched. Search terms were reported.

Study selection
Case-control and controlled studies that assessed any form of acupuncture therapy in patients with various depressive disorders (as defined by standardised diagnostic criteria, further details provided) were eligible for inclusion. Trials of non-traditional acupuncture modalities only (such as acupressure and laser acupuncture) were excluded.

Most included studies were published in English or Chinese. Diagnostic instruments used were International Classification of Diseases (ICD), Chinese Classification of Mental Disorders (CCMD) and Chinese Classification of Cerebrovascular Diseases (CCCD). Changes in severity of depression were assessed using Hamilton Rating Scale for Depression (HAMD); pathological changes were verified using computed tomography (CT) and magnetic resonance imaging (MRI).

Included trials were mostly of patients with either major depressive disorder or post-stroke depression. Most trials compared acupuncture monotherapy to antidepressants; others compared interventions against waiting list controls or sham acupuncture. Acupuncture plus antidepressants was compared to antidepressants alone. Antidepressants included fluoxetine (20mg/day), paroxetine (20 to 40mg/day) and amitriptyline (25 to 300mg/day). Acupuncture therapies used either manual or electrical stimulation of combinations of bilateral body and scalp acupoints. The four most frequently used acupoints were Baihui (Du-20), Yintang (EX-HN3), Taichong (LR-3), and Shenmen (HT-7). The number of treatment sessions ranged from 15 to 60. Treatment duration ranged from four to 12 weeks. Response rates, depressive symptoms and adverse events were assessed.

The authors did not state how many reviewers performed the selection.

Assessment of study quality
Methodological quality was assessed using a modified five-point Jadad scale that consisted of the following criteria: type of randomisation method; adequate and appropriate randomisation method; single/double blinding; blinding of assessors; and description of withdrawals and dropouts. Each study was awarded a score up to 5 points. Studies that scored 3 or more points were included in the meta-analysis.

Assessments were carried out by at least two reviewers. Any disagreements were resolved through discussion with a third reviewer.

Data extraction
Dichotomous data (response rates) were generally extracted as at least a 50% reduction in depression scale scores from baseline to endpoint between active acupuncture and controlled groups, and used to calculate risk ratios (RRs) with 95% confidence intervals (CIs). Continuous data (changes in depressive symptoms) were extracted as mean baseline-to-endpoint changes in depression scale scores; Cohen’s d effect sizes and pooled standard deviations were calculated for each study arm.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Studies were combined by type of depressive disorder and outcome. Pooled risk ratios and 95% CIs were calculated for dichotomous outcomes; weighted mean differences (WMDs) with 95% CIs were calculated for continuous data. Statistical heterogeneity was assessed using Z values and \( \chi^2 \) distributed Cochrane Q values. Where significant heterogeneity was evident, the Mantel–Haenszel random-effects model was used to pool data; otherwise, a fixed model was applied. The I\(^2\) test for heterogeneity was used to describe low (values less than 25%), medium (values between 25% and 50%) and high (values over 50%) levels of heterogeneity. Subgroup analyses were performed by trial comparator. Publication bias was assessed using funnel plots and the Egger's test.

Results of the review
Thirty-nine RCTs of high quality (Jadad score \( \geq 3 \)) were included in the review: 20 RCTs of major depressive disorder (n=1,998); 15 RCTs of post-stroke depression (n=1,680); two RCTs of pre-menstrual depression; and one RCT for peri-natal depression and comorbid depression. Only studies of major depressive disorder and post-stroke depression were included in the meta-analysis, due to the small numbers of studies and participants in the other disease subgroups. Four studies were awarded a maximum Jadad score of 5 points, four scored 4 points and the remaining studies scored 3 points.

For patients with major depressive disorder there were no statistically significant differences between acupuncture monotherapy and control groups for clinical response or symptom severity. Subgroup analyses failed to find any statistically significant differences between acupuncture and antidepressants, sham acupuncture and waiting list control. Two pooled trials of acupuncture plus antidepressants versus antidepressants alone showed a statistically significant improvement in HAMD scores in favour of the combination treatment (WMD 2.38, 95% CI 0.62 to 4.12, p=0.007, I\(^2\)=0%)

For patients with post-stroke depression there was a statistically significant difference favouring acupuncture monotherapy in comparison with control groups for clinical response (RR 1.36, 95% CI 1.24 to 1.50, p<0.00001, I\(^2\)=36%; 13 RCTs) and symptom severity (WMD 2.54, 95% CI 1.11 to 3.97, p=0.0005, I\(^2\)=79%; 14 RCTs). Both these pooled analyses were associated with moderate to high levels of heterogeneity.

Subgroup analyses showed statistically significant differences in favour of acupuncture monotherapy in comparison with antidepressants and waiting list controls for both clinical response and symptom severity (further details reported in the review).

Incidence of adverse events was lower with acupuncture and sham acupuncture than with antidepressants (10.2% versus 40.4%, \( \chi^2 = 389.457, \text{d.f.} = 1, p<0.001 \)).

There was no evidence of publication bias.

Authors’ conclusions
Acupuncture therapy appeared to be a safe and effective treatment for major depressive disorders and post-stroke depression; evidence for other depressive disorders was lacking.

CRD commentary
This review answered a clear research question. Inclusion criteria for study design were broad, but only highest-quality randomised controlled trials were included in the meta-analysis. Attempts were made to search for both published and unpublished studies, which reduced risk of publication bias (confirmed by the authors’ assessments). The authors’
searches reflected a predominance of Chinese- and English-language publications, but they did not report whether searches were restricted to these languages and so risk of language bias was unclear. It was unclear how up to date the literature searches were, although start dates were given for each database searched. Multiple reviewers were involved in assessment of study quality; it was unclear whether similar precautions were taken to reduce risk of reviewer error and bias during study selection and data extraction. Heterogeneity between studies was assessed. Subgroup analyses considered differences in study comparators. The meta-analyses included only the highest-quality data, but many studies included only small numbers of patients and subgroup analyses were based on a limited number of studies, which may have affected their reliability. There was evidence of significant heterogeneity between many of the studies included in the pooled analyses. Most analyses found no significant differences between acupuncture therapies and antidepressants and sham acupuncture, which did not support the authors' conclusions that acupuncture therapy was effective. Overall, the authors' findings did not reflect the evidence presented and limitations in study numbers, sample sizes and study pooling, particularly in some subgroup analyses, suggested that the conclusions are not reliable.

Implications of the review for practice and research

Practice: The authors stated that acupuncture may be considered as an alternative therapy for patients with major depressive disorder and post-stroke depression, but its use in combination with antidepressants was controversial.

Research: The authors stated that further research in the form of large well-designed controlled trials to assess effectiveness of standardised acupuncture therapies for depressive disorders were required. Studies should attempt to identify which demographic and methodological factors affected treatment effects.

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