A meta-analysis of acupuncture combined with opioid receptor agonists for treatment of opiate-withdrawal symptoms

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CRD summary
This review concluded that acupuncture combined with opioid receptor agonists for the treatment of opiate-withdrawal symptoms could effectively be used to manage withdrawal symptoms. A lack of good quality data, a lack of clarity over parts of the review process and uncertainty over the generalisability of the findings suggest that this conclusion should be interpreted with caution.

Authors' objectives
To assess the efficacy of acupuncture combined with opioid receptor agonists for the treatment of opiate-withdrawal symptoms.

Searching
EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), CBM, CNKI Wanfang and VIP database were searched from January 1990 to February 2008 for English-language and Chinese-language studies; search terms were reported. Reference lists of included studies were searched and experts consulted for additional studies.

Study selection
Randomised controlled trials (RCTs) that compared acupuncture with opioid receptor agonists against a control group that received any opioid receptor agonists or partial opioid receptor agonists and which focused on opioid detoxification were eligible for inclusion. Eligible studies comprised at least 15 participants in each group that met criteria for opioid-heroin dependence and were in the acute stage of the abstinence syndrome. Opioid-heroin dependence was defined by DSM-IIIR or DSM-IV criteria and opioid-abuse history, documented abstinence syndrome and positive urine test.

In included trials, symptoms of acute stage abstinence syndrome included lachrymation, yawning, sweating, diarrhoea, insomnia and fatigue. Included interventions comprised acupuncture combined with either methadone, buprenorphine or opiate. Acupoints most frequently used in the included studies were neiguan, zusanli, shenmen, hegu and sanyinjiao. On average, acupuncture stimulation lasted from 20 to 50 minutes once or twice per week over 10 to 15 days. A range of eligible outcomes included: total score for opioid-withdrawal symptoms; relapse rate; side-effects; and medicine dosage required to allay withdrawal. Average ages of participants in the included studies ranged from 24.0 to 34.2 years of age; 82% were male. All studies dealt with participants dealing with heroin abuse; the average daily amount of heroin use was 0.45g to 1.80g and average duration of use was 38.9 to 98.4 months. All studies were undertaken in China.

Two reviewers selected the studies for inclusion in the review. Disagreements were resolved by discussion.

Assessment of study quality
Randomisation, blinding and withdrawal were assessed according to the Jadad criteria. Studies could score up to a maximum of 5 points; trials that scored at least 3 points were considered to be of high quality.

The authors did not state how many reviewers assessed study quality.

Data extraction
Data were extracted to derive the relative risk (RR) for dichotomous outcomes (such as relapse rate) and mean differences for continuous outcomes (such as scores on rating scales).

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

Methods of synthesis
The studies were combined in meta-analyses. Pooled relative risks and weighted mean differences (WMD), and their 95% confidence intervals (CI), were calculated using a fixed-effects model. A random-effects model was used if
significant heterogeneity was present. Heterogeneity was assessed using the $\chi^2$ and $I^2$ tests. Fail-safe numbers were calculated to assess publication bias.

**Results of the review**

A total of 11 RCTs (n=1,175, range 57 to 200) were included in the review. Quality score was 2 in all studies; no studies reported details of randomisation or blinding. For statistically significant WMD in total withdrawal symptom scores (days one, seven and final two days only) fail-safe N ranged from 12 to 242. There was some discrepancy in patient numbers between the tables and the text.

Withdrawal-symptom scores were lower in combined treatment trials than in agonist-alone trials (seven studies) on withdrawal day one (WMD -3.67, 95% CI -5.83 to -1.52), day seven (WMD -9.54, 95% CI -17.99 to -1.09), penultimate day of treatment day nine/day 14 (WMD -9.50, 95% CI -16.15 to -2.84) and final day of treatment (WMD -7.51, 95% CI -11.80 to -3.22), but not at other time points. There was no significant difference in relapse rates after six months (RR 0.60, 95% CI 0.32 to 1.10; four studies).

There was insufficient data to combine safety or medicine dosage outcomes.

**Authors' conclusions**

Acupuncture combined with opioid agonists could effectively be used to manage the withdrawal symptoms, but there was no strong evidence that the combination is superior to treatment with an opioid agonist alone.

**CRD commentary**

Inclusion and exclusion criteria were clear. The authors searched a range of sources for publications in English and Chinese, so language bias could have been present. Some attempts were made to locate unpublished studies. The risk of publication bias was assessed through fail-safe N; the results were reported for each time point, but not discussed. The authors reported that they used methods to reduce error and bias in the selection of studies, but it was unclear whether this extended to the extraction of data and assessment of study quality.

An appropriate assessment of trial quality was reported; all trials were of poor quality. Standard statistical methods were used to pool the data. Heterogeneity was explored, but not reported in the results; significant heterogeneity was present for the analyses.

Generally this was a well-conducted review but, as acknowledged by the authors, the findings were limited by a lack of good-quality data, a lack of clarity over parts of the review process and uncertainty over the generalisability of the findings away from China. In light of these shortcomings the authors' conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that high-quality research was required for more definitive conclusions.

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