

# Research Snapshots

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## COCHRANE REVIEW ON THE EFFECTS OF CHINESE HERBAL MEDICINES ON IMPAIRED GLUCOSE TOLERANCE AND IMPAIRED FASTING GLUCOSE

Higher than normal blood glucose levels – Impaired glucose tolerance (IGT; fasting blood glucose <7.0 mmol/L and two-hour post-load blood glucose 7.8-11.0 mmol/L) and impaired fasting glucose (IFG; fasting blood glucose 6.1-6.9 mmol/L) – are often present for several years before formal diagnosis of diabetes mellitus.

**OBJECTIVES:** This systematic review was undertaken to determine the efficacy (effects and safety) of Chinese herbal medicines for people with IGT or IFG.

**METHODS:** Protocols stipulated in the 2008 Cochrane Handbook for Systematic Reviews were adopted. Sensitive validated search strategies were used to source randomised clinical trial (RCTs) studies up to February 2009 from The Cochrane Library, PubMed, EMBASE, AMED, Chinese language databases, SIGLEA and databases of ongoing trials.

**RESULTS:** Of 1926 initially identified records, 83 were examined further and 16 studies ( $n = 1391$ ) met inclusion criteria for full review. These 16 had all been conducted from 2001 onwards, over a period from four weeks to two years, and involved 42–168 participants ranging in age from 44 to 66 years who had been recruited from hospitals or clinics in China (15) and Japan (1). Interventions all included complex herbal formulas as decoctions, pills/capsules or granules. The most common ingredients were *Huangqi* (*Radix Astragali Membranaceus*; 10 RCTs), *Shanyao* (*Radix Dioscoreae Opposita*; 8 RCTs) and *Gegen* (*Radix Puerariae*; 4 RCTs). Lifestyle modification was mostly used as co-intervention ( $n = 12$ ) and control (10) – though no studies gave comprehensive descriptions of these. Other controls were placebo (3) and pharmacology (metformin [2]; acarbose [1]; antihypertensive medication [1]). The most apparent finding was that participants receiving herbal medicine and lifestyle modification ( $n = 8$  RCTs; 625 participants) were more than twice as likely to have normalised blood glucose by the end of the trial than those undertaking lifestyle modification. Of note, however, is the potential bias on outcomes, none of these eight studies

having blinding in their designs. Of the 3 out of 16 trials with double blinding and low risk of bias, significant results were found for some but not all biomedical markers.

**CONCLUSION:** This review points to the promise of a group of Chinese herbal medicines to lower blood glucose and to prevent diabetes mellitus. The general heterogeneity of samples, herbal complexes tested, methodologies and results does not allow generalisation or validation for clinical practice guidelines. However, this review does indicate the need for continued research using well-designed RCTs which build rate of reversion to normal blood glucose into statistical calculations, and which include measures of glycosylated haemoglobin A1c, the preferred diagnostic test for diabetes.

*Grant SJ, Bensoussan A, Chang D, Kiat H, Klupp NL, Liu JP and Li X. Chinese herbal medicines for people with impaired glucose tolerance or impaired fasting blood glucose (Review). Cochrane Database Syst Rev 2009(4).*

**Kerry Bennett**

TRADITIONAL CHINESE ACUPUNCTURE AND PLACEBO (SHAM) ACUPUNCTURE ARE DIFFERENTIATED BY THEIR EFFECTS ON  $\mu$ -OPIOID RECEPTORS IN PATIENTS WITH FIBROMYALGIA

**BACKGROUND:** Controversy remains regarding the mechanisms of acupuncture analgesia. A prevailing theory, largely unproven in humans, is that it involves the activation of endogenous opioid antinociceptive systems and on  $\mu$ -opioid receptors (MORs). In addition, endogenous opioid peptides have been found to mediate placebo-induced analgesia. This overlap may explain a lack of differentiation between traditional acupuncture (TA) and sham acupuncture (SA) in many controlled clinical trials.

**OBJECTIVE:** The authors compared both short and long-term effects of TA with SA treatment on in vivo MOR binding availability in patients diagnosed with fibromyalgia.

**DESIGN/SETTING/SUBJECTS:** 20 female patients were randomized to receive eight either TA or SA treatments over four weeks. SA intervention was performed on non-acupuncture points and did not break the skin. Positron emission tomography (PET) with  $^{11}\text{C}$ -carfentanil was performed once during the first treatment session and once at one month later following the eighth treatment.

**OUTCOME MEASURES:** The severity of clinical pain was assessed immediately before PET1 and after PET2 with the Short form of the McGill Pain Questionnaire.

**RESULTS:** TA evoked short-term increases in MOR binding potential in multiple pain and sensory processing regions including the cingulate (dorsal and subgenual), insula, caudate, thalamus, and amygdala. TA also evoked long-term increases in MOR binding potential in some of the same structures including the cingulate (dorsal and perigenual), caudate, and amygdala. The enhanced MOR binding potential were absent in the SA group where small

reductions were observed, an effect more consistent with previous placebo PET studies. Long-term increases in MOR binding potential following TA were also associated with greater reductions in clinical pain. Intensity of pain was, however, not statistically significantly different between TA and SA groups.

**CONCLUSION:** Overall the data strongly imply divergent opioid receptor mechanisms in true acupuncture and sham acupuncture interventions. Although the fundamental mechanism underlying these processes await further investigation, central opioid receptors appear to be involved in both treatments, albeit with differing effects within the same brain structures.

*Harris RE, Zubieta JK, Scott DJ, Napadow V, Gracely RH, Clauw DJ. Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on  $\mu$ -opioid receptors (MORs). *NeuroImage* 2009;47:1077–85.*

*John Deare*

### ACUPUNCTURE IS NOT EFFECTIVE IN INDUCING CHILD BIRTH

**OBJECTIVE:** The aim of this study was to evaluate the effectiveness of acupuncture in stimulating foetal delivery by shortening the time from acupuncture treatment to delivery, encouraging spontaneous delivery or decreasing the rate of caesarean-section.

**METHODS:** Women at 38 to 41 weeks of their first child pregnancy were recruited. Subjects were randomised to receive traditional Chinese medicine (TCM) acupuncture, sham acupuncture, or usual care. Acupuncture treatments included bilateral needling on LI4, SP6, BL32, and BL54 and retained for 30 minutes for five times over two weeks. Sham acupuncture treatments included non-acupuncture points with shallow insertion. The usual care group received routine pre-natal care from their care provider. Primary outcome was time from enrolment of first acupuncture session to time of delivery. Secondary outcomes included pregnancy related complications, rate of caesarean-section and spontaneous delivery.

**RESULTS:** Eighty-nine women who had their first child were recruited from prenatal chart review and web-based advertising. Thirty, 29 and 30 women were randomised into TCM acupuncture, sham acupuncture and usual care, respectively. There were no significant differences among the groups in time from first acupuncture session to delivery although sham acupuncture group had a shorter delivery time on average. There were no significant differences among groups in pregnancy related complications, rates of caesarean-section, and spontaneous delivery.

**CONCLUSION:** TCM acupuncture was not effective in inducing spontaneous labour or reducing the rate of caesarean section in comparison with sham acupuncture or usual care.

**COMMENT:** The authors have previously conducted an acupuncture study on inducing labour with positive finding and supporting the use of acupuncture. The main difference between the two studies is that the previous study included higher risk patients and acupuncture was delivered close to the delivery time (mean: 40 1/7 weeks); whereas this trial included fewer high risk patients and the treatment was given early (mean: 38 5/7 weeks). It is possible the closer to the delivery time, the more ready it is for labour to be induced.

*Asber GN, Coeytaux RR, Chen W, Reilly AC, Loh YL and Harper TC. Acupuncture to initiate labor (Acumoms 2): A randomized, sham-controlled clinical trial. J Matern Fetal Neonatal Med 2009;22(10):843-8.*

### IS SHAM ACUPUNCTURE REALLY INERT? A CHALLENGING QUESTION

This is a commentary of current acupuncture studies comparing the effect of real and sham/minimal acupuncture on clinical conditions. Three multicentred randomised studies and one meta-analysis on migraine have shown that both real and sham acupuncture were as effective as each other and both were more effective than standard treatment, placebo medication or waiting list controls. Healthy subjects responded to sham acupuncture treatment with activation of the limbic system whereas patients with pain responded to sham acupuncture treatment with deactivation of the limbic system. Patients also responded to sham acupuncture differently depending on their conditions. With IVF, sham acupuncture produced higher pregnancy rate than real acupuncture did. With irritable bowel syndrome, both real and sham acupuncture groups showed no difference in quality of life assessment. With patients suffering from environmental illnesses, cortisol

concentration increased without any group difference. Acupuncture ritual also induced a psychological re-orientation which might make sham acupuncture as powerful as real acupuncture because both interventions altered functional connectivity.

Both experimental and clinical studies showed placebo acupuncture was not psychophysiological inert. The authors argue that placebo-controlled acupuncture studies introduce bias against the finding instead of reducing bias. The authors recommend acupuncture to be compared with standard treatments before establishing whether acupuncture is effective against placebo interventions.

*Lundeberg T, Lund I, Sing A and Naslund J. Is Placebo Acupuncture What It is Intended to Be? Evid Based Complement Alternat Med 2009 DOI: 10.1093/ecam/nep049*

### ACUPUNCTURE CAN HELP PATIENTS IN THE EMERGENCY DEPARTMENT (ED)

**OBJECTIVE:** This is a non-randomised pilot study assessing the efficacy of acupuncture to reduce ED patients' pain and the feasibility of performing acupuncture in ED.

**METHODS:** Acupuncture was used to treat ED patients with acute non penetrating extremity injury. All patients received ice, elevation and splinting when appropriate. Pain was assessed before acupuncture treatment, right after (time 0) and every 30 minutes thereafter by using visual analogue scale (VAS) for the duration of their stay in ED. Telephone calls were also made within 72 hours after discharge to assess patients' intensity of pain, complications, and satisfaction with acupuncture. Average time spent in the fast track area and the average time in the department (TID) for all fast track patients with similar

injury were compared. ED physicians were asked not to administer analgesics before or during acupuncture treatment. If patients requested and administered analgesics before or during acupuncture treatment, patients were withdrawn from study.

**RESULTS:** 47 patients were approached and 20 consented to participate. Of the 20 participants, mean age was 33 and 14 of them were male. They suffered from musculoskeletal contusion, injury, sprain or closed fracture. Three of them did not complete the protocol and were not included in the analysis. The median VAS score was reduced by 16mm (range

0-60mm) out of 100 at time 0. Median numerical rating scale at follow-ups was 3 out of 10. Median TID was 135 minutes (range 55 to 255 minutes). Median TID of patients who did not receive acupuncture was 90 minutes (range 52 to 270 minutes). There was no significant difference in TID between acupuncture and the history control group who did not receive acupuncture. The author did not define the control group clearly in the paper. The median satisfaction score was 5 (range 3 to 5).

**CONCLUSION:** Acupuncture can be an effective analgesic intervention for patients with acute extremity injuries

and acupuncture did not increase patient's TID. Patients were satisfied with acupuncture treatment. Minor complications were experienced by acupuncture participants.

*Arnold AA, Ross BE, and Silka PA. Efficacy and feasibility of acupuncture for patients in the ED with acute, nonpenetrating musculoskeletal injury of the extremities. Am J Emerg Med 2009;27(3):280-4.*

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