Clinical trials of effectiveness

Acute low back pain


Multicentre RCT (n=275) comparing three types of acupuncture and conventional treatment (CT).

Methods

Patients with new onset low back pain (LBP) within the previous 2 weeks were recruited from four primary care health centres in Spain. They were randomised to four groups: CT alone, true acupuncture+CT (TA), sham acupuncture+CT (SA) and ‘placebo’ acupuncture+CT (PA). Patients in the acupuncture groups were blinded to the treatment they received, but the CT group were not. The CT, SA and PA groups were considered as control groups with the SA and PA groups being used to assess the specificity of acupuncture points and technique.

CT consisted of analgesics, non-steroidal anti-inflammatory drugs, muscle relaxant drugs, posture recommendations and asking patients to maintain normal activity. Treatment in the three acupuncture groups consisted of five 20-min sessions over a period of 2 weeks performed by physicians with considerable experience in acupuncture. Patients in the TA group had individualised acupuncture points treated according to Traditional Chinese Medicine (TCM) criteria. Non-specific points for the treatment of LBP were chosen in the SA patient group and needled in the same way as the TA group. Points in the PA group were treated by applying momentary pressure with a semi-blunted needle fitted within a guide tube.

The main outcome measure was the clinically relevant improvement in LBP at 3 weeks following randomisation, defined as a 35% reduction in the Roland Morris Disability Questionnaire (RMQ) score.

Results

The mean duration of pain before treatment was 6 days. The proportions of subjects achieving a significant improvement in their RMQ baseline score were 75.5%, 75.0%, 65.2% and 44.3% in the TA, SA, PA and CT groups, respectively. In the adjusted analysis, the relative risks for efficacy were 5.04 (95% CI 2.24 to 11.32), 5.02 (95% CI 2.26 to 11.60) and 2.57 (95% CI 1.21 to 5.46) in the TA, SA and PA groups, respectively, relative to CT. All acupuncture groups responded better than CT alone. However, for percentage improvement, TA was statistically superior to PA (figure 1).

Comment

Previous studies have demonstrated the efficacy of acupuncture over placebo in the treatment of chronic LBP. This well-conducted study demonstrates its effectiveness in the context of acute LBP with a significant superiority over CT alone. The results imply that traditional acupuncture is not more effective than SA. However, the authors themselves state that the study was statistically powered only to detect a difference between acupuncture and CT. A much larger sample size (the literature suggests about 800) would be required to demonstrate any differences between the different types of acupuncture.

Dry eye


RCT (n=150) of acupuncture compared with artificial tears.

Methods

One hundred and fifty patients (mean age approximately 47 years) with moderate to severe dry eye were recruited; just under half had had no previous treatment for the condition. Participants were randomly allocated to 4 weeks of acupuncture treatment at 17 points (decided by consensus: bilateral BL2, GB14, TE 23, Ex1, ST1, GB20, LI4, LI11 and midline GV23) or to the artificial tears group (sodium carboxymethylcellulose). De qi was elicited and needles were left for 20 min; 12 treatments were given over 4 weeks. The main outcome measures at various times up to 12 weeks were the 12-question ocular surface disease index (OSDI), tear film break-up time (TBFUT) and Schirmer I test for tear secretion.

Results

The acupuncture group showed a gradually increasing superiority in OSDI scores over the artificial tears group which was most marked at the 12-week point, 8 weeks

---

**Figure 1** Percentage improvement in Roland Morris score at 3 weeks. Based on Vas et al. *Pain* 2012;153:1883–9.
Acupuncture research update

Figure 2  Dry eye score (OSDI). Based on Kim et al. PLoS One 2012;7:e36638.

after the end of treatment (figure 2). Acupuncture was also superior to tears in one of the objective tests (TFIBUT) but not the other (Schirmer I).

Comment
This seems to be the first clinical trial of acupuncture for dry eye—a condition which interferes with life and is not fully controlled by artificial tears. This study was well designed, but inevitably there are uncertainties: patients with single dry eye were included although they may have a different pathology; ‘patients who needed active treatment’ were excluded; and an even longer follow-up would be interesting.

Considering that there is no cure for dry eye except youth (and that we cannot give patients), the fact that there was improvement even 4 weeks after discontinuation of the acupuncture treatment is significant. Although non-specific effects of acupuncture were not accounted for in this study, in fact acupuncture cannot be delivered without them. Clearly acupuncture is at least as effective as tear drops, although hyaluronic acid is now increasingly used as artificial tears and may be superior to carboxymethylcellulose used here.

The next research questions are whether the results of acupuncture treatment justify the resources needed and even whether self-treatment is possible, for example, with acupressure or electrical stimulation.

Functional dyspepsia

Multicentre randomised trial (n=64) comparing traditional acupuncture with sham for functional dyspepsia and attempting correlation with brain activity.

Methods
Sixty-four patients with functional dyspepsia were randomly allocated to either traditional acupuncture (ST34, ST36, ST40, ST42) or sham (penetrating needling at non-acupuncture points, three on upper extremity, one near proximal tibia) for 4 weeks (30 min per session, 5 sessions per week; manual and electrical stimulation). Outcome measures were changes in Symptom Index of Dyspepsia (SID, assessing symptoms) and Nepean Dyspepsia Index (NDI, assessing quality of life). Ten patients from each group underwent assessment of changes in glucose metabolism before and after treatment in various brain areas by positron emission tomographic (PET) scan.

Results
SID and NDI scores improved significantly in the acupuncture group. In the sham group, the SID score for postprandial distension and the NDI score improved significantly, but not the SID score for early satiety. SID scores improved significantly more in the acupuncture group than in the sham group. NDI score changes did not differ significantly between groups, but only the improvement in the acupuncture group was considered clinically significant. Metabolic activity decreased significantly in both acupuncture and sham groups, but in different areas of the brain. Improvement in the NDI score in the acupuncture group was associated with a significant decrease of metabolism in the brainstem and thalamus. The reduction in SID scores in the acupuncture group was associated with reduced activity in parts of the brain which form the homeostatic afferent network.

Comment
This was a small trial, done without the benefit of power calculation. Only a third of patients in each group underwent PET scan assessment. Clinical findings are in keeping with other studies (eg, Ma et al1 summarised in Acupuncture Research Update in June 2012). The authors say that the improvement in symptoms correlates with changes in brain areas which have increased activity in functional dyspepsia, and that acupuncture restores homeostasis. This may be of interest when researching the mechanisms by which acupuncture works, but it has to be remembered that the pathophysiology of functional dyspepsia is unclear. A better defined syndrome may have been a better subject for such a study, which ought to have included more participants.

Reference

Migraine: economic analysis

Economic analysis of RCT (n=480) with a questionable finding.
Methods

The multicentre RCT of acupuncture treatment in patients with migraine was summarised in the Acupuncture Research Update column in March 2012. A total of 480 patients with migraine were randomised to four groups: ‘appropriate’ points on the most appropriate meridian (Shaoyang); other points on the same meridian; points on an ‘inappropriate’ meridian (Yangming); or off-meridian ‘sham’ locations. All groups received 20 treatments over 4 weeks, all had electroacupuncture and de qi was elicited in the first three. The number of days with migraine at 5–8 weeks was the primary outcome, and there were no differences between groups. At the 13–16-week follow-up, all acupuncture groups had greater reductions than the sham group, but there were no differences between the groups (figure 3).

This new paper reports the cost-effectiveness ratio, expressed as cost per day reduction of headache days from baseline to week 16. Cost-comparison analyses, differences in the migraine-specific quality of life questionnaire (MSQ) and the incremental cost-effectiveness ratio were secondary outcome measurements. In addition, a sensitivity analysis was conducted.

Results

The total cost per patient was CNY1273.2 (95% CI 1171.8 to 1375.1) in the Shaoyang specific group, CNY1427.7 (95% CI 1311.8 to 1543.6) in the Shaoyang non-specific group, CNY1490.8 (95% CI 1327.1 to 1654.6) in the Yangming specific group and CNY1470.1 (95% CI 1358.8 to 1581.3) in the sham acupuncture (SA) group. The reduced days with migraine were 4.0±2.7, 3.6±2.8, 3.8±3.6, and 2.2±3.7 in the four groups (p<0.05 for each genuine acupuncture points group vs the sham group) at week 16. Days lost from work are not reported.

The cost-effectiveness ratios of the four groups were 356, 320.5, 401.6, 393.1 and 682.2, respectively. The results of the sensitivity analysis were consistent with that of the cost-effectiveness analysis. The Shaoyang specific group significantly improved in all three MSQ domains compared with the SA group.

Comment

The trial is reported as showing a positive economic analysis for treatment at ‘appropriate’ points compared with various groups treated at ‘inappropriate’ points. If true, this is an important finding. The abstract even describes the improvement in quality of life as ‘dramatic’, which is an uncommon term (being subjective) in a scientific report and one that hardly seems justified since the improvement was described as ‘clinically minor’ in the original report.

On close inspection, the figures are not convincing. The difference between the groups was entirely in ‘indirect’ costs; these are not precisely defined but seem mainly to involve the costs of lost days at work. The paper admits there were great difficulties in measuring lost days at work, there were significant baseline differences and data were not collected for 4 of the 12 follow-up weeks. Surprisingly, the paper does not report the actual numbers of days lost (only the number of days with migraine—which is not the same thing). The original reviews of this paper are available for all to read in the online version of the paper. Chance seems to have played a distinct part in this finding.

Another concern about this paper is that it refers to the original report as having shown the ‘efficacy’ of acupuncture; but the differences in the main outcome measures were not significant, only trends.

Reference


Carpal tunnel syndrome


RCT (n=41) comparing verum acupuncture and sham acupuncture (SA), together with nocturnal splints.

Methods

Forty-one subjects with mild to moderate carpal tunnel syndrome were randomised to receive either verum acupuncture or SA. The severity of carpal tunnel syndrome was determined on the basis of symptoms and electrodiagnostic studies, with severe cases being excluded.

Two physician acupuncturists were involved in the treatment of the subjects in both arms of the study but not in data collection or analysis. The subjects were physically blinded using an opaque cover over their eyes during the treatment sessions. The assessors were also blinded. Subjects in both groups received weekly treatments for a total of 6 weeks. The points used were: affected side PC6, PC7 and SP6 and opposite side TE5, LI4, LI11 and GB34, and were selected on the basis of TCM. SA was performed using retracting non-penetrating Streitberger placebo needles which were held in place by a small plastic ring and Steri-strip tape. They were manipulated for 2 s and held in place for 20 min. Verum
acupuncture was performed using sterile acupuncture needles along with the same plastic ring and Steri-strip tape. Needles were manipulated manually until de qi was achieved and also left in place for 20 min.

The Carpal Tunnel Self-Assessment Questionnaire (CTSAQ) Symptom and Function Scales were used as primary outcome measures. Secondary outcome measures included key and tip pinch assessment and combined sensory index using a dynamometer. All outcome measures were performed immediately after the end of treatment, at 2 weeks and at 3 months. Subjects in both groups were also instructed to wear wrist splints nightly.

Results
Both the verum acupuncture and SA groups showed significant improvements in CTSAQ scores. Subjects in the verum acupuncture group had an improvement of 0.58 (p=0.05) in the CTSAQ Symptom Scale at 3 months compared with 0.81 (p=0.001) in the SA group (figure 4). There was an improvement of 0.45 (p=0.17) in the CTSAQ Function Scale in the verum acupuncture group compared with 0.48 (p=0.02) in the SA group. However, no statistically significant differences were found in scores of secondary outcome measures between baseline and 3 months.

Comment
Verum acupuncture was not found to be superior to SA in this study, with both groups showing a clinically relevant improvement. Since wrist bracing itself is known to be effective in relieving symptoms of carpal tunnel syndrome, it is not possible to verify how much of the improvement in the two acupuncture groups was due to this variable. The study design could have been improved by having a third conservative treatment group which used wrist bracing alone. It would also have been interesting to obtain objective electrodiagnostic measures at 3 months to compare with baseline in addition to the subjective CTSAQ scores. A higher ‘dose’ of acupuncture could also have been used in the verum acupuncture group using electroacupuncture to demonstrate a potential difference, but the authors found the Streitberger needles would not stay upright with leads attached.

Migraine and cranial blood flow


RCT (N=35) comparing Traditional Chinese Medicine (TCM) with sham acupuncture (SA) for migraine prophylaxis and to assess the response in cranial blood flow to either treatment.

Methods
Adults with established migraine were randomly assigned to either TCM acupuncture (n=18) at 6–10 points selected from a list, eliciting de qi, or a sham procedure (n=17) needled superficially at non-acupuncture points. Treatments were given weekly for 8 weeks. Clinical outcome was the reduction in migraine frequency. In addition, flow through the middle cerebral artery at rest and during a Valsalva manoeuvre was assessed by transcranial Doppler ultrasonography; previous studies suggest that an abnormal response may be present in patients with migraine, reflecting haemodynamic changes.

Results
The TCM acupuncture group experienced a reduction of 52.2% in the number of headache days in 3 months (from 7.86±3.32 days to 3.76±3.03 days) compared with 28.2% (from 6.05±2.88 days to 4.34 days) in the SA group; the reduction was significant in both groups. Duration of attacks was reduced from 89.2±42.2 h to 43.9±34.3 h/month in the TCM group and from 68.5±39.5 h to 51.8±36.4 h/month in the SA group, which was not a significant difference.

Vasotonus, as measured by flow velocity in the middle cerebral arteries at rest, was not changed significantly in either group. The cerebrovascular response (CVR) to Valsalva, defined as maximum end-diastolic flow velocity acceleration during straining, was reduced from 7.61±3.11 cm/s² (right MCA)/7.62±3.93 cm/s² (left MCA) in the pre-acupuncture phase to 5.21±2.51 (right)/7.62±3.95 cm/s² (left) in the TCM group; this was significant (p<0.004). The response observed in the SA group was non-significant (p=0.94; figure 5).

The authors conclude that their study confirms other observations of the clinical benefit of acupuncture in the prophylaxis of migraine and the significant CVR with TCM may have a role in the mechanism of the acupuncture.

Comment
This is a fairly small study, performed without the benefit of a power calculation, so it is perhaps not ideal to assess efficacy. However, a number of such studies on
migraine have already been performed. A non-penetrating control may have been better than non-traditional points with superficial needling. It is, however, encouraging that efforts are being made to establish the mechanisms by which acupuncture might work.

**Systematic reviews**

**Acupuncture for pain**


Meta-analysis (29 studies) of four chronic pain conditions: back and neck pain, osteoarthritis, chronic headache and shoulder pain.

**Methods**

Researchers from the Acupuncture Trialists’ Collaboration, a group that was established to analyse RCTs of acupuncture for chronic pain, selected high-quality studies (ie, that used allocation concealment) and contacted the authors for individual patient data; 29 of 31 eligible RCTs were included, with a total of 17,922 participants—the largest ever study on acupuncture.

**Results**

In the primary analysis, acupuncture was superior to both sham and no-acupuncture control for each pain condition (*p*<0.001 for all comparisons).

The researchers found modest but statistically significant effect size differences between acupuncture and sham (ie, specific effects) for spinal pain (0.37) (figure 6), osteoarthritis (0.26), chronic headache (0.15) and shoulder pain (0.62). This indicates that acupuncture is more than a placebo.

The effect sizes in comparison to no-acupuncture controls—which reflect the effect that would be seen in practice—were considerably larger: spinal pain (0.55), osteoarthritis (0.57) and chronic headache (0.42). There were no trials for shoulder pain.

These results were robust to a variety of sensitivity analyses, including those related to publication bias, and to fixed or random effects analysis.

**Comment**

This study provides the most distinct evidence to date that acupuncture is more than just a placebo. The overall effect of acupuncture (specific and non-specific), as
ever benefited of healing. The task of exploring more carefully all the mechanisms of pain and, in the meantime, let researchers proceed with this result as the effect of bias but, if you have experienced dislike acupuncture for any reason you can dismiss the effect size of acupuncture against sham is small (0.2), it after randomisation.

This is solid robust evidence. However, because the effect size of acupuncture against sham is small (0.2), it can be interpreted according to your prejudice: if you dislike acupuncture for any reason you can dismiss the result as the effect of bias but, if you have experienced the effect of acupuncture in clinical practice, you will see this result as confirming your opinion.

The most productive stance would be to provide whatever benefits our patients can have in their struggle with pain and, in the meantime, let researchers proceed with the task of exploring more carefully all the mechanisms of healing.

NICE guidance on headaches


These new National Institute for Health and Clinical Excellence (NICE) guidelines cover assessment, diagnosis and management of different types of headache.

In their evidence of effectiveness, they only considered sham controlled trials. For tension headache, three studies (n=673) showed that verum acupuncture is more clinically effective than sham acupuncture (SA) in reducing the number of headache days at 3 months follow-up. For migraine, three studies (n=1299) suggested that verum acupuncture is more effective than SA in reducing the number of migraine days at 3 months follow-up, but there is some uncertainty.

Summarising the economic evidence, one study conducted in the UK showed that acupuncture is cost-effective when compared with no treatment in people with migraine or tension-type headache. Although the population in this study was primarily people with migraine (95%), there is a recognised overlap between chronic tension-type headache and chronic migraine. Therefore chronic migraine results can be extrapolated to chronic tension-type headache and vice versa, so NICE considered the findings to be applicable to the overall population included in the RCT.

Recommendations for management of tension headache include:

▸ Consider a course of up to 10 sessions of acupuncture over 5–8 weeks for the prophylactic treatment of chronic tension-type headache.

Recommendations for management of migraine with or without aura include:

▸ If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks or gabapentin (up to 1200 mg/day) according to the person’s preference, comorbidities and risk of adverse events.

Acupuncture for cancer pain: systematic review


Fifteen RCTs were included (n=1157).

Methods

Fourteen databases were searched for RCTs where acupuncture was used as the sole intervention or as an adjunct to standard treatment if the control group received the same concomitant treatment as the acupuncture group. Sensible exclusion of papers was used including non-RCTs, trials with designs preventing true evaluation of the effectiveness of acupuncture and trials which included cancer pain mixed with other types of pain or postoperative pain.

Results

Fifteen papers were included (n=1157), all of which were associated with a high risk of bias; 14 studies were conducted in China and one in France. The majority of acupuncture treatments or combination therapies exhibited favourable effects compared with standard treatments, although a meta-analysis suggested acupuncture did not generate a better effect than drug therapy (n=886; RR 1.12; 95% CI 0.98 to 1.28; p=0.09). However, comparison between acupuncture combined with drug therapy and drug therapy alone showed a significant difference in favour of combination therapy (n=437; RR 1.36; 95% CI 1.12 to 1.64; p=0.003; figure 7). The authors conclude that the number of RCTs included was too small and that the methodological quality was too low for meaningful conclusions to be drawn.

Comment

This is a well-justified systematic review, given that the two previously published reviews did not include all relevant data. Information is included regarding the number of sessions of acupuncture given and points used.

The main problem encountered, clearly described by the authors, was the poor quality of most of the RCTs.
All had a high risk of bias; for example, only one trial demonstrated adequate allocation concealment, six trials did not describe the randomisation process at all, assessor blinding was only described in two of the trials and—perhaps most damaging—adverse events were only described in two of the trials.

Several RCTs have previously suggested that acupuncture can improve cancer pain, but this has not been confirmed by this systematic review which has highlighted the fact that available evidence from RCTs is of poor methodological quality and based on small sample sizes. Perhaps as the results of the meta-analysis are positive, further large and good quality RCTs are justified for this important area.

### Insomnia


Thirty-three RCTs of any form of acupuncture (n=2293 participants).

#### Methods

RCTs evaluating any form of acupuncture for insomnia were analysed.

#### Results

Thirty-three trials were included with 2293 participants aged 15–98 years, some with medical conditions contributing to insomnia (stroke, end-stage renal disease, perimenopause, pregnancy, psychiatric diseases). The trials evaluated needle acupuncture, electroacupuncture, acupressure or magnetic acupressure.

Compared with no treatment (two studies, 280 participants) or sham/placebo (two studies, 112 participants), acupressure resulted in more people with improvement in sleep quality (compared with no treatment: OR 13.08, 95% CI 1.79 to 95.59; compared with sham/placebo: OR
6.62, 95% CI 1.78 to 24.55). However, when assuming that dropouts had a worse outcome in sensitivity analysis, the beneficial effect of acupuncture was inconclusive. Compared with other treatment alone, acupuncture as an adjunct to other treatment might marginally increase the proportion of people with improved sleep quality (15 studies, 883 participants, OR 3.08, 95% CI 1.98 to 4.90), as shown in figure 8. On subgroup analysis, needle acupuncture but not electroacupuncture showed a benefit.

Comment
All trials had a high risk of bias and were heterogeneous in the definition of insomnia so no conclusions can be drawn.

Adrian White,1 Sharon Burton,2 S Hoo Kwee,3 Michael Meinen,4 Edith Rom,5 Amer Sheikh6

1Department of Primary Care, Peninsula Medical School, Plymouth University, Plymouth, UK
2Wilson Street Surgery, Derby, UK
3Crijnssenstraat 61–3, Amsterdam, The Netherlands
4Denton Park Health Centre, Newcastle upon Tyne, UK
5Wye Valley Trust, Hereford, UK
6Tricorne Stables, Wokingham, Berkshire, UK

Correspondence to Dr Adrian White, Department of Primary Care, Peninsula Medical School, Plymouth University, N21 ITTC Building, Tamar Science Park, Plymouth PL6 8BX, UK; Adrian.white@pms.ac.uk
