Acupuncture research update

Recent papers summarised by Adrian White

CLINICAL EFFECTIVENESS

Acute migraine


Auricular acupuncture for acute migraine (n=94).

Methods

The research group have piloted a technique called the Needle Contact Test (NCT): tender points on the ear are identified, for example, with the Sedatelec algometer, then a needle is held in contact with each tender point in turn for 10 s – looking for the one which produces the greatest immediate reduction in pain. That is the point chosen for needle insertion. In patients with acute migraine attacks, they found the majority of the points were located on the antero-internal part of the antitragus (area M in figure 1) on the same side of pain, so that limited area was used in this study.

Ninety-four women were recruited in a Headache Centre in the first 4 h of an attack of migraine without aura. In the test (verum) group, tender points were located in area M and a needle held in contact. Any areas that produced a 25% reduction in pain was needled with a semipermanent ASP Sedatelec needle.

In the control group, non-tender areas were located in an inappropriate area (sciatic nerve, S in figure 1) with the algometer, and needled in the same way. Changes in pain intensity were measured using a Visual Analogue Scale for the next 24 h.

Results

As shown in the figure 2, there was a significant and clinically relevant greater reduction in pain over 24 h in the group needled at the tender points.

Comment

The authors conclude that this is evidence supporting the point specificity (somatotopic representation) of auricular acupuncture; the evidence could, however, be in support of treating tender points. That said, their NCT is innovative and appears valuable, so certainly justifies testing in the hands of other practitioners.

Medically unexplained symptoms


Pragmatic randomised controlled trial (n=80) comparing acupuncture and waiting list controls.

Method

Patients were included if had consulted at least eight times in the past year and with a ‘medically unexplained symptom’ – a physical symptom for at least 3 months that caused significant distress or impairment and could not be explained by physical disease. They were recruited from four London general practitioner (GP) practices. The acupuncture, using traditional five element style, was given 12 times over 6 months – immediately in the acupuncture-first group, and after 6 months wait in the deferred-acupuncture group. The average treatment session lasted 60 min.

The primary outcome was Measure Your own Medical Outcomes Profile (MYMOP) together with well-being (W-BQ12) and the generic health status measure (EQ5D). The Patient Enablement Instrument was used but not completed reliably because participants misunderstood it.

Results

After 6 months, figure 3 shows there was a significant difference between the groups for the MYMOP scores, (p<0.05), using the available data. However, when missing data had been substituted, the difference was no longer statistically significant. There were robust differences between the scores for well-being (W-BQ12), most marked for anxiety and depression. GP consultation rates and medications reduced in both groups with no significant differences.

At 12 months, the improvements in the acupuncture-first group were maintained and the deferred-acupuncture group had caught up.
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In the nested qualitative study, the 20 patient interviews found that patients reported valuing the caring practitioner; half of them valued the fact that the treatment was seen to include the whole person, and there were behavioural changes – most patients took an increasingly active role in their own treatment, were thinking positively, and followed advice on exercise and diet. Half reported they had more energy and increased their social interactions. Some found their pain unchanged but said they themselves better able to cope with it.

Comment

The authors point out that patients with medically unexplained symptoms not only have their own distress, but also use a significant amount of health resources: for example, they constitute up to 50% of new outpatient referrals. Their symptoms often overlap with the kind of symptoms that acupuncture has been shown effective for, such as tension headache and chronic back pain.

All trends were in favour of acupuncture: the small sample size (smaller than planned, due to slow recruitment) and short follow-up might mean insufficient time to show any effects on consultation rates. Clearly, larger and longer studies are now needed to determine the long term effects and provide an economic evaluation.

Male sexual dysfunction


Acupuncture for premature ejaculation (n=90).

Methods

Ninety patients referred to the urology clinic at a tertiary training and research hospital with premature ejaculation were randomly assigned into paroxetine, acupuncture and sham acupuncture groups. Heterosexual, sexually active men aged between 28 and 50 years were included. Men with other sexual disorders, including erectile dysfunction were excluded.

The medicated group received paroxetine 20 mg/day. The acupuncture group were treated at ST36, LI4, KI3, LR3, bilaterally, and CV3 and Yintang in the midline, leaving needles for 20 min after de qi had been elicited. The sham-acupuncture (‘placebo’) group were given a pricking sensation without penetration of the needle – at point locations that were not reported. Both these groups were treated twice a week for 4 weeks.

A questionnaire known as Premature Ejaculation Diagnostic Tool (PEDT) was applied before and after treatment. Intravaginal ejaculation latency times (IELTs) were measured by using a stopwatch held by the partner.

Results

As figure 4 shows, there were significant improvements in performance measured by IELT of the paroxetine and acupuncture (both p=0.001 compared to sham acupuncture). Median PEDT scores of paroxetine, acupuncture and placebo groups were 17.0, 16.0 and 15.5 before treatment, and 10.5, 11.0 and 16.0 after treatment, respectively (p=0.001, p=0.001 and p=0.314, respectively).

Comment

This result might stimulate more research rather than change practice. But this may be a difficult area to research – for example, a stopwatch is normally used to measure how quick something is, so might have a bad influence. The success of blinding was not tested. The result seems unlikely to be convincing: the latency time results depend on just one measurement before and one after the treatment, and there was no follow-up.

Xerostomia


A small (n=24) controlled trial in radiotherapy (RT) patients.

Methods

A total of 24 consecutive patients with head and neck cancer receiving RT treatment in a dose of more than 5000 cGy involving the salivary glands were assigned to either the acupuncture group (n=12), treated with acupuncture before and during RT, or the usual care control group (n=12). 29 points were needled, needles were stimulated to elicit de qi and retained for 20 min. The points used were local (ST3, ST4, ST5, ST6, ST7, GB2, SI19, TE21), distal (LI4, LI11, LR3, ST36, KI5, GV20) and auricular (ShenMen, Central Nervous System, Neurovegetative System, Kidney, Spleen, Pancreas and Mouth). Acupuncture was given before and twice weekly during RT, for a total of 16–20 sessions.

The clinical response was assessed by syalometry, measuring the resting (RSFR) and stimulated (SSFR) salivary flow rates. Patients also completed a questionnaire scoring dry mouth-related symptoms with a Visual Analogue Scale.
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Results
Although all patients exhibited some degree of impairment in salivary gland functioning after RT. Patients in the acupuncture group showed improved salivary flow rates (see figure 5, SSFR; p<0.001). They also reported decreased xerostomia related symptoms (p<0.05) compared with patients in the CT group.

Comment
The results suggest that acupuncture focused in a preventive approach can be a useful therapy in the management of patients with head and neck cancer undergoing RT. Acupuncture was well tolerated in these patients. We need to know the longer term results, and some people will be interested in comparing acupuncture with sham acupuncture.

Herpes zoster pain


Methods
Patients with herpes zoster who scored their pain as at least 7/10 on a Visual Analogue Scale (VAS) were eligible. One hundred two patients were randomised to receive either acupuncture (n=52) or standard care (n=50) for 4 weeks.

The acupuncture group were treated twice weekly; they were not allowed strong analgesics and patients who used them were withdrawn.

The standard care group were prescribed pregabalin rising from 75 to 600 mg/day according to patient need, together with local anaesthesia provided by peridural or perineural block depending on location. Perineural blocks were repeated up to five times, on alternate days.

Pain was assessed over 4 weeks using VAS and by the McGill Pain Questionnaire (MPQ). Activities of Daily Living were also assessed, as was the Short Form McGill Pain Questionnaire (SF-MPQ).

Results
The trial was curtailed before the planned sample size (160) was reached because of difficulty in recruiting participants. The EA group had significantly greater reduction in pain intensity at 3 and 6 months, 0.9 cm (p=0.05) and 1.3 cm (p=0.007) respectively, than the sham EA group, see figure 7. The EA group also showed greater improvement in Activities of Daily Living. There were trends in favour of EA for Neck Disability Index and for SF-MPQ, and trends in favour of the sham control group for SF-36.

Whiplash injury


Methods
One hundred twenty-four adults with a history of whiplash associated disorder (WAD) of more than 1 month but without arm pain were recruited through newspaper advertisements. They had to have subacute or chronic WAD (grade I or II, ie, without neurological signs). They were randomly allocated to real or sham electroacupuncture (EA) treatment for 12 sessions over a 6-week period. For real acupuncture, the points used were GB39, GB20, LI14 and SI6, bilaterally: stimulation was given at 2–5 Hz and 1.5 volts, but the patients were unable to feel the current. For sham acupuncture, needles were inserted 20–30 mm away from these points, and an inactivated EA machine was attached in the same way. Treatment duration was an average of 30 min, range 20–60 min.

Primary outcome measures were pain intensity (Visual Analogue Scale), disability (Neck Disability Index) and health related quality of life (Short Form 36 (SF-36)). Activities of Daily Living were also assessed, as was the Short Form McGill Pain Questionnaire (SF-MPQ).

Results
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Comment
This trial met difficulties: recruitment was slow and in the final months of the study patients who had previously had acupuncture were included (though likely to have a poor prognosis). In addition, some participants were unable to attend twice weekly. Otherwise the trial seems well conducted though blinding was not tested.

The authors concluded that the reduction in pain and improvement in activity were probably not clinically significant, and it is clear from the figure that the changes in pain scores were small.

Economic analysis: knee pain


Analysis of study data (n=352) of Foster et al. 1

Methods
The aim of this study was to assess the cost utility of adding acupuncture to a course of advice and exercise (AE) delivered by National Health Service (NHS) physiotherapists to people with osteoarthritis (OA) of the knee who had been referred to them for treatment. Patients were recruited from 2003 to 2005. A total of 352 adults (aged 50 years or older) were randomly assigned to receive one of three interventions: AE alone, or AE plus six sessions of true acupuncture (AE+true Ac), or AE plus six sessions of non-penetrating sham acupuncture (AE+sham Ac). The main outcome measures were quality adjusted life years (QALYs), measured by the EQ5D, and UK NHS costs.

The trial found no difference between the three treatment approaches when measuring clinical effectiveness. A cost-utility analysis was also performed. The main comparison is AE against AE+true Ac, not against AE+sham Ac, since health economics is essentially a practical method and sham acupuncture is not actually ‘deliverable’ in the NHS.

The findings were expressed as the incremental cost per QALY (units are 1 extra year of normal quality life, often measured with the EQ5D) gained over 12 months. Sensitivity analyses included a broader cost perspective to incorporate private out-of-pocket costs.

Results
NHS costs were higher for AE+true Ac (£314) than for AE alone (£229), but so was the improvement in EQ5D score, as shown in figure 8. The difference in mean QALYs was superior for AE+true Ac (mean difference 0.022). The cost per QALY gained was £3889. This value was associated with a 77% probability that AE+true Ac would be more cost-effective than AE alone, using a threshold of £20 000 per QALY. This result is robust to several sensitivity analyses. Cost utility data for AE+sham Ac provided cost-effectiveness estimates similar to those for AE+true Ac.

Comment
Readers are likely to remember the original report of the study, which found ‘No effect of acupuncture in addition to exercise’ (and was accompanied by a BMJ leader with that title). So, in contrast, the economic analysis is actually positive. They may also remember that the main reason that National Institute for Health and Clinical Excellence guideline on OA did not recommend acupuncture for OA knee was the lack of good information on economic evaluation: and here it is. But now, the context of the NHS has changed and even though acupuncture is clearly cost effective, it still incurs additional costs so is unlikely to be offered. Unless of course it reduces other NHS costs such as knee replacement surgery.

Readers may also be surprised by the tiny size of the changes in EQ5D scores, but this is a feature of the method of measurement – one QALY is one additional year of good quality life, so the benefits of acupuncture are, of course, going to be an order of magnitude smaller than unity.

Note that these figures are not directly comparable to those obtained in the German series of studies because these took a societal perspective.

In the authors’ words, the economic benefits ‘could not be attributed to the penetrating nature of conventional acupuncture’. However, the comments on the limitations of the trial included that electroacupuncture was not used so the treatment might have been inadequate, and that exercise was given which might have hidden any differences between the two types of acupuncture (ceiling effects).

Reference

SYSTEMATIC REVIEWS

Premenstrual syndrome

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**Methods**

The authors undertook a secondary analysis of existing qualitative interviews with 27 patients drawn from a study of western and traditional acupuncture in usual practice (for a range of painful conditions), and 27 drawn from a qualitative study nested in an RCT of western acupuncture for osteoarthritis of the hip or knee. The authors used qualitative analysis software to facilitate an inductive thematic analysis in which we identified three main themes.

**Results**

In usual practice, starting acupuncture was more likely to be embedded in an active and ongoing search for pain relief, whereas in the RCT starting acupuncture was opportunistic. Usual practice patients were likely to have been personally recommended treatment by a health professional or friend, whereas those in the RCT received an invitation ‘out of the blue’. The usual practice patients reported few uncertainties about the treatment and these had minimal consequences for them. In the RCT, patients experienced considerable uncertainties about their treatment and its effectiveness, and were particularly concerned about whether they were receiving real (or placebo) acupuncture. Patients stopped acupuncture only at the end of the fixed course of treatment in the RCT, which was similar to those receiving acupuncture in the public sector National Health Service. In comparison, private sector patients re-evaluated and re-negotiated treatments, particularly when starting to use acupuncture.

**Comment**

The influence of the context seems particularly strong on the outcome of acupuncture, and on the prognosis in chronic illness. The authors conclude that differences in psychosocial context between RCTs and usual practice could reduce the impact of acupuncture in RCT settings and/or lead to under-reporting of benefit by patients in trials. An effort should be made to make RCTs more likely usual care: the design of recruiting a large cohort for observation, then selecting some at random for treatment, could provide the setting for such a study.

**BASIC RESEARCH**

**Glial cells**


Cerebral ischaemia was induced in rats by a surgical intervention, as a laboratory model of ischaemic stroke. The effect of the ischaemia was assessed in terms of the injury to synapses up to 21 days, seen through the electronic microscope. One group of animals was given electroacupuncture (EA) at GV14 and GV20 every day. These animals scored significantly higher than the untreated controls in every one of the measures used. The authors speculate that the improvement with EA may be related to its effect on astrocytes and promoting the beneficial interaction between astrocytes and synapses.

Stroke is one of the major indications for acupuncture in China, and although the evidence of its effect is still in doubt, at least one can have confidence in knowing that there are potential mechanisms for the effect, so justifying further clinical studies. Acupuncture’s effect on the cells in the brain other than the neurons is interesting.

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**QUALITATIVE METHODS**

**Patients’ attitudes in clinical trials**


This qualitative study (N=54) explored differences in psychosocial context between randomised controlled trial (RCT) and usual practice settings.

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**Figure 9**  Acupuncture for premenstrual distress.

Ten randomised controlled trials (RCTs) included.

**Methods**

Ten databases were searched electronically, and relevant reviews were searched by hand through June 2009. The review included RCTs of women with premenstrual syndrome (PMS); these RCTs compared acupuncture with sham acupuncture, medication, or no treatment. Study outcomes were presented as mean differences (for continuous data) or ORs (for dichotomous data) with a 95% CI. The risk of bias was assessed using the assessment tool from the Cochrane Handbook.

**Results**

Ten RCTs were included, and together showed a high risk of bias in terms of random sequence generation, allocation concealment and blinding. The pooled results demonstrated that acupuncture is superior to all controls (figure 9; eight trials, pooled RR 1.55, 95% CI 1.33 to 1.80, p<0.00001); and superior to sham acupuncture (two trials, RR 5.99, 95% CI 2.84 to 12.66, p<0.00001). Further, the effect of acupuncture was superior to different doses of progesterin and/or anxiolytics (four trials, RR 1.49, 95% CI 1.27 to 1.74, p<0.00001).

**Comment**

Premenstrual syndrome ranges in severity from mild to serious enough to impair the ability to function normally. Patients should be diagnosed carefully by a diary of at least 2 months’ duration: the ‘core disorder’ shows relief of symptoms by menstruation with a symptom-free week in the follicular phase. Cognitive behavioural therapy is effective and commonly used. The authors speculate that the improvement with acupuncture is due to its effect on astrocytes and promoting the beneficial interaction between astrocytes and synapses.
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Nerve growth factor


Western descriptions of the effects of acupuncture on pain, inflammation, motor dysfunction, mood disorders and seizures are based on the stimulation of sensory afferent fibres.

This article, which is openly accessible, reviews the research group’s work on nerve growth factor (NGF) over 20 years. NGF is a neurotrophin that regulates the function of peripheral sensory and sympathetic neurons and of forebrain cholinergic neurons.

The group have shown effects of electroacupuncture (EA) on biological processes related to: male and female reproduction; peripheral neuropathy; the central nervous system; and in the immune system – where EA reversed the effect of compound 48/80 in a model of anaphylaxis (see figure 10) which relies on the release of NGF from mast cells.

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Figure 10 Effect of EA on anaphylaxis.