

Over the past 12 months, two studies on acupuncture for patients with hypertension have been published. One of them showed a significant difference between acupuncture and sham acupuncture results, but the other did not. In this Journal Club, three internationally renowned experts with different scientific backgrounds – acupuncture, anthropology, and statistics – will provide insight into both studies.

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Acupuncture for Hypertension: A Tale of Two Trials

Macklin EA, Wayne PM, Kalish LA, Valaskatgis P, Thompson J, Pian-Smith MCM, Zhang Q, Stevens S, Goertz C, Prineas RJ, Buczynski B, Zusman RM: Stop Hypertension with the Acupuncture Research Program (SHARP) – Results of a Randomized, Controlled Clinical Trial. Hypertension 2006;48:838–845.

Case studies and small trials suggest that acupuncture may effectively treat hypertension, but no large randomized trials have been reported. The Stop Hypertension with the Acupuncture Research Program pilot trial enrolled 192 participants with untreated blood pressure (BP) in the range of 140/90 to 179/109 mm Hg. The design of the trial combined rigorous methodology and adherence to principles of traditional Chinese medicine. Participants were weaned off antihypertensives before enrollment and were then randomly assigned to 3 treatments: individualized traditional Chinese acupuncture, standardized acupuncture at preselected points, or invasive sham acupuncture. Participants received ≤ 12 acupuncture treatments over 6 to 8 weeks. During the first 10 weeks after random assignment, BP was monitored every 14 days, and antihypertensives were prescribed if BP exceeded 180/110 mm Hg. The mean BP decrease from baseline to 10 weeks, the primary end point, did not differ significantly between participants randomly assigned to active (individualized and standardized) versus sham acupuncture (systolic BP: -3.56 versus -3.84 mm Hg, respectively; 95% CI for the difference: -4.0 to 4.6 mm Hg; $P = 0.90$; diastolic BP: -4.32 versus -2.81 mm Hg, 95% CI for the difference: -3.6 to 0.6 mm Hg; $P = 0.16$). Categorizing participants by age, race, gender, baseline BP, history of antihypertensive use, obesity, or primary traditional Chinese medicine diagnosis did not reveal any subgroups for which the benefits of active acupuncture differed significantly from sham acupuncture. Active acupuncture provided no greater benefit than invasive sham acupuncture in reducing systolic or diastolic BP.

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Flachskampf FA, Gallasch J, Gefeller O, Gan J, Mao J, Pfahlberg AB, Wortmann A, Klinghammer L, Pfloderer W, Daniel WG: Randomized Trial of Acupuncture to Lower Blood Pressure. Circulation 2007;115:3121–3129.

Background: Arterial hypertension is a prime cause of morbidity and mortality in the general population. Pharmacological treatment has limitations resulting from drug side effects, costs, and patient compliance. Thus, we investigated whether traditional Chinese medicine acupuncture is able to lower blood pressure.

Methods and Results: We randomized 160 outpatients (age, 58 ± 8 years; 78 men) with uncomplicated arterial hypertension in a single-blind fashion to a 6-week course of active acupuncture or sham acupuncture (22 sessions of 30 minutes' duration). Seventy-eight percent were receiving antihypertensive medication, which remained unchanged. Primary outcome parameters were mean 24-hour ambulatory blood pressure levels after the treatment course and 3 and 6 months later. One hundred forty patients finished the treatment course (72 with active treatment, 68 with sham treatment). There was a significant ($P < 0.001$) difference in post-treatment blood pressures adjusted for baseline values between the active and sham acupuncture groups at the end of treatment. For the primary outcome, the difference between treatment groups amounted to 6.4 mm Hg (95% CI, 3.5 to 9.2) and 3.7 mm Hg (95% CI, 1.6 to 5.8) for 24-hour systolic and diastolic blood pressures, respectively. In the active acupuncture group, mean 24-hour ambulatory systolic and diastolic blood pressures decreased significantly after treatment by 5.4 mm Hg (95% CI, 3.2 to 7.6) and 3.0 mm Hg (95% CI, 1.5 to 4.6), respectively. At 3 and 6 months, mean systolic and diastolic blood pressures returned to pretreatment levels in the active treatment group.

Conclusions: Acupuncture according to traditional Chinese medicine, but not sham acupuncture, after 6 weeks of treatment significantly lowered mean 24-hour ambulatory blood pressures; the effect disappeared after cessation of acupuncture treatment.

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From the Perspective of the Acupuncturist – MacPherson, York, UK

The challenges of conducting trials of acupuncture for hypertension are numerous and the authors (Flachskampf et al. and Macklin et al.) should be commended for tackling what is I believe a particularly difficult area of research. Some of these challenges are generic to acupuncture trials, while other challenges are specific to treating the condition of hypertension with acupuncture. In this review I will concentrate more on the latter.

A major problem is that hypertension is often symptom free, a point noted in the article on the Flachskampf trial where the authors state that 'hypertension rarely affects a patient's well-being.' The difficulty of making a diagnosis in symptom free patients is not addressed in either trial. The core process of diagnosis in traditional Chinese medicine is based on developing an understanding of the imbalance by eliciting the relevant signs and symptoms and then pulling these together in a grouping that reflects the underlying pattern of disharmony. It is theoretically impossible to diagnose in this traditional way when there are no signs and symptoms. This problem will limit the extent to that these trials are generalisable or indeed will influence practice, as acupuncturists will not be able to construct diagnoses where signs and symptoms are absent.

A second problem is related to the actual diagnostic syndromes of traditional Chinese medicine that are used as a framework by these two trials. While much is made of the importance of the tradition that acupuncture is based on, the treating of hypertension is a relatively new phenomenon. This lack of tradition is not raised by either set of authors, the tacit implication being that (the symptoms of) hypertension has been treated for 2,000 years. The reality is that compared to many other conditions, especially those for which patients have been consulting for treatment over many centuries, there is limited clinical experience and literature in the area. Therefore, the clinical syndromes that are put forward as likely to be involved in hypertension have not been subjected to any evidence based filtering. This is of course a problem for all conditions, but the disadvantage of using such syndromes in these two trials is that there has been a much more limited process of empirical development in selection and validation. Interestingly both trials quote the Chinese text edited by Cheng Xinnong as a source text for the syndromes thought to underlie hypertension, a copy of which I do not have to hand. Nevertheless I would be interested in how and when these patterns were developed, and what process of testing they went through prior to being published in this text.

A third problem is with the 'individualised' acupuncture intervention, which is described in more detail in an earlier paper [1]. Despite the claim that there was 'adherence to principles of TCM acupuncture' (Macklin et al.), there were several

ways that the trial acupuncture did not adhere, with the consequence of reducing generalisability of the results. First the treating acupuncturists were not the same as the diagnosing acupuncturists; second what were deemed as non-specific effects were 'standardised across the randomised groups' [1]; third the treatments were not individualised at every session, as re-assessment occurred but not before the 5th session; and fourth there were restrictions on point selection. The problem seems to be that the authors would like it both ways, to do an explanatory trial to determine whether there are specific effects associated with acupuncture, and a trial that delivers authentic acupuncture to 'mimic actual practice.' However, it is unlikely that acupuncturists will be impressed with the approach taken to acupuncture in this trial, even in the so-called 'individualised' arm.

It is worth noting that the SHARP trial [Macklin et al.] was described as a 'pilot' (in the abstract), yet set out to determine whether there were differences between groups at 10 weeks (after an average of 7 weeks of treatment), not something one would expect to determine in a pilot. This confusion of purpose is problematic. The SHARP authors did outline in a separate paper [1] some power calculations for the study and for the size of the difference that they did in fact find in this pilot, a 3.5–4.0 mm Hg reduction in systolic blood pressure when comparing standardised and individualised acupuncture versus control, would have required a trial of around 900 patients. In other words, this pilot was underpowered as a full-scale study.

One of the questions raised by the two trials is why does one study (Flachskampf) show an effect and the other (SHARP) not. There are clearly many parallels between the trials, as well as some differences. One reason that may explain the difference in outcomes is that the Flachskampf trial provided around twice as many treatments over roughly the same time period, i.e. 22 treatments over 6 weeks, while the SHARP trial delivered 12 treatments over 6–8 weeks (average 7 weeks). Another important difference was that the Flachskampf trial had its primary end point immediately after the 6 weeks of treatment, while the SHARP trial measured blood pressure on average 3 weeks after the treatment had been completed, i.e. at the 10-week time point. Interestingly, Flachskampf found that the effects of acupuncture had disappeared by 12 weeks, however it is unclear how quickly these effects were ameliorated. It could be that the effects wore off fairly quickly. If this also happened in the SHARP trial, then it is plausible that the SHARP patients also had an effect at the end of the 7-week period, but it had worn off by 10 weeks. This is one interpretation that provides a more consistent story on the effects of acupuncture for hypertension: namely that there are likely to be short-term effects but these do not last beyond the end of a course of treatment.

Based on the experience of many acupuncturists in the field, and my own in particular, it is commonly believed that it is very difficult to reduce high blood pressure once it has devel-

oped as full-blown condition. Of course we treat many people with hypertension where the condition is considered as a comorbidity, but it is not common for us to be treating hypertension as a primary complaint [2]. The problem seems to be that irreversible changes have taken place, a situation that is also true for various other conditions. A common example is varicose veins where visually it can be seen that profound changes have taken place, changes that are not likely to be reversed by acupuncture. If this is also true for hypertension, then it may make more sense to see the scope for acupuncture as a form of prevention, in other words before the irreversible changes have taken place.

The consequence of this combination of concerns that I have raised in this review is that the professional acupuncture communities will be likely to have less confidence in the results of these trials than say for example trials for conditions where there is a more lengthy tradition of treatment, where obvious and immediate symptoms are presenting, where one can be more confident that an appropriate diagnosis is being made, where treatment is more generalisable to normal practice, and for conditions where our experience is that the imbalance (disharmony) is commonly experienced to be reversible.

References

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- 2 MacPherson H, Sinclair-Lian N, Thomas K: Patients seeking care from acupuncture practitioners in the UK: A national survey. *Complement Ther Med* 2006; 14:20–30.

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From the Perspective of the Statistician – Andrew Vickers, New York, NY, USA

When two trials of acupuncture show conflicting results, it is tempting to look at fine details of the acupuncture and control treatments. Indeed, acupuncturists and others have frequently reviewed the literature examining treatment differences between trials and ascribing variations in outcome to these differences. Almost without exception, such reviews have concluded that: a) acupuncture treatments were superior in ‘positive’ trials and b) sham treatments were often actually active in the ‘negative’ trials.

The problem with such research, and the reason why the conclusions are always the same, is that reviewers were not blinded to outcome. It is not difficult to make a plausible case why any particular trial might be positive or negative. As an example, I published a trial a few years back showing that acupunc-

ture was effective for chronic headache disorders. But let’s imagine that I had found no difference between acupuncture and controls. This might be explained in terms of the practitioners: these were physiotherapists with additional training in acupuncture, and traditional acupuncturists have long criticized those with a conventional approach. Alternatively, we limited treatment sessions to a total of 12 over a 3-month period: is this really enough to treat patients with a 20-year history of migraine?

I once tried an experiment with students at an acupuncture school: I described two trials to them, told them that one was positive and one negative, and asked them to guess which was which and explain their reasoning. One of the trials involved stimulation of acupuncture point P6 for postoperative vomiting; the other was a pain trial in which practitioners could ‘treat as normal’. The students uniformly chose the pain trial as the one showing positive results, deriding the vomiting trial as ‘watered-down Westernized acupuncture.’ Of course, I then revealed that statistically significant differences between groups had been found for vomiting, but not pain, as a simple way of demonstrating that the point of science is to tell us things we don’t know, not just confirm our beliefs.

So what about these two hypertension trials? One could argue that the superior results in the Flachskampf trial related from the more intensive acupuncture regimen (22 treatments rather than 12). However, the reduction in blood pressure was of similar magnitude in both trials, the difference was that in Flachskampf, there was not much change in the controls (leading to a statistically significant difference between groups), whereas in Macklin, both groups experienced similar levels of improvement. So if the results were reversed, we might argue that the intensive treatment in Flachskampf led to an enhanced placebo effect. Or perhaps the reason for the difference in outcome between the control groups in each trial was that non-acupuncture points were used in one trial, but non-indicated points in another. Perhaps true acupuncture points, even if not indicated for hypertension, could produce a general relaxant effect that would lower blood pressure. Which sounds very plausible until you work out that it was the non-acupuncture points that seemed to have the better results than the non-indicated points.

But there may be no reason to explain the difference between Flachskampf and Macklin simply because perhaps no such difference exists. Macklin concluded ‘active acupuncture provided no greater benefit than invasive sham acupuncture’; Flachskampf found small differences between groups immediately after treatment, but no difference at 3 months. It is implausible that anyone would find it worthwhile to administer acupuncture 22 times in 6 weeks to bring about a small, transient improvement in blood pressure. Indeed, a small, transient improvement is of essentially no benefit for a chronic risk factor such as hypertension. Thus one would be tempted to conclude from Flachskampf’s trial that ‘active acupuncture provided no greater benefit than invasive sham acupuncture.’

My take-home message is straightforward: It is easy to over-interpret differences between a couple of acupuncture trials and generate spurious relationships between treatment characteristics and trial outcome. The only sound basis for determining what aspects of acupuncture, or sham, are associated with a clinical effect is a meta-analysis of a large number of trials. That formal statistical analyses of a large amount of data is superior to informal analyses of a small data set should hardly be news, but it is worth repeating nonetheless.

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From the Perspective of the Anthropologist – Volker Scheid, London, UK

From a perspective anchored in the cultural studies of science, technology and medicine my main interest in these papers is their status as cultural artifacts that provide access to the life-worlds of a particular research community. If any, life-world debate and argument marks sites of contestation. Silence, on the other hand, leads us to what is shared, taken-for-granted, considered to be self-evident, and thus not in need of explanation. It is to these silences that my comment addresses itself.

The most striking silence at the centre of both studies pertains to the very object they claim to examine, namely the practice of acupuncture in the treatment of hypertension. That silence speaks all the louder because of the attention simultaneously lavished on discussions of research design and the analysis of outcomes.

Both Flachskampf et al. and Macklin et al. define acupuncture with reference to traditional Chinese medicine and legitimise its value in the treatment of hypertension by recourse to its long-time usage. Flachskampf et al. describe it as ‘an ancient treatment technique anchored in traditional Chinese medicine’ and as ‘an ancient system of medical knowledge and skills,’ while Macklin et al. note that acupuncture ‘has been used in traditional Chinese medicine (TCM) to treat symptoms of hypertension for 2,500 years.’ Bibliographic references supporting these claims are minimal and of a token nature, satisfying customary practice rather than actually supporting the authors’ specific claims. Flachskampf et al., for instance, refer readers to two Chinese papers from the 1990s, in which acupuncture is ‘reported to have potential for treating cardiovascular diseases, including arterial hypertension.’ What about these two papers is significant, or why a tradition claiming to be based on centuries of clinical experience is unable to offer more than two papers suggesting ‘potential’ rather than ‘real’ effects is not explained. Macklin et al., likewise, reference their claim to a single introductory text on Chinese medicine dating from the 1980s, long since superseded by more detailed historical studies.

This cursory treatment hides a most serious conundrum of which both authors do not seem to be aware. Namely, how is it possible to claim that physicians in pre-modern China successfully treated a condition diagnosed by means of technological devices imported into China only in the course of the 20th century? A condition, furthermore, that frequently has no symptoms and of which both patients and their practitioners will have been unaware. Not surprisingly, there exist no discussions of hypertension and its treatment by means of acupuncture in the pre-modern Chinese medical literature. The contemporary TCM textbook approaches that inform both studies were defined not earlier than the 1960s, when they were imported into acupuncture practice from pharmacologically-based internal medicine (内科 *neike*). Likewise, the core paradigm of TCM acupuncture according to which acupuncture points have specific functions dates from not earlier than the 1930s. It was created in an explicit attempt to reconfigure acupuncture on the model of Chinese internal medicine in order to promote the systematisation and thereby modernisation of Chinese medicine as a whole. Because the modernisation of Chinese medicine in the course of the 20th century has been largely politically driven, doubts regarding its clinical effectiveness are increasingly being voiced in both contemporary China and the West. Certainly, observing practice ‘on the ground’ one encounters a much greater variety of clinical and diagnostic styles than represented by the TCM textbook approaches used in these studies that, nevertheless, claim to represent TCM acupuncture in toto.

Given the ready availability of the information outlined in the previous paragraph, the obvious question is why is it being ignored. Would the researchers and their peer group audience tolerate similar lacunae of background knowledge in areas such as research methodology or the biomedical understanding of hypertension? If not, why not and what are the consequences of doing so?

These are complex issues and cannot be discussed here in detail. Pragmatically, the historical diversity of Chinese medicine and its complex relation to biomedically defined realities such as hypertension would make studies such as these even more difficult. Given that CAM research occupies a marginal space in a community dominated by and oriented towards biomedicine, researchers will naturally seek to address the core concerns of their peer group. For this purpose, simple definitions of Chinese medicine that match the audience’s ideas about what medicine should look like are clearly preferable.

As likely, however, is the possibility that the researchers themselves were not aware of Chinese medicine’s complex history and the problems this raises for practice and research. How, otherwise, could Macklin et al. suggest that physicians in China 2,500 years ago treated the symptoms of an oftentimes symptomless condition? Flachskampf et al., meanwhile, might have wanted to consider more closely the implications of the

premise underpinning their study: 'We had the unique opportunity,' they write, 'to test the therapeutic potential of acupuncture administered by Chinese experts to Western hypertensive outpatients.' From other information supplied in the paper one can deduct that these 'experts' were relatively recent graduates as they had only been practicing 'for several years.' Expert status in acupuncture, one assumes, is thus in some imperceptible way linked to being Chinese. This, again, is only possible if 'being Chinese' and 'Chinese medicine' are

linked by their possession of some kind of cultural essence, something that is unchangeable and persists across space and time. Would, one is entitled to ask, a similar definition of biomedicine in racial terms – 'Caucasian medicine' perhaps – be acceptable to Flachskampf et. al.'s peer group?

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