Complementary Therapies in Medicine (2006) **14**, 39–46

ELSEVIER

Complementary Therapies in Medicine

www.elsevierhealth.com/journals/ctim

Acupuncture for tinnitus: A series of six *n* = 1 controlled trials

Andrew Jackson[a], **Hugh MacPherson**[b,c,*], **Seokyung Hahn**[c,d]

[a] *Northern College of Acupuncture, York, UK*
[b] *Foundation for Traditional Chinese Medicine, York, UK*
[c] *Department of Health Sciences, 2nd Floor, Seebohm Rowntree Building, University of York, Heslington, York YO10 5DD, UK*
[d] *Medical Research Collaborating Center, Seoul National University Hospital, Seoul National University College of Medicine, South Korea*

Available online 19 September 2005

KEYWORDS
Acupuncture;
Tinnitus;
n = 1;
Cases series;
Bayesian statistics

Summary
Objective: To explore patient perceived benefits of acupuncture for tinnitus.
Design: Controlled *n* = 1 trials, with two phases A and B.
Subjects: Six patients with tinnitus.
Outcome measures: Primary outcome was Daily Diary records related to four tinnitus symptoms: loudness of tinnitus; pitch of tinnitus; waking hours affected with tinnitus; quality of sleep. Secondary outcomes were the Tinnitus Handicap Inventory (THI) and Measure Your Medical Outcome Profile (MYMOP).
Methods: Patients received a course of 10 acupuncture treatments over a 2-week period. Daily Diary entries related to the four tinnitus symptoms were recorded by patients for 14 days pre-treatment (phase A) and 14 days post-treatment (phase B). A hierarchical Bayesian model was used to combine the results from the individual patients to obtain estimates of the population and individual patient treatment effects, incorporating random variations at both levels (between patients and within patient). Tinnitus Handicap Inventory (THI) and Measure Your Medical Outcome Profile (MYMOP) were recorded at assessment points pre-treatment and post-treatment.
Results: Six patients participated in the trials, each receiving 10 treatments and completing all Daily Diary entries and outcome measures. For the of symptoms of loudness and pitch, there were variable treatment effects between patients, with a trend for the median overall reduction for loudness of −2.49 (−5.04, 0.02) and for pitch −1.39 (−3.74, 0.89), 95% credibility intervals being shown in brackets. For the other two symptoms, the waking hours affected and quality of sleep, patients' responses were more consistent, with amore credible overall median reduction for affected waking hours of −2.76 (−3.94, −1.63) and for quality of sleep −2.72 (−3.45, −2.03). The THI and MYMOP measures showed a trend of improvement after treatment.

* Corresponding author. Tel.: +44 1904 321394; fax: +44 1904 321388.
E-mail address: hm18@york.ac.uk (H. MacPherson).

0965-2299/$ – see front matter
doi:10.1016/j.ctim.2005.07.005

Conclusion: The $n = 1$ trial methodology, with an AB design and Bayesian analysis, can be considered of value in exploring treatment effects for small numbers of patients receiving individualised treatments, as is common within complementary medicine. When the treatment effects from six patients were synthesized, the results of this study suggest that acupuncture may have a beneficial role in the treatment of tinnitus.

Introduction

Tinnitus, from the Latin ''tinnere'' meaning to ring, has a reputation for being a difficult disease to treat, whether by conventional medicine or by acupuncture. For people with tinnitus, the condition can vary from a low level buzzing to a noise of such intensity it can lead to severe anxiety, despair and even suicidal tendencies.

Acupuncture has been much used for tinnitus over the years, however recent attempts to demonstrate acupuncture's effectiveness have not provided definitive evidence. A systematic review by Park et al.[1] found that the evidence from six eligible randomised controlled trials was not adequate to make a judgment as to acupuncture's effectiveness for tinnitus. Their commentary highlighted various shortcomings from these trials, including ''disappointing'' methodology. They criticised the inappropriate use of crossover designs in four of these trials, because carryover effects can be expected from acupuncture. Inadequate reporting meant that the rationale for points used was not always stated. No authors quoted the classical literature and the trials using individualized points did not report traditional diagnostic frameworks nor related procedures for point selection. One trial used only ear points.[2] Another used the same points for both the real and ''sham'' acupuncture, but with the so-called sham points being inserted subcutaneously,[3] an approach that has largely been rejected on the grounds that such sham treatments can be expected to result in acupuncture effects.[4] Extraordinarily, this trial received the highest quality rating on Park et al.'s methodology scale. Despite the problematic nature of the reviewed trials, Park et al's research has led to a questionable reinterpretation and unsubstantiated conclusion that acupuncture is ineffective for tinnitus.[5]

On the basis that there is inadequate evidence to draw conclusions to date, we have designed a simple study on a limited budget to explore patient's perceptions of outcome from acupuncture. We utilised an $n = 1$ design which can fit well with a treatment approach based on individualised acupuncture, and where point selection is usually reformulated at each ongoing session based on changes to presenting symptoms over time.[6] If the condition under investigation is chronic, then we can argue that sufficient baseline measures might demonstrate reasonable stability to the pre-treatment chronicity. If so, improvements cannot therefore so easily be dismissed as due to the natural history of the disease.

In the investigation of new drugs, the usual $n = 1$ trials are double blind, cross-over, randomised, and controlled. They are generally used for chronic, stable conditions for which the proposed treatment has a rapid onset of action and ceases to act soon after it is discontinued, that is with no carry-over effect.[7] The patient undergoes a series of pairs of treatment periods, one period of each pair with the active drug and one with matched placebo, assigned at random. Pairs of treatment periods, sometimes labelled ABAB, etc., are continued until effectiveness is proved or refuted. There are a number of problems with importing this model into complementary and alternative medicine, even though it has been argued that $n = 1$ designs are ''suitable for some research initiatives in complementary medical practice''.[8] First the treatment effects in CAM may be slow, with a number of treatments usually being required as a minimum ''dose'' for the full beneficial effects to manifest. For example the impact of acupuncture for the treatment of chronic pain seems to require a minimum of six treatments.[9] A second problem is that the ABAB designs require no carry-over effect, so that the effect of treatment in say phase B needs to be sufficiently ''washed out'' to not affect the measurements in the subsequent phase A. However, we know that CAM therapies, and acupuncture in particular,[10] can be expected to have ongoing and progressing change both during and after a course of treatment. No time period would be long enough to ''wash out'' the effect.

As a result of these concerns, we have drawn on earlier research into behavioural therapy (Barlow and Hersen, 1984), a tradition that has continued in rehabilitation research,[11] and chosen the simple AB design as our $n = 1$ framework. The unique feature of $n = 1$ controlled trials is that each trial is of a single patient who acts as his/her own control.

Because we expected the acupuncture ''dose'' to require a series of treatments, and the effect to be sustained after the end of treatment, our measurements can be collected in a pre-treatment phase A and a post-treatment phase B. However these measurements will not be amenable to ordinary statistical tests, primarily because the data in each phase will not be independent, i.e. there is likely to be auto-correlation.[12] As an alternative to the usual frequentist statistical approach, we have utilised a Bayesian approach, one that has been developed for combining $n = 1$ trial data in a meta-analysis, but here used to evaluate individual responses to treatment as well as estimate an overall population treatment effect.[13]

Methodology

Design

The design was a series of six $n = 1$ controlled trials of acupuncture for patients with tinnitus. Each patient acted as their own control, enabling pre-treatment scores for specified symptoms to be compared with post-treatment scores, and the results of all six trials pooled.

Eligibility and recruitment

Patients were recruited at an acupuncture clinic in the North West of England by the local researcher, one of the authors (AJ). The patients met the eligibility criteria if they identified themselves as people with tinnitus, were available to meet the stringent monitoring and treatment requirements of the trial, were over 18, had not previously been treated by acupuncture for their tinnitus, could speak and write in English, and were not pregnant. Informed consent was obtained prior to participation, with ethics approval provided by the Northern College of Acupuncture Research Ethics Committee.

Treatment

The acupuncture was provided by the local researcher (AJ) who was in his first year of practice after recently completing a 3-year training at the Northern College of Acupuncture, York England. The patients received treatment for two sets of five consecutive days, receiving ten treatments in all. While this might be seen as an unusual treatment regime in the West, it is considered normal in China. Treatments were available morning, afternoon and evening, which allowed people at work to fit in with the research timetable. Given this flexibility, the patients' were willing to receive treatment on this basis, despite its more demanding schedule than is usual in the West. For each patient, the acupuncturist undertook a traditional acupuncture diagnosis, based on the principles of Traditional Chinese Medicine, identifying the underlying patterns or syndromes to the patient's tinnitus, and incorporating tongue and pulse diagnostics.[14] The selection of points was individualised for each patient and at each treatment, based on the diagnosis and presenting symptoms. Moxibustion and auricular acupuncture were provided based on theoretical considerations, but not electro-acupuncture. Two types of stainless steel coil handle needles were used, 15 mm × 0.20 mm and 40 mm × 0.28 mm, the depth of insertion varied between points, and de qi was normally sought at each point. Needles were retained for approximately 20 min. All aspects of diagnosis and treatment were recorded.

Outcomes

Primary outcome

The Daily Diary required patients to score four tinnitus-related symptoms on a daily basis. While not validated as stand-alone items, two symptoms were taken from the Tinnitus Handicap Inventory,[15] the loudness and the pitch of the tinnitus (both rated 0—10, where 10 was worst possible). The other two items were the number of waking hours affected with tinnitus (0—24 h), and the quality of sleep (0—10 where 10 was worst possible). Key to the analysis for each patient was the 14 pre-treatment scores (phase A) and 14 post-treatment scores (phase B), all on four of the above tinnitus related symptoms.

Secondary outcomes

The Tinnitus Handicap Inventory[15] is widely used as an instrument for research into tinnitus. It is scored on a scale of 0—100 where ''mild'' tinnitus lies in the range 18—36 and ''moderate'' in the range 38—56. The Measure Your Own Medical Profile (MYMOP)[16] is an instrument that allows patients to generate their own key symptoms that are then monitored for change over time. It is scored from 1—25.

Data collection

At the start of Week 1, recruited patients completed THI and MYMOP. Patients were also at this time given instructions to complete their Daily Diary, scoring four symptoms towards the end of each day for the following 6 weeks. At the start of Week 3, the patient returned to the clinic and

once again completed THI and MYMOP, followed by receiving their first of 10 acupuncture treatments. Patients then completed THI and MYMOP at the start of Weeks 5, 7 and 11, the last of these being the final follow up 6 weeks after completing treatment.

Analysis

A hierarchical Bayesian model for analysis of $n = 1$ trials[13] was used to combine the results from the six individual patients' Daily Dairy data for the four tinnitus related symptoms. The model incorporates variations at both levels, namely within patient and between patient. The observed responses y_{ij} from the ith patient at the jth assessment are assumed to follow a normal distribution centred around the mean μ_{ij} with variance ${\sigma_i}^2$, where μ_{ij} is modelled as $\mu_{ij} = \theta_{0i} + \theta_i X_{ij}$. X_{ij} is assigned to be one if the data are from the post-treatment and zero if from the pre-treatment. θ_{0i} represents the pre-test mean symptom score in the patient i and θ_i represents the treatment effect in that patient. The various patients' true treatment effects θ_i follow a normal distribution centred around an overall mean θ with between patient variance τ^2. The model derives a posterior distribution for τ to describe the extent of the between patient variation. In extreme cases, when $\tau^2 = 0$, all of the individual treatment effects θ_i will be equal to the population level effect θ, and if τ^2 is very large (∞), then the individual patient treatment effect θ_i are unrelated to each other. Prior distributions for θ and θ_{0i} were specified as non-informative normal distributions, and for σ^2 and τ^2, non-informative inverse gamma distributions.

For THI and MYMOP, we did not attempt to make inferences using formal statistical test, but instead plotted the data at each of the five assessment points for visual comparison.

Results

Six patients were recruited with an average age of 52 years, and additional characteristics as presented in Table 1.

All patients received ten treatments, each in two consecutive five weekday blocks. They were diagnosed with a mixture of two predominant syndromes: Liver Qi Stagnation and Kidney Deficiency, with full details of diagnosis and treatment reported elsewhere.[17] Point selection for each patient was based on (1) these two syndromes, with commonly used points for the former including LIV-3 and for the latter KID-3 and BL-23 used bilaterally, (2) local points, most commonly GB-2 and SJ-17, used bilaterally if both ears were affected, otherwise unilaterally, and (3) other points based on the patients' diagnosis and their additional symptoms. The number of points selected per session ranged from 6 to 13. Five patients received moxibustion and two auricular acupuncture.

For each patient 14 pre-treatment Daily Diary scores (Weeks 1 and 2) for each symptom were analysed with the 14 post-treatment scores (Weeks 5 and 6). In Tables 2—5 for each symptom the patient

Table 1 Details of patients treated by acupuncture for their tinnitus.

Patient	Age	Male/female	Duration of tinnitus	Unilateral or bi-lateral tinnitus
A	35	M	2 years	Bi-lateral
B	79	M	Over 20 years	Right ear
C	69	M	Over 20 years	Bi-lateral
D	59	M	15 years	Bi-lateral
E	32	F	12 months	Bi-lateral
F	36	M	9 years	Bi-lateral

Table 2 Details of treatments provided for patients.

Patient	Typical point prescription	Moxibustion	Auricular acupuncture
A	SJ-17, GB-2, SJ-6, BL-23, ST-36, LIV-3	Yes	No
B	SJ-17, GB-2, ST-36, SP-6, H-7	Yes	No
C	SJ-17, GB-2, KID-6, KID-3, ST-36	No	Yes
D	SJ-17, GB-2, REN-4, REN-6, ST-36, SP-6, LIV-3	Yes	Yes
E	SJ-17, GB-2, ST-36, SP-6, LIV-3, LIV-8	Yes	No
F	SJ-17, SI-19, KID-3, REN-4, ST-36, ST-40, H-7, ST-25	Yes	No

Table 3 Patient and combined treatment difference in loudness.

Parameter	Mean	Standard deviation	Median	95% Credibility interval
θ	−2.490	1.298	−2.492	(−5.040, 0.019)
θ_1	−2.978	0.502	−2.984	(−3.941, −1.982)
θ_2	0.270	0.503	0.273	(−0.724, 1.254)
θ_3	−0.671	0.505	−0.667	(−1.664, 0.309)
θ_4	−1.829	0.512	−1.840	(−2.831, −0.821)
θ_5	−6.447	0.508	−6.445	(−7.465, −5.450)
θ_6	−3.323	0.498	−3.325	(−4.310, −2.353)
τ^2	9.900	1.750	6.596	(2.096, 35.890)

Table 4 Patient and combined treatment difference in pitch.

Parameter	Mean	Standard deviation	Median	95% Credibility interval
θ	−1.39	1.198	−1.388	(−3.736, 0.893)
θ_1	−0.737	0.411	−0.743	(−1.524, 0.082)
θ_2	1.818	0.413	1.821	(1.001, 2.627)
θ_3	−0.889	0.411	−0.885	(−1.704, −0.092)
θ_4	−1.231	0.419	−1.241	(−2.048, −0.407)
θ_5	−4.866	0.412	−4.864	(−5.694, −4.060)
θ_6	−2.466	0.408	−2.466	(−3.270, −1.672)
τ^2	8.490	14.900	5.665	(1.842, 30.970)

treatment effect estimate (θ_i, for $i = 1, 2, \ldots, 6$) and the overall treatment effects (θ) were expressed as the mean and the standard deviation as well as the median with the 95% credibility interval, which can be interpreted as Bayesian equivalent of the confidence interval. The treatment effect estimates are displayed in Tables 3—6 and 'forest' diagrams of medians for each symptom with 95% credibility intervals are presented in Figs. 1—4.

The combined treatment effect favours acupuncture, with the median overall reduction of −2.49 (−5.04, 0.02) for loudness and −1.39

Table 5 Patient and combined treatment difference in waking hours affected.

Parameter	Mean	Standard deviation	Median	95% Credibility interval
θ	−2.769	0.590	−2.764	(−3.936, −1.625)
θ_1	−2.698	0.675	−2.718	(−4.016, −1.227)
θ_2	−2.714	0.658	−2.734	(−4.007, −1.307)
θ_3	−3.139	0.739	−3.048	(−4.873, −1.911)
θ_4	−2.934	0.690	−2.903	(−4.429, −1.620)
θ_5	−3.178	0.754	−3.078	(−4.937, −1.954)
θ_6	−1.919	1.046	−2.169	(−3.396, 0.553)
τ^2	1.200	3.280	0.319	(0.001, 7.159)

Table 6 Patient and combined treatment difference in quality of sleep.

Parameter	Mean	Standard deviation	Median	95% Credibility interval
θ	−2.723	0.369	−2.715	(−3.448, −2.029)
θ_1	−2.744	0.383	−2.737	(−3.513, −1.962)
θ_2	−2.940	0.411	−2.902	(−3.848, −2.188)
θ_3	−2.725	0.387	−2.721	(−3.527, −1.958)
θ_4	−2.594	0.394	−2.620	(−3.336, −1.743)
θ_5	−2.091	0.544	−2.140	(−2.984, −0.961)
θ_6	−3.233	0.513	−3.177	(−4.362, −2.400)
τ^2	0.567	2.080	0.252	(0.002, 2.88)

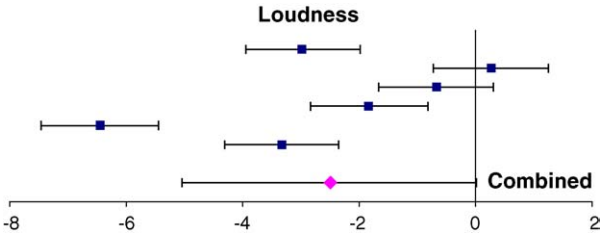

Figure 1 Patient and combined treatment difference in loudness. Median treatment differences and 95% credibility intervals.

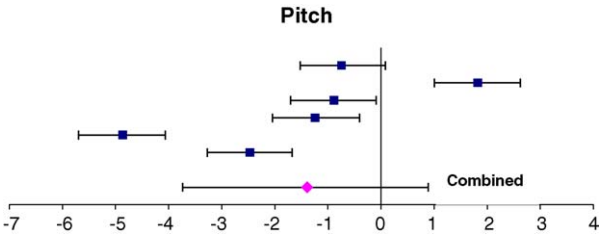

Figure 2 Patient and combined treatment difference in pitch. Median treatment differences and the 95% credibility intervals.

(−3.74, 0.89) for pitch, both with fairly wide 95% credibility intervals. For the other two symptoms, number of waking hours affected and quality of sleep, patients' responses were more consistent

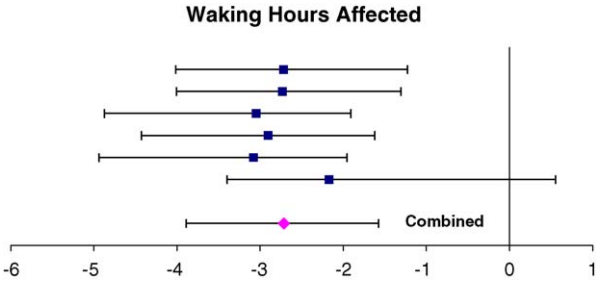

Figure 3 Patient and combined treatment difference in waking hours affected. Median treatment differences and the 95% credibility intervals.

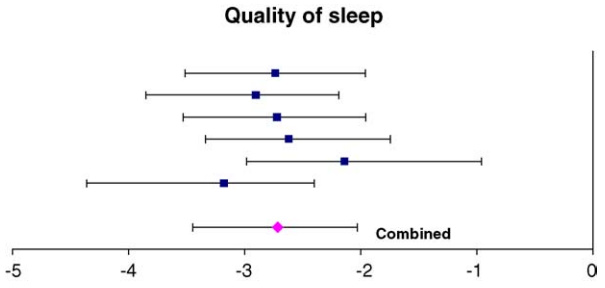

Figure 4 Patient and combined treatment difference in quality of sleep. Median treatment differences and the 95% credibility intervals.

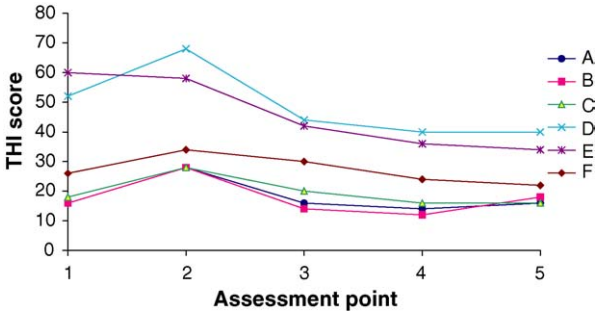

Figure 5 Scores of THI for six patients at each assessment point.

and the significant improvement with higher credibility is clearly indicated from the results of the analysis, with the overall median reduction of −2.76 (−3.94, −1.63) for waking hours and −2.72 (−3.45, −2.03) for improved quality of sleep.

All patients completed THI and MYMOP at all assessment points. In Figs. 5 and 6 are presented the actual THI and MYMOP scores for each patient at each of the five assessment points. Although there is an initial slight rise (worsening) in the THI, both scales show a clear trend towards lower scores (i.e. less tinnitus) after treatment for all patients.

In terms of the THI outcome measure, five patients recorded a worsening in their condition at the end of Week 2, before steady improvements subsequently. Interestingly, this initial worsening was identified by patients as being related to their heightened awareness resulting from the requirements of recording data on their tinnitus every day. There was an overall tendency after treatment of decreasing THI scores (i.e. reduced symptom burden), though four patients did show little change due to treatment. The MYMOP scores, showed a clearer trend of decline (i.e. reduced symptom burden) after treatment.

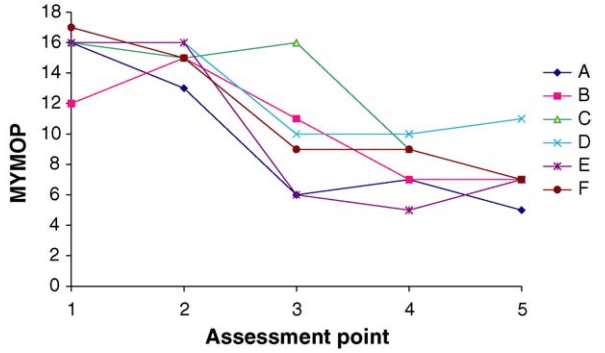

Figure 6 Scores of MYMOP for six patients at each assessment point.

Discussion

There are aspects of the $n = 1$ design which make it methodologically suited to clinical contexts where patients receive customised treatments, as is the case in complementary medicine.[8] Our approach represents an evolution of the classic case study that has been a primary method of disseminating knowledge in traditional Chinese medicine.[18] Because acupuncture can have more than a short-term impact,[10] it has been necessary in this study to utilise a specific type of $n = 1$ study, an AB design, rather than the more conventional approach with repetitive ABAB phases. This has enabled us to circumvent the problems associated with the slow but cumulative impact of acupuncture treatment and the subsequent carry-over effects. And finally we have avoided difficulties associated with different levels of variations by using a hierarchical complex model utilising a Bayesian approach. It should be noted that this approach is only appropriate for self-limiting conditions that are relatively stable, and not going through periods of improvement and regression.

For this group of six patients, some improvements were reported by the majority of patients for the four symptoms of tinnitus recorded in their Daily Diaries. One patient felt worse on average after the treatment, he was the oldest patient (79 years), and had had tinnitus over 20 years. Another patient showed a particularly noticeable improvement, and she was the youngest with the shortest duration of tinnitus (12 months). However the small size of this sample precludes us drawing the conclusion that younger and/or female patients who have had tinnitus for shorter periods of time respond better to acupuncture.

The results of this study are encouraging even though the improvements could be explained by factors other than acupuncture, including the time and attention given to the patients, a social desirability response, expectancy effects, etc., all of which might be expected to have a positive effect. This study was not designed to break down the components that contributed to the changes. We do not know, for example, what specific contribution came from the needling per se. What we have measured is the whole package of care, which from a pragmatic point of view, is the very package that might be expected by a patient who had consulted this practitioner.

The extent that this practitioner and these six patients are representative of the wider population of practitioners and people who have tinnitus needs careful consideration. The acupuncturist was relatively inexperienced. The patients, all recruited in the Manchester area, were willing and able to meet the relatively arduous requirements of the study, including a regime of 2 weeks of five weekday treatments. It was only with difficulty, and because of their determination to support this research, that the six patients were able to complete all assessments and treatments. Therefore there is the potential that the patients in this study were not necessarily typical. The generalisability of the findings of this study will be limited by the extent to which this treatment regime can be adopted as a norm in the West. While we can argue it is likely that acupuncture led to changes in these patients, as evidenced by the significant improvement to many symptoms, we do not have the evidence to claim that patients with tinnitus in general may experience benefits from acupuncturists generally.

It is hoped that this study will encourage renewed interest in acupuncture's potential for treating people with tinnitus. Recent negative[5] and neutral[1] reviews have created a climate where acupuncture might be assumed to be ineffective. While some people might remain confused about the difference between ''no evidence of an effect'' and ''evidence of no effect'', it is our conclusion that there is as yet inadequate evidence on which to base a judgment on acupuncture's effectiveness for tinnitus. Further research is needed, in particular well-designed randomised controlled trials where patients are representative of people with tinnitus in the general population. Such trials will need to have sufficient sample sizes, adequate acupuncture, validated outcome measures, and appropriate follow up periods in order to make a useful contribution to the field.

Conclusion

The $n = 1$ methodology with an AB design supported by Bayesian statistics has provided a useful approach to exploratory research when patient numbers are small and individualised treatments are provided, as is common in complementary medicine. Most patients in this study perceived significant benefits in their self-reported symptoms related to tinnitus. When the treatment effects from all six patients were synthesized, by taking the effect variations between patients into account, the results support the case that acupuncture might be beneficial for tinnitus. Further research to evaluate acupuncture's effectiveness for tinnitus is merited.

Acknowledgments

We acknowledge Anne Signol for her advice and experience in the treatment of tinnitus with acupuncture, Julie Harvey for her administrative support, and Andrew Vickers who helpfully criticised a number of aspects of an earlier version of this paper in an open review.

References

1. Park JB, White A, Ernst E. Efficacy of acupuncture for tinnitus—a systematic review. *Arch Otopharyngol* 2000;**126**:489—92.
2. Podoshin L, Ben-David Y, Frances M, Gerstel R, Felner H. Idiopathic subjective tinnitus treated by biofeedback, acupuncture and drug therapy. *Ear Nose Throat* 1991;**0**(5):284—9.
3. Hansen PE, Hansen JH, Brentzen O. Acupuncture treatment of chronic unilateral tinnitus: a double blind cross-over trial. *Clin Otolaryngol* 1982;**7**:325—9.
4. Birch SJ, Felt RL. *Understanding acupuncture*. London: Churchill Livingstone; 1999. p. 335.
5. Centre for Reviews and Dissemination, ''Acupuncture'' Effective Health Care Bulletin, vol. 7(2), University of York, UK, 2001.
6. MacPherson H, Kaptchuk TJ. *Acupuncture in practice: case history insights from the West*. Edinburgh: Churchill Livingstone; 1997, 282.
7. Guyatt G, Sackett D, Adachi J, et al. A clinician's guide for conducting randomized trials in individual patients. *Can Med Assoc J* 1988;**139**(6):497—503.
8. Aldridge D. Single case research designs. In: Lewith GT, Aldridge D, editors. *Clinical research methodology for complementary therapies*. London: Hodder & Stoughton; 1993.
9. Ezzo J, Berman B, Hadhazy VA, et al. Is acupuncture effective for the treatment of chronic pain? A systematic review. *Pain* 2000;**86**(3):217—25.
10. Carlsson C. Acupuncture mechanisms for clinically relevant long-term effects—reconsideration and a hypothesis. *Acupunct Med* 2002;**20**(2—3):82—99.
11. Zhan S, Ottenbacher KJ. Single subject research designs for disability research. *Disab Rehabil* 2001;**23**(1):1—8.
12. Barlow D, Hersen M. *Single case experimental designs: strategies for studying behavior change*. New York: Pergamon Press; 1984.
13. Zucker DR, Schmid CH, McIntosh RB, Agostino HP, Lau J. Combining single patient (N-of-1) trials to estimate population treatment effects and to evaluate Individual patient responses to treatment. *Clin Epidemiol* 1997;**50**(4):401—10.
14. Maciocia G. *The practice of Chinese medicine*. London: Churchill Livingstone; 1994.
15. Baguley DM, Norman M. Tinnitus handicap inventory. *Am Acad Audiol* 2001;**12**(7):379—80.
16. Paterson C. Measuring outcome in primary care: a patient generated measure MYMOP. *Br Med J* 1996;**312**:1016—22.
17. Jackson A. The use of acupuncture for in treating people with tinnitus. A series of six $n = 1$ case studies. MSc Dissertation. Northern College of Acupuncture, York, 2003.
18. Unschuld P. *Medicine in China A History of Ideas*. Berkeley, Los Angeles, London: University of California Press; 1985.