

Primary care

Acupuncture for chronic headache in primary care: large, pragmatic, randomised trial

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Abstract

Objectives To determine the effects of a policy of “use acupuncture” on headache, health status, days off sick, and use of resources in patients with chronic headache compared with a policy of “avoid acupuncture.”

Design Randomised, controlled trial.

Setting General practices in England and Wales.

Participants 401 patients with chronic headache, predominantly migraine.

Interventions Patients were randomly allocated to receive up to 12 acupuncture treatments over three months or to a control intervention offering usual care.

Main outcome measures Headache score, SF-36 health status, and use of medication were assessed at baseline, three, and 12 months. Use of resources was assessed every three months.

Results Headache score at 12 months, the primary end point, was lower in the acupuncture group (16.2, SD 13.7, n = 161, 34% reduction from baseline) than in controls (22.3, SD 17.0, n = 140, 16% reduction from baseline). The adjusted difference between means is 4.6 (95% confidence interval 2.2 to 7.0; P = 0.0002). This result is robust to sensitivity analysis incorporating imputation for missing data. Patients in the acupuncture group experienced the equivalent of 22 fewer days of headache per year (8 to 38). SF-36 data favoured acupuncture, although differences reached significance only for physical role functioning, energy, and change in health. Compared with controls, patients randomised to acupuncture used 15% less medication (P = 0.02), made 25% fewer visits to general practitioners (P = 0.10), and took 15% fewer days off sick (P = 0.2).

Conclusions Acupuncture leads to persisting, clinically relevant benefits for primary care patients with chronic headache, particularly migraine. Expansion of NHS acupuncture services should be considered.

Introduction

Each week 10% of general practitioners in England either refer patients to acupuncture or practise it themselves,¹ and chronic headache is one of the most commonly treated conditions.² A recent Cochrane review of 26 randomised trials of acupuncture for headache concluded that, although existing evidence supports the value of acupuncture, the quality and

amount of evidence are not fully convincing.³ We conducted a large pragmatic randomised trial to estimate the effects of acupuncture in practice.⁴

Methods


The study included 12 separate sites, each consisting of a single acupuncture practice and two to five local general practices. Study sites were located in Merseyside, London and surrounding counties, Wales, and the north and south west of England.


Accrual of patients

Practices identified potential participants, and general practitioners wrote to suitable patients. A researcher conducted recruitment interviews, eligibility screening, and baseline assessment by telephone. Patients' conditions were diagnosed as migraine or tension-type headache, following criteria of the International Headache Society (IHS).⁵ Patients aged 18-65 who reported an average of at least two headaches per month were eligible. Patients were excluded for any of the following: onset of headache disorder less than one year before or at age 50 or older; pregnancy; malignancy; cluster headache (IHS code 3); suspicion that headache disorder had specific aetiology (IHS code 5-11); cranial neuralgias (IHS code 12); and acupuncture treatment in the previous 12 months. Eligible patients completed a baseline headache diary for four weeks. Patients who provided written informed consent, had a mean weekly baseline headache score of 8.75 or more, and completed at least 75% of the baseline diary were randomised to a policy of “use acupuncture” or “avoid acupuncture.”

Randomisation

We used fully concealed randomised minimisation (“biased coin”) to allocate patients. Minimised variables were age, sex, diagnosis (migraine or tension type), headache score at baseline, number of years of headache disorder (chronicity), and number of patients already allocated to each group, averaged separately by site.

 Additional tables A and B and a description of the sensitivity analyses are on bmj.com

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Treatment

Patients randomised to acupuncture received, in addition to standard care from general practitioners, up to 12 treatments over three months from qualified, experienced acupuncturists. The acupuncture point prescriptions used were individualised to each patient. Patients randomised to “avoid acupuncture” received usual care from their general practitioner but were not referred to acupuncture.

Outcome assessment

Patients completed a daily diary of headache and medication use for four weeks at baseline and then three months and one year after randomisation. Severity of headache was recorded four times a day on a six point Likert scale (0 = no headache, 5 = intense incapacitating headache) and the total summed to give a headache score. The SF-36 health status questionnaire was completed at baseline, three months, and one year. Every three months after randomisation, patients completed additional questionnaires that monitored use of headache treatments and days sick from work or other usual activity. One year after randomisation patients were asked to give a global estimate of current and baseline headache severity on a 0-10 scale.

Statistical considerations

The primary outcome measure was headache score at the one year follow up. Secondary outcome measures included headache score at three months, days with headache, use of medication scored with the medication quantification scale (MQS),⁶ the SF-36, use of resources, and days off usual activities. (see bmj.com).

Results

Recruitment took place between November 1999 and January 2001. Compliance of patients was good: only three patients in the control group reported receiving acupuncture outside the study. Acupuncture patients received a median of nine (interquartile range 6-11) treatments, with a median of one treatment per week. The dropout rate was close to that expected and approximately balanced between groups. Patients who dropped out were similar to completers in terms of sex, diagnosis, and chronicity, but they were slightly younger (43 v 46 years, $P=0.01$) and had higher head-

ache score at baseline (29.3 v. 25.6, $P=0.04$). Baseline characteristics for the 301 patients who completed the trial were similar between groups. Thirty one of the patients who withdrew provided three month data, and an additional 45 provided a global assessment. Only 6% of patients (12 in each group) provided no data for headache after randomisation.

The table shows results for medical outcomes for patients completing 12 month follow up. In the primary analysis mean headache scores were significantly lower in the acupuncture group. Scores fell by 34% in the acupuncture group compared with 16% in controls ($P=0.0002$). This result was highly robust to sensitivity analysis for missing data (smallest difference between groups of 3.85, $P=0.002$; see appendix on bmj.com). When we used the prespecified cut off of 35% as a clinically significant reduction in headache score, 22% more acupuncture patients improved than controls, equivalent to a number needed to treat of 4.6 (95% confidence interval 9.1 to 3.0). The difference in days with headache of 1.8 days per four weeks is equivalent to 22 fewer days of headache per year (8 to 38). The effects of acupuncture seem to be long lasting: headache scores were lower at 12 months than at the follow up after treatment.

Medication scores at follow up were lower in the acupuncture group, although differences between groups did not reach significance for all end points. When we summed and scaled all medication taken by patients after randomisation and compared groups by ANCOVA, medication scores fell by 23% in controls but by 37% in the acupuncture group (adjusted difference between groups 15%; 95% confidence interval 3%, 27%; $P=0.01$). SF-36 data generally favoured acupuncture, although differences reached significance only for physical role functioning, energy, and change in health (see bmj.com).

We conducted interaction analyses to determine which patients responded best to acupuncture. Although improvements in mean headache score over control were much larger for migraine patients (4.9; 95% confidence interval 2.4, 7.5, $n=284$) than for patients who did not meet the criteria for migraine (1.1; 95% confidence interval -2.4, 4.5, $n=17$), the small numbers of patients with tension-type headache

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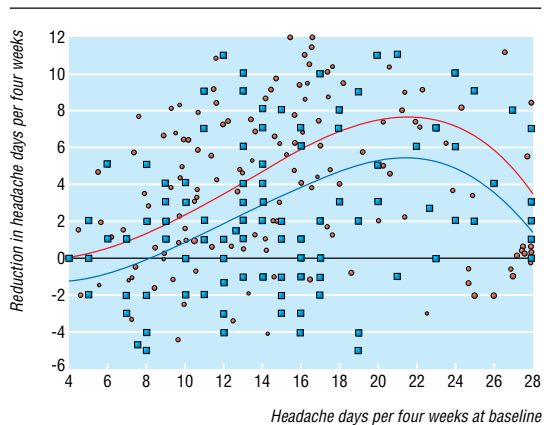
Headache and medication outcomes. Higher scores indicate greater severity of headache and increased use of medication. Differences between groups are calculated by analysis of covariance. Values are means (SD) unless otherwise indicated

End point	Baseline		After treatment (at three months after randomisation)				At 12 months					
	Acupuncture (n=161)	Controls (n=140)	Acupuncture (n=159)	Controls (n=136)	Difference‡	95% CI	P value	Acupuncture (n=161)	Controls (n=140)	Difference‡	95% CI	P value
Weekly headache score	24.6 (14.1)	26.7 (16.8)	18.0 (14.8)	23.7 (16.8)	3.9	1.6 to 6.3	0.001	16.2 (13.7)	22.3 (17.0)	4.6	2.2 to 7.0	0.0002
Days of headache in 28 days	15.6 (6.6)	16.2 (6.7)	12.1 (7.2)	14.3 (7.3)	1.8	0.7 to 2.9	0.002	11.4 (7.5)	13.6 (7.5)	1.8	0.6 to 2.9	0.003
Clinically relevant improvement in score*	—	—	65 (41%)	37 (27%)	14%	3% to 24%	0.014	87 (54%)	45 (32%)	22%	11% to 33%	0.0001
Clinically relevant improvement in frequency†	—	—	36 (23%)	17 (13%)	10%	2% to 19%	0.024	49 (30%)	21 (15%)	15%	6% to 25%	0.002
Scaled pain medication (weekly)	16.5 (18.1)	14.3 (17.6)	11.0 (13.6)	11.4 (14.1)	1.6	-0.7 to 3.9	0.16	8.5 (12.2)	8.7 (12.6)	1.2	-0.6 to 3.1	0.19
Scaled prophylactic medication (weekly)	9.0 (17.8)	13.3 (22.2)	7.9 (17.6)	11.5 (21.3)	0.7	-2.4 to 3.8	0.7	5.0 (14.4)	11.1 (21.3)	3.9	0.5 to 7.4	0.026
Use of any prophylactic medication in 28 days	40 (25%)	45 (32%)	34 (21%)	39 (29%)	7%	-3% to 17%	0.15	22 (14%)	37 (26%)	13%	4% to 22%	0.005

*As defined in study protocol: 35% or greater improvement in headache score from baseline.

†International Headache Society definition: 50% or greater reduction in days with headache.⁷

‡Adjusted difference: positive favours acupuncture.



Frequency of headache at baseline and after treatment. Red dots are actual values for patients in the acupuncture group; blue squares are for controls. The straight line represents no change: observations above the line improved. The curved lines are regression lines (upper red line for acupuncture, lower blue line for controls) that can be used as predictions. Some outliers have been removed

preclude us from excluding an effect of acupuncture in this population. The interaction term for baseline score and group was positive and significant ($P=0.004$), indicating larger effects of treatment on patients with more severe symptoms, even after controlling for regression to the mean. The figure shows comparable data for days with headache.

Data on use of resources show that patients in the acupuncture group made fewer visits to general practitioners and complementary practitioners than those not receiving acupuncture and took fewer days off sick (see bmj.com). The only adverse event reported for acupuncture was five cases of headache after treatment in four subjects.

Discussion

Main findings

Acupuncture in addition to standard care results in persisting, clinically relevant benefits for primary care patients with chronic headache, particularly migraine, compared with controls. We also found improvements in quality of life, decreases in use of medication and

visits to general practitioners, and reductions in days off sick. Methodological strengths of our study include a large sample size, concealed randomisation, and careful follow up.

Limitations

Control patients did not receive a sham acupuncture intervention. One hypothesis might be that the effects seen in the acupuncture group resulted from the placebo effect. Such an argument is not relevant since in everyday practice, patients benefit from placebo effects. None the less, good evidence from randomised trials shows that acupuncture is superior to placebo in the treatment of migraine.^{3 8} Furthermore, this study was modelled on Vincent's earlier double blind, placebo controlled trial in migraine,⁹ and direct comparison implies that our findings perhaps cannot be explained purely in terms of the placebo effect.

Patients in the trial were not blinded, so measures to minimise bias included minimum contact between trial participants and the study team, extended periods of anonymised diary completion and coaching patients about bias. The difference between groups is far larger (odds ratio for response 2.5) than empirical estimates of bias from failure to blind (odds ratio 1.2).¹⁰ The similarity of our results to those of the prior blinded study provides further evidence that bias does not completely explain the apparent effects of acupuncture.

Use of medication and other therapies (such as chiropractic) was lower in patients assigned to acupuncture, indicating that the superior results in this group were not due to confounding by off-study interventions.

Comparison with other studies

Effects found in this study that have been previously reported include: differences between acupuncture and control for migraine^{3 8 11} that increased between follow up after treatment and one year⁸; unconvincing effects for tension-type headache¹²⁻¹⁵; improvements in severity as well as frequency^{8 16} and increased benefit in patients with more severe headaches.⁸

Conclusion

A policy of using a local acupuncture service in addition to standard care results in persisting, clinically relevant benefits for primary care patients with chronic headache, particularly migraine. Expansion of NHS acupuncture services for headache should be considered.

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Competing interests: NE provides acupuncture as part of her private physiotherapy practice.

Ethical approval: South West Multi-centre Research Ethics Committee and appropriate local ethics committees.

- 1 Thomas KJ, Nicholl JP, Fall M. Access to complementary medicine via general practice. *Br J Gen Pract* 2001;51:25-30.
- 2 Wadlow G, Peringer E. Retrospective survey of patients of practitioners of traditional Chinese acupuncture in the UK. *Complement Ther Med* 1996;4:1-7.

What is already known on this topic

- Acupuncture is widely used to treat chronic pain
- Several small trials indicate that acupuncture may be of benefit for chronic headache disorders
- The methodological quality of these studies has been questioned

What this study adds

- Acupuncture led to persisting, clinically relevant reduction in headache scores
- Patients receiving acupuncture used less medication, made fewer visits to general practitioners, and took fewer days away from work or other usual activities
- Expansion of NHS acupuncture services for chronic headache, particularly migraine, should be considered

- 3 Melchart D, Linde K, Fischer P, Berman B, White A, Vickers A, et al. Acupuncture for idiopathic headache. *Cochrane Database Syst Rev* 2001;(1):CD001218.
- 4 Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003;290:1624-32.
- 5 International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 1988;8:1-96.
- 6 Kee WG, Steedman S, Middaugh SJ. Medication quantification scale (MQS): update of detriment weights and medication additions. *Am J Pain Management* 1998;8:83-8.
- 7 Tfelt-Hansen P, Block G, Dahlof C, Diener HC, Ferrari MD, Goadsby PJ, et al. Guidelines for controlled trials of drugs in migraine: second edition. *Cephalalgia* 2000;20:765-86.
- 8 Melchart D, Thormaehlen J, Hager S, Liao J, Linde K, Weidenhammer W. Acupuncture versus placebo versus sumatriptan for early treatment of migraine attacks: a randomized controlled trial. *J Intern Med* 2003;253:181-8.
- 9 Vincent CA. A controlled trial of the treatment of migraine by acupuncture. *Clin J Pain* 1989;5:305-12.
- 10 Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408-12.
- 11 Allais G, De Lorenzo C, Quirico PE, Airola G, Tolardo G, Mana O, et al. Acupuncture in the prophylactic treatment of migraine without aura: a comparison with flunarizine. *Headache* 2002;42:855-61.
- 12 White AR, Eddleston C, Hardie R, Resch KL, Ernst E. A pilot study of acupuncture for tension headache, using a novel placebo. *Acupuncture Med* 1996;14:11-5.
- 13 Karst M, Rollnik JD, Fink M, Reinhard M, Piepenbrock S. Pressure pain threshold and needle acupuncture in chronic tension-type headache—a double-blind placebo-controlled study. *Pain* 2000;88:199-203.
- 14 Karakurum B, Karaalin O, Coskun O, Dora B, Ucler S, Inan L. The “dry-needle technique”: intramuscular stimulation in tension-type headache. *Cephalalgia* 2001;21:813-7.
- 15 Karst M, Reinhard M, Thum P, Wiese B, Rollnik J, Fink M. Needle acupuncture in tension-type headache: a randomized, placebo-controlled study. *Cephalalgia* 2001;21:637-42.
- 16 Lenhard L, Waite P. Acupuncture in the prophylactic treatment of migraine headaches: pilot study. *N Z Med J* 1983;96:663-6. (Accepted 21 January 2004)

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Cost effectiveness analysis of a randomised trial of acupuncture for chronic headache in primary care

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Abstract

Objective To evaluate the cost effectiveness of acupuncture in the management of chronic headache.

Design Cost effectiveness analysis of a randomised controlled trial.

Setting General practices in England and Wales.

Participants 401 patients with chronic headache, predominantly migraine.

Interventions Patients were randomly allocated to receive up to 12 acupuncture treatments over three months from appropriately trained physiotherapists, or to usual care alone.

Main outcome measure Incremental cost per quality adjusted life year (QALY) gained.

Results Total costs during the one year period of the study were on average higher for the acupuncture group (£403; \$768; €598) than for controls (£217) because of the acupuncture practitioners' costs. The mean health gain from acupuncture during the one year of the trial was 0.021 quality adjusted life years (QALYs), leading to a base case estimate of £9180 per QALY gained. This result was robust to sensitivity analysis. Cost per QALY dropped substantially when the analysis incorporated likely QALY differences for the years after the trial.

Conclusions Acupuncture for chronic headache improves health related quality of life at a small additional cost; it is relatively cost effective compared with a number of other interventions provided by the NHS.

Introduction

Migraine and chronic tension headache represent a considerable societal burden in terms of costs to the health service and costs of lost productivity because of reduced effectiveness and time off work.¹⁻⁴ A decade ago the annual costs to the health service were estimated to be between £23m¹ and £30m,² and have probably increased since, given the prescription of

more expensive drugs (such as the triptans). A much greater burden is the cost to the economy of lost productivity: in the early 1990s this was estimated to be between £250m² and £611m⁴ annually.

Interest is increasing in acupuncture as an approach for chronic headache disorders. Although several randomised studies have been conducted,⁵ few reliable data are available on the cost effectiveness of this intervention. We present a cost effectiveness analysis carried out alongside a randomised trial that seeks to assess the value for money of acupuncture for chronic headache.

Methods

In the trial 401 patients aged 18-65 who reported an average of at least two headaches per month were recruited from general practices in England and Wales and randomly allocated to receive either up to 12 acupuncture treatments over three months from appropriately trained physiotherapists or usual care alone.⁶

For the purposes of this evaluation we assume that the acupuncture intervention is provided in the community by the NHS; hence we measure costs from both an NHS perspective and a societal perspective. We measured effectiveness in terms of the quality adjusted life years (QALYs) gained. For our base case, we have taken a conservative approach by excluding savings in productivity costs and by adopting a time horizon of 12 months, the length of the trial follow up. We measured costs in UK prices (£) for 2002-3. We used a single index measure of health related quality of life (HRQoL)—the SF-6D—to calculate HRQoL for each patient at baseline, three months, and 12 months from patients' responses to the SF-36 at each of these time points.⁷

The patients themselves reported unit costs associated with non-prescription drugs and private health-

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