

The effectiveness of acupuncture for osteoarthritis of the knee – a systematic review

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Abstract

Objective To determine the effectiveness of acupuncture treatment for pain and function of patients with osteoarthritis of the knee.

Methods A systematic review of randomised controlled trials was performed, including a meta-analysis which combined the results of trials that used adequate acupuncture treatment and used WOMAC scores to measure the effect. The internal validity (quality) and heterogeneity of studies were taken into account.

Results Thirteen studies were available, of which eight, involving 2362 patients, could be combined. For both reduction of pain and improvement of function, acupuncture was significantly superior to sham acupuncture ($P < 0.05$ for all comparisons) in both the short term and the long term. Compared with no additional intervention (usual care), acupuncture was again significantly superior for pain and function. The treatment effects were maintained after taking account of quality and heterogeneity in sensitivity analyses.

Conclusion Acupuncture is an effective treatment for osteoarthritis of the knee. Its overall effect size is 0.8, and it can be considered instead of non-steroidal anti-inflammatory drugs for patients whose symptoms are not controlled by education, exercise, weight loss if appropriate and simple analgesics. Further research is necessary into the most efficient way of delivering acupuncture, and its longer term benefits.

Keywords

Acupuncture, knee osteoarthritis, systematic review, meta-analysis.

Introduction

A systematic review is a research project in which all the publications on a particular subject are sought, their results are combined and the findings are summarised in a way that is useful for patients and policymakers who are making decisions about health care.¹

The methodology for reviews is now firmly established internationally, and is described most fully in the Cochrane Collaboration handbook.² A particular strength of a systematic review is that it reduces the influence of the researcher's own bias by using a strict methodology that has been set up in advance. A systematic review can be reproduced by anyone who cares to, although minor decisions that

have to be made during the process of the review may affect the conclusions.³

Two features that are basic to a systematic review are: 1) a method of assessing the validity (quality) of each study, so that the validity of the conclusions can in turn be assessed; and 2) a valid and reliable method for combining the results of studies, the most efficient being to combine individual study results mathematically in a meta-analysis. The result of this combined analysis has more power than those of individual trials because of the larger sample size. A meta-analysis also allows an estimate of the consistency of the findings between different studies, eg in settings, patients or treatments. However, deciding whether to combine studies needs caution

and judgement, as it is not justifiable to combine the results of studies that are clearly heterogeneous. The overall quality of systematic reviews can be assessed using known key objective criteria.⁴

This paper summarises a systematic review of the effectiveness of acupuncture for osteoarthritis of the knee, a study which has been accepted for publication in full elsewhere.⁵

Methods

The aim of this systematic review was to evaluate the effectiveness of acupuncture in treating pain and improving function in patients with osteoarthritis of the knee. We planned to include only randomised controlled trials that compared acupuncture with sham acupuncture, other sham treatments, or other forms of care – including waiting list or standardised care with analgesic drug treatment. By ‘sham’, by analogy with ‘sham surgery’, we mean any intervention that is intended to appear the same to the patients but to have a very small physiological effect. A truly inactive ‘placebo’ control for acupuncture is not easy to devise.⁶

Our primary aims were to evaluate the effect of acupuncture: 1) compared with sham acupuncture and 2) as an addition to any other treatment. Regulatory approval of a new drug depends on showing firstly that it is more effective than a placebo drug, and then that the effect is clinically useful. However, comparing acupuncture with placebo acupuncture is more complex because placebo acupuncture is more effective than placebo drug.⁷ The overall effect of acupuncture treatment depends also on factors such as heightened expectation and the effects of intentional touch on the pain control centres in the limbic system.^{6,8} The effects of these factors seem quite separate from the effect of needle location, which is what is tested in most RCTs. Therefore, comparison with sham acupuncture may be regarded as proof of principle that acupuncture can have biological effects, whereas comparing acupuncture with controls who do not receive acupuncture provides information on the place that acupuncture might play in health care.

We searched six electronic databases in June 2006: Medline, Embase, Cochrane CENTRAL, AMED, and CINAHL and PEDro. Asian databases were not accessed because of insufficient resources, but we believe that this omission had a conservative

effect on our results since published Chinese studies of acupuncture are largely or invariably positive.⁹ Two authors independently reviewed the search results and selected titles and abstracts which appeared to be relevant. We then obtained original copies of those articles, and again two authors independently selected the articles which met our criteria for inclusion in the review. These were: the participants were adults with a clinical or radiological diagnosis of osteoarthritis of the knee (or chronic knee pain for at least three months); they were treated with a course of body (not just auricular) acupuncture; the comparison group(s) received sham acupuncture, or another sham treatment, or no additional treatment, or an alternative active intervention; and the outcomes included pain or function.

We then extracted data from the studies into spreadsheets which we had previously prepared and piloted. Again, data were extracted by two authors independently; the data were then combined and any differences were resolved by discussion. An assessment of the quality (internal validity) of each study was undertaken using a standardised assessment of randomisation, blinding, control for co-interventions, dropouts, timing of measures and method of analysis.

The next step of the process – the decision about combining the data – was governed by two important principles. Firstly, it is recognised that some trials of acupuncture have used treatment that is inadequate.¹⁰ Therefore we established criteria for ‘adequate’ acupuncture, from our own clinical experience and from previous studies.^{11,12} We defined acupuncture as ‘adequate’ if it consisted of at least six treatments, was given at least once per week, with at least four points needed for each painful knee for a minimum of 20 minutes, and either needle sensation (*de qi*) achieved in manual acupuncture, or electrical stimulation used at sufficient intensity to produce more than minimal sensation. Secondly, we decided to include only the results of trials that used Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores for pain and function, because WOMAC is recognised as the most reliable and sensitive measure for knee pain trials, and is generally accepted as the preferred measure.¹³ The data from studies that only used the Visual Analogue Scale (VAS) or other scales to assess pain were not combined.

We therefore combined in a meta-analysis the data of those studies which used adequate acupuncture and which applied WOMAC scores, using the standard software provided by Review Manager 4.2.7 (The Cochrane Collaboration, 2005). We used a random effects model since this produces a more conservative analysis if studies are not homogeneous. The result of the analysis is presented in the form of a mean difference of WOMAC score between the groups with 95% confidence intervals, together with a P value for statistical significance.

We performed multiple comparisons between the studies, first for pain and then for function, both for the short term (we defined this from the end of treatment to six months, using the data point nearest to 12 weeks) and then for long term (we defined this between six months and one year, using the last data point).

We then performed sensitivity analyses to account for two possible limitations. Firstly, we wanted to know whether the results of the analysis would be over-dependent on studies that were of low quality: so we repeated the analyses after removing any study that scored less than 50% on the quality score. Secondly, we wanted to take account of any heterogeneity between the studies. The effect of heterogeneity is assessed routinely by the software using a statistic known as I^2 (the chi square value divided by the degrees of freedom). In general, I^2 values of greater than 50% indicate that heterogeneity between the studies is marked. We took this into account by repeating the analysis after removing any

studies that were responsible for the heterogeneity. Finally, we checked the results of the meta-analysis against the results of those studies that were excluded from it, to check the consistency of the findings.

Results

We found 13 studies that could be included in the review, involving 2362 patients.¹⁴⁻²⁶ Five of these (Table 1) were not suitable for combining in the meta-analysis: in one,¹⁸ the acupuncture involved only two needles and therefore did not meet our criteria for adequacy; in four,^{16;17;19;26} the WOMAC measure was not used. This left eight studies (Table 2), which were sufficiently clinically similar in terms of settings, patients and treatments, to be combined. All but two of these were of high quality.^{14;22} The outcomes of all studies are shown in Table 3, and the results of the various meta-analyses are presented in the Figures and summarised in Table 4.

Comparisons with sham acupuncture

For pain reduction, five studies with short-term outcomes (Figure 1a) and three with long-term outcomes (Figure 2a), showed that acupuncture was significantly superior to sham acupuncture. Removing the one study of lower quality made little difference to this result.²² The test shows high heterogeneity, which appears to be due to a single study.²⁴ It is not clear why this study shows a much greater effect of acupuncture than the others, but it may be related to the fact that the patients had more severe symptoms at baseline, or that the acupuncture

Table 1 Characteristics of RCTs of acupuncture for chronic knee pain not included in meta-analysis

Reference	Mean age (y)	Experimental group: intervention (n=)	Control group: intervention (n=)	Study quality (max 9)	Result
Christensen et al 1992	69.2	MA (14)	waiting list (15)	4	MA superior
Molsberger et al 1994	59.7	MA (71)	off-point superficial MA (26)	4	MA superior
Ng et al 2003	85.0	EA (8)	TENS (8) education (8)	3	no significant difference trend for EA
Petrou et al 1988	63	MA (16)	off-point superficial MA (15)	3	MA superior (some measures)
Yurtkuran & Kocagil 1999	58.1	EA (25)	sham TENS (25) acupuncture-like TENS (25)	3	EA superior no significant difference

y = years; EA = electroacupuncture; MA = manual acupuncture

Table 2 Characteristics of RCTs of acupuncture for chronic knee pain included in meta-analysis

Reference	Mean age (y)	Experimental group intervention (n=)	Baseline pain, function (mean WOMAC)	Control group intervention (n=)	Study quality (max 9)
Berman et al 1999	65	MA, EA (37)	9.6, 34.6	current medication (36)	3
Berman et al 2004	65.5	MA, EA (190)	8.9, 31.3	true sham EA, MA (191) education groups (189)	6
Sangdee et al, 2002 (a)	63.0	EA + placebo (48)	10.3, 38.0	on-point sham TENS + placebo (47)	6
Sangdee et al, 2002 (b)		EA + diclofenac (49)	10.5, 37.9	sham TENS + diclofenac (49)	
Scharf et al, 2006	62.8	MA + physiotherapy (330)	10.6, 37.4	off-point superficial MA + physio (365) conservative + physio (342)	7
Takeda & Wessel 1994	61.6	MA (20)	7.8, 24.6	off-point superficial MA (20)	3
Tukmachi et al, 2004 (a)	61.0	MA, EA (10)	10.2, n/a	current drug (10)	6
Tukmachi et al, 2004 (b)		MA, EA + 12.2, n/a current drug (10)			
Vas et al, 2004	67.0	EA + diclofenac (48)	12.4, 40.5	true sham EA, MA + diclofenac (49)	8
Witt et al, 2005	64	MA (150)	9.9, 34.5	off-point superficial MA (76) waiting list (74)	7

y = years; WOMAC = Western Ontario and McMaster Osteoarthritis Index; EA = electroacupuncture; MA = manual acupuncture; n/a = not assessed

(a) and (b) = different active arms, see text for full explanation

involved more intensive electrical stimulation than other studies, or that the control group had a new form of sham needle which does not penetrate the skin. On removing this study, all heterogeneity disappears and acupuncture is still superior to sham acupuncture for pain relief (Table 3).

For improvement of function, the results are similar to pain both in the short term (Figure 1b) and the long term (Figure 2b). Acupuncture shows a small but statistically significant superiority to sham acupuncture over both follow up periods.

Two studies comparing acupuncture with sham acupuncture that were excluded from the meta-analysis are consistent with it: Molsberger and colleagues found acupuncture significantly superior to sham acupuncture for pain;¹⁷ and Petrou and colleagues found a superiority in starting and walking pain, though not in pain on descending stairs or night pain.¹⁹

These results are also consistent with the results of two other studies that compared acupuncture with sham TENS:^{20,26} acupuncture was either significantly superior, or showed a strong trend for pain^{20,26} and function.²⁰

Comparisons with no additional treatment

Four studies compared acupuncture with no additional treatment for pain, and three for function (Figure 3). In three studies, current medication including non-steroidal anti-inflammatory drugs was permitted in both groups, and in the fourth study diclofenac was prescribed to all patients.²¹

Acupuncture was significantly superior for pain, with a weighted mean difference of 3.4 (CI 2.6, 4.3) points on the WOMAC pain scale (0-20), with moderate heterogeneity. This result was similar when combining only the higher quality studies.

For improvement of function, acupuncture was significantly superior to no additional treatment (three studies), with a weighted mean difference of 11.7 (CI 6.5, 16.8) points on the WOMAC function scale (0-68). The marked heterogeneity is mainly due to one large study,²¹ in which patients in all groups also received six sessions of physiotherapy (isometric exercises, walking school, exercises with medical equipment).²⁷ Since acupuncture probably exerts some effect through muscle ergoreceptors,²⁸ simultaneous physiotherapy might diminish its

Table 3 Difference in outcomes between acupuncture and control groups

Reference	Control intervention	Time point (w)	Difference in pain scale 0-20 (95% CI), measure if not WOMAC	Difference in function, WOMAC 0-68 (95% CI)
Berman et al 1999	current medication	12	3.8 (1.5, 6.0)	12.0 (5.6, 18.3)
Berman et al 2004	true sham EA, MA education groups	14 14	1.0 (0.1, 1.8) 2.1 (1.2, 3.0)	2.8 (0.2, 5.4) 6.6 (3.8, 9.4)
Christensen et al 1992	waiting list	8	6.2*, VAS	
Molsberger et al 1994	off-point superficial MA	15	4.0 (0.1, 7.9), VAS	
Ng et al 2003	TENS education	4	1.6 (-0.4, 3.6), NRS 2.4*, NRS	
Petrou et al 1988	off-point superficial MA	3	1.2*, 4-item scale	
Sangdee et al, 2002 (a)	on-point sham TENS + placebo	4	2.3 (0.6, 4.1)	6.8 (1.4, 12.3)
Sangdee et al, 2002 (b)	sham TENS + diclofenac	4	1.4 (-0.5, 3.2)	4.6 (-0.5, 9.7)
Scharf et al, 2006	off-point superficial MA conservative	12 12	0.6 (-0.1, 1.3) 2.8 (2.1, 3.5)	1.4 (-0.9, 3.6) 8.2 (6.0, 10.3)
Takeda & Wessel 1994	off-point superficial MA	7	1.2 (-1.1, 3.4)	-1.8 (-10.1, 6.6)
Tukmachi et al, 2004 (a)	current drug	5	4.3 (0.2, 8.4)	
Tukmachi et al, 2004 (b)	current drug	5	7.9 (2.1, 13.7)	
Vas et al, 2004	true sham EA, MA + diclofenac	12	5.0 (2.9, 7.1)	16.6 (9.5, 23.7)
Witt et al, 2005	off-point superficial MA waiting list	8 8	1.4 (0.3, 2.6) 4.1 (1.5, 6.0)	5.0 (1.3, 8.8) 15.2 (11.9, 18.6)
Yurtkuran & Kocagil 1999	sham TENS acupuncture-like TENS	2 2	4.6*, PPI 1.4*, PPI	

w = weeks; WOMAC = Western Ontario and McMaster Osteoarthritis Index; EA = electroacupuncture; MA = manual acupuncture; VAS = Visual Analogue Scale; NRS = Numerical Rating Scale; PPI = Present Pain Index

(a) and (b) = different active arms, see text for full explanation

*confidence interval cannot be calculated from published data

Table 4 Results of meta-analyses (and sensitivity analyses) of acupuncture for chronic knee pain

	Studies n= (excluded)	Participants n=	Heterogeneity I ² %*	Weighted mean difference (95% CI)
Pain, short term				
vs sham	5 (2)	1334	74.5	1.54 (0.49, 2.60)
excluding outlying study	4	1246	0	0.87 (0.40, 1.34)
high quality studies	4	1294	80.9	1.06 (0.59, 1.53)
vs no additional treatment	4 (1)	927	37.5	3.42 (2.58, 4.25)
high quality studies	3	854	56.3	3.42 (2.36, 4.48)
Pain, long term				
vs sham	3	1178	0	0.54 (0.05, 1.04)
Function, short term				
vs sham	5	1333	78.4	4.32 (0.60, 8.05)
excluding outlying study	4	1245	20.2	2.41 (0.60, 4.21)
high quality studies	4	1293	82.6	3.10 (1.59, 4.61)
vs no additional treatment	3	907	83.8	11.65 (6.48, 16.81)
high quality studies	2	834	91.7	11.58(4.64, 18.51)
Function, long term				
vs sham	3	1178	0	2.01 (0.36, 3.66)

three right hand columns show numbers combined, heterogeneity and weighted mean difference (random effects)

*heterogeneity scores >50% indicate meaningful heterogeneity

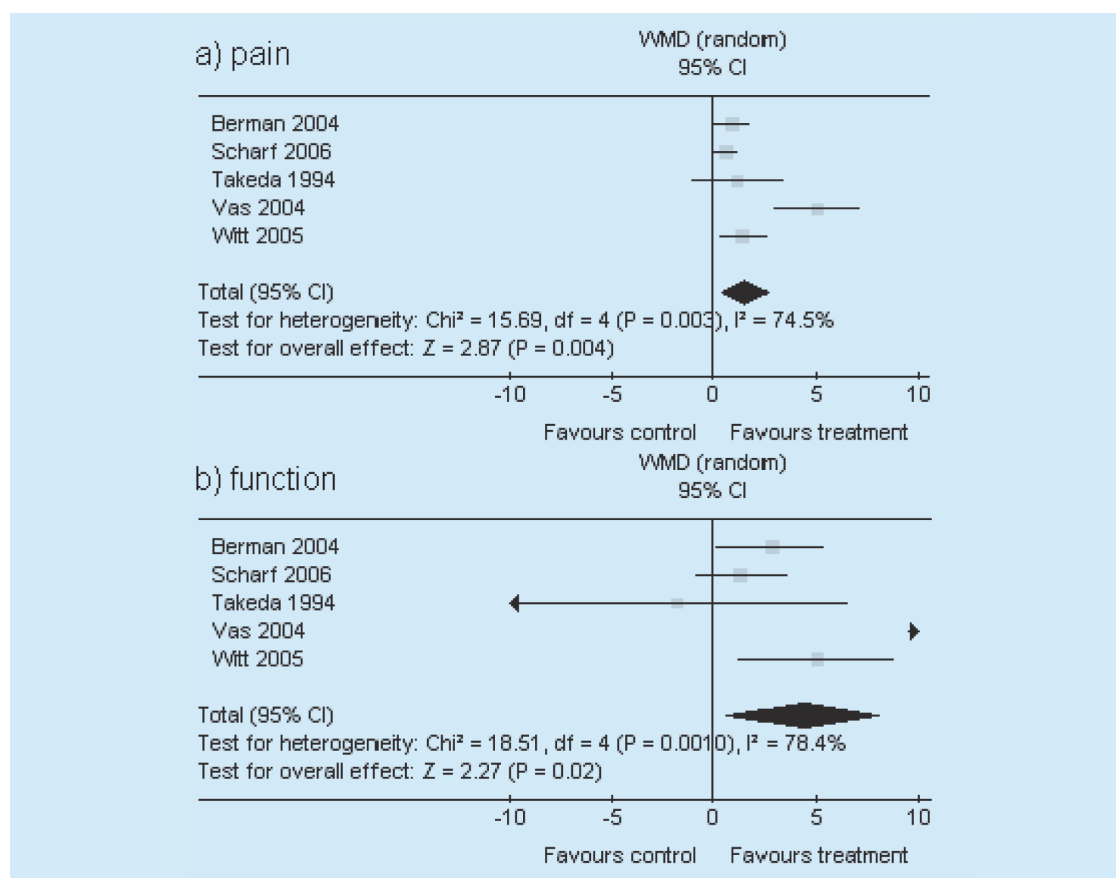


Figure 1 Meta-analysis of short term WOMAC pain and function scores: acupuncture compared with sham acupuncture.

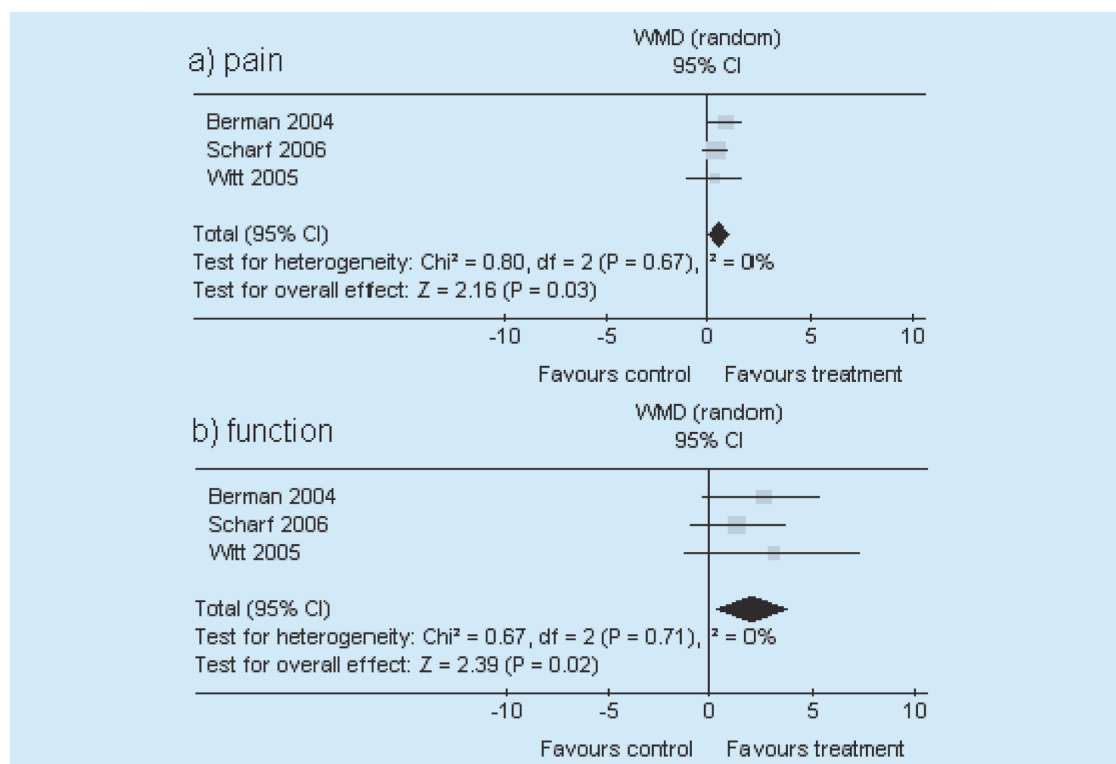


Figure 2 Meta-analysis of long term WOMAC pain and function scores: acupuncture compared with sham acupuncture.

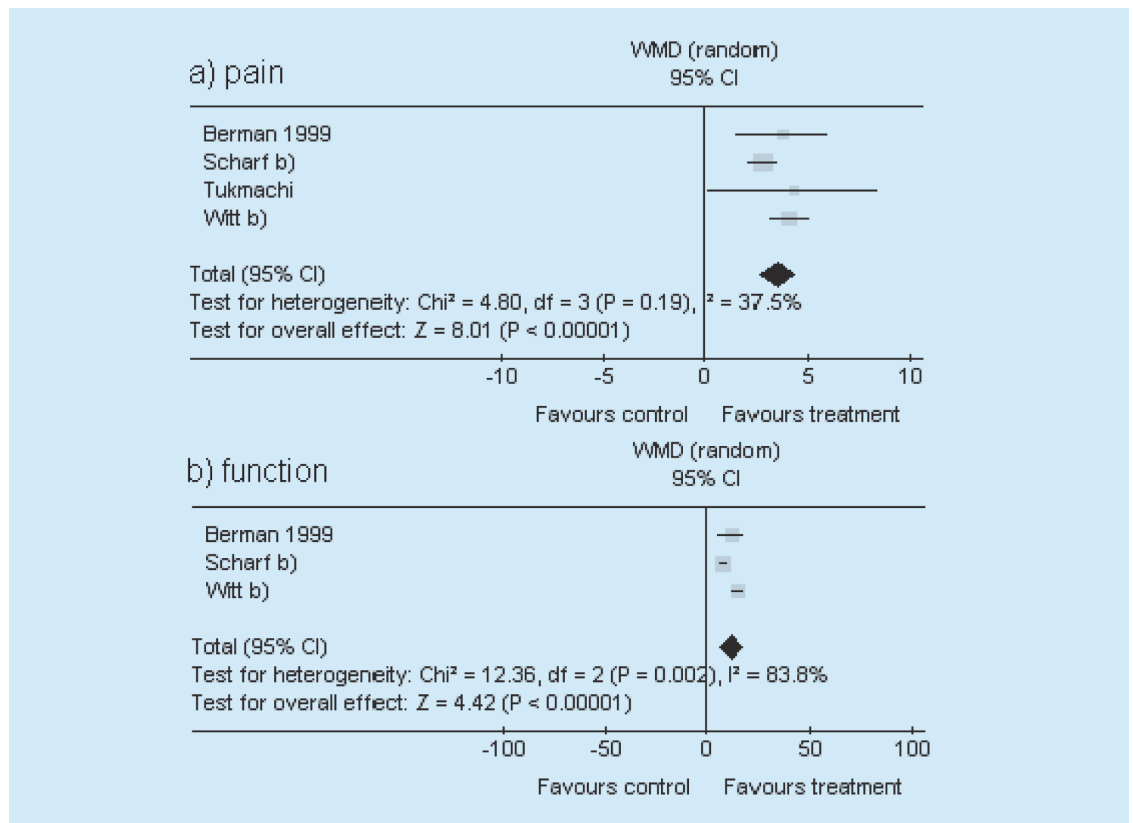


Figure 3 Meta-analysis of short term WOMAC pain and function scores: acupuncture compared with usual care (note different scales for pain and function).

apparent effect. This study was the only one which compared acupuncture with no additional treatment for more than six months, and found that the effect was sustained.

These results were consistent with the one study not included in the meta-analysis, which found acupuncture significantly superior to usual care for pain.¹⁶

Comparison with other interventions

Only one study included in the review compared acupuncture with another active intervention, six two hour sessions of an education programme,¹⁵ true acupuncture was significantly better for reducing pain and improving function in both short term and long term.

Discussion

The results of this systematic review show that adequate acupuncture treatment is significantly superior to placebo (sham acupuncture) and to no additional treatment for osteoarthritis of the knee, both in reducing pain and in improving function.

There is good reason to regard the positive results of this meta-analysis as reliable: they are supported by good quality studies of reasonable size performed in centres in several different countries, and the study results were themselves generally consistent. Although one study was formally reported as not showing a statistically significant effect of acupuncture compared with sham acupuncture in responder rate,²¹ the trend towards acupuncture was strong and its confidence intervals overlapped those of most other studies (Figures 1 and 2). This amounts to category 1 evidence in support of acupuncture over sham acupuncture, according to the usual criteria for evaluating evidence.²⁹

There are also several reasons to believe that these results are generalisable: about two thirds ($n=1337$) of the patients in the meta-analysis had presented routinely in primary care,^{21,25} and a further tenth ($n=200$) had been directly referred to clinics from primary care. Although in most studies the acupuncture was given by one practitioner, in one study 297 practitioners were involved,²¹ and in another the acupuncture was provided by 28 centres.²¹ The

acupuncture treatments were similar in all studies, with the exception of strong electroacupuncture in one study as mentioned.²⁴

Implications for practice

The size of the effect of acupuncture for pain compared with sham is small, (standardised mean difference) 0.36 (0.12, 0.60). This is comparable to the effect size of 0.32 (0.24, 0.39) for non-steroidal anti-inflammatory drugs against placebo.³⁰

However, it is more meaningful to consider the size of the effect when compared to no additional treatment, as this reflects the benefit likely to be seen in practice, and includes all the various effects of acupuncture.⁸ Here the effect size was 0.80 (0.59, 1.02), which is regarded as large.³¹ The mean improvement in pain after acupuncture was 3.4 WOMAC points, which is about a one-third reduction in the average baseline pain. The mean improvement of function was 11.7 WOMAC points, again promising an overall improvement in disability of about one third of the average baseline value.

These average benefits are impressive, particularly when taking the known safety record of acupuncture³² into account. In one of these studies in which events were carefully reported, the rate of adverse events in the acupuncture group were the same as those in both the sham acupuncture and no treatment groups.²¹ One patient in the acupuncture group died of myocardial infarction: this was judged to be not related to the acupuncture, but more likely to the rofecoxib that she had started taking four weeks before the study.

Implications for research

Although the overall result of studies is positive, some questions remain that could enable acupuncture to be targeted more efficiently in practice. It would be useful to know if particular subgroups of patients may respond better to a particular form of treatment. For example, do patients with more severe symptoms respond better to electroacupuncture? Some questions about the application of acupuncture include the best form of treatment for bilateral symptoms, or cases where osteoarthritis is affecting several joints.

On the present evidence, acupuncture seems effective when given in conjunction with medication,^{23:25} but it is possible that a smaller effect

is seen when it is used in conjunction with physiotherapy.²¹ It is likely that combinations of treatments for osteoarthritis have additive effects,³³ and it would be useful to explore acupuncture as an adjunct to other evidence-based interventions within the same package of care. Additionally, it is important to determine the most efficient schedule for applying acupuncture over the long time course that is commonly seen with OA, for example comparing a single block course of treatment with intermittent treatments over six months or more.^{25:15}

Simple comparative studies will be the best way to establish the most efficient way to offer acupuncture, and these questions could readily be addressed within an acupuncture service that is set up for patients with osteoarthritis. One conclusion from the data in this systematic review is that sham (placebo) controlled studies are no longer necessary for acupuncture in knee pain; in fact it is probably not ethical to deny patients the benefit of acupuncture.

In conclusion, we have shown that acupuncture provides significant beneficial effects in pain and function over sham acupuncture and no additional treatment, for patients with knee osteoarthritis. In view of this, it should be considered as a practical alternative to treatment with non-steroidal anti-inflammatory drugs.

Summary points

Eight studies of acupuncture for OA knee (N= 2362) were combined in a meta-analysis

Acupuncture was significantly superior to sham (placebo) acupuncture for pain and function

Acupuncture has a large effect compared with no acupuncture (effect size = 0.8)

The beneficial effects appear to last for at least six months

Acupuncture can be considered an alternative to NSAIDs

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