ORIGINAL ARTICLE

Randomized controlled trial of nettle sting for treatment of base-of-thumb pain

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SUMMARY

There are numerous published references to use of nettle sting for arthritis pain but no randomized controlled trials have been reported. We conducted a randomized controlled double-blind crossover study in 27 patients with osteoarthritic pain at the base of the thumb or index finger. Patients applied stinging nettle leaf (*Urtica dioica*) daily for one week to the painful area. The effect of this treatment was compared with that of placebo, white deadnettle leaf (*Lamium album*), for one week after a five-week washout period. Observations of pain and disability were recorded for the twelve weeks of the study.

After one week's treatment with nettle sting, score reductions on both visual analogue scale (pain) and health assessment questionnaire (disability) were significantly greater than with placebo (P=0.026 and P=0.0027).

INTRODUCTION

The sting of the common stinging nettle has long been used for self-treatment of arthritic pain. We have previously reported two cases seen in general practice[1] and an interview study of 18 patients using this treatment[2]. There are anecdotal reports of urtication (external stinging) for joint pain world wide[3–7], including use by soldiers in Roman times[8], but we find no record of a randomized controlled trial.

In preparation for our own trial we conducted in-depth interviews with 18 patients who had used nettle sting for their joint pains, analysing the results by a grounded theory approach[9]. The information obtained (in particular, method, duration and frequency of application) was used to plan a randomized controlled double-blind crossover trial of common stinging nettle versus white deadnettle (placebo).

METHODS

The nQuery Advisor computer statistical package was used to calculate sample size. We estimated that the difference in health assessment questionnaire score between nettle-treated and placebo-treated patients would be 0.4 units. A sample size of 18 in each group would have 80% power to detect a difference in means of −0.40 (the difference between a group 1 mean of 0.00 and a group 2 mean of 0.40), on the assumption that the common standard within-patient deviation is 0.40 with a group t-test on the period I–period II differences with a 0.05 one-sided significance level.

The inclusion criteria were persistent pain at the base of thumb or index finger of at least ten weeks' duration consistent with a clinical diagnosis of osteoarthritis, in a patient over 18 years old and English-speaking. Exclusion criteria were a history of drug dependency, severe systemic disease, diabetes, pregnancy/lactation, and learning disability. Patients were given or sent an information leaflet before being seen, to offer further information and facilitate enrolment with written consent. The study was approved by the local ethics committee.

Patients

All the patients who were invited to participate accepted, and 27 patients were recruited. 22 were attending rheumatology outpatient departments and 5 were attending a general practice. None had previously used nettles as a treatment. There were 4 men and 23 women, mean age 60 years (range 45–82), mean duration of the complaint 3.8 years (0.2–16). 26 patients had persistent pain in the base of the thumb consistent with osteoarthritis; in addition 2 of these had rheumatoid arthritis and 1 had ankylosing spondylitis. A further patient had osteoarthritis of the base

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of the index finger and wrist. At the start of the study 19 were taking analgesics and 13 anti-inflammatories. 10 patients had received steroid injections for their hand osteoarthritis but none of these had had a steroid injection in the previous three months. Existing treatment was continued during the trial as required by the level of pain.

Trial design

A first week of treatment was followed by a washout period of five weeks. There was then a second treatment week with a further washout period of five weeks. Patients and assessing doctor were blinded to the treatment order. A final assessment was made at the end of the twelve-week trial.

Intervention

White deadnettle (*Lamium album*) plant was chosen as a placebo since when non-flowering it is almost indistinguishable from the common stinging nettle but does not sting. Plants were grown in pots and distributed non-flowering to the patients who were randomly allocated at initial clinic attendance (by numbers drawn from an envelope) to stinging nettle first or white deadnettle first. Patients were instructed how to cut a leaf (with hand in a plastic bag) and apply the underside to the painful area of thumb or index finger base with gentle pressure for about 30 seconds, moving the leaf twice. This was to be done once a day. Patients were given an instruction leaflet. We told them we were investigating the potential beneficial effects of two types of 'nettle' and warned them they might experience stinging which would not be harmful.

Assessment

Patients were assessed clinically at each attendance and completed a pain diary and a health assessment questionnaire. They were observed over the twelve weeks of the study as shown in Figure 1. Multiple outcome measures were used, as recommended by Bradley[10]. The visual analogue scale and verbal rating scale for pain, and the Stanford Health Assessment Questionnaire for disability, are well validated criteria[10–13]. The visual analogue scale consists of a 100 mm horizontal line with endpoints that are anchored by descriptors 'no pain' and 'worst pain ever'. The patient was asked to mark the point on the scale that represented the intensity or unpleasantness of his or her

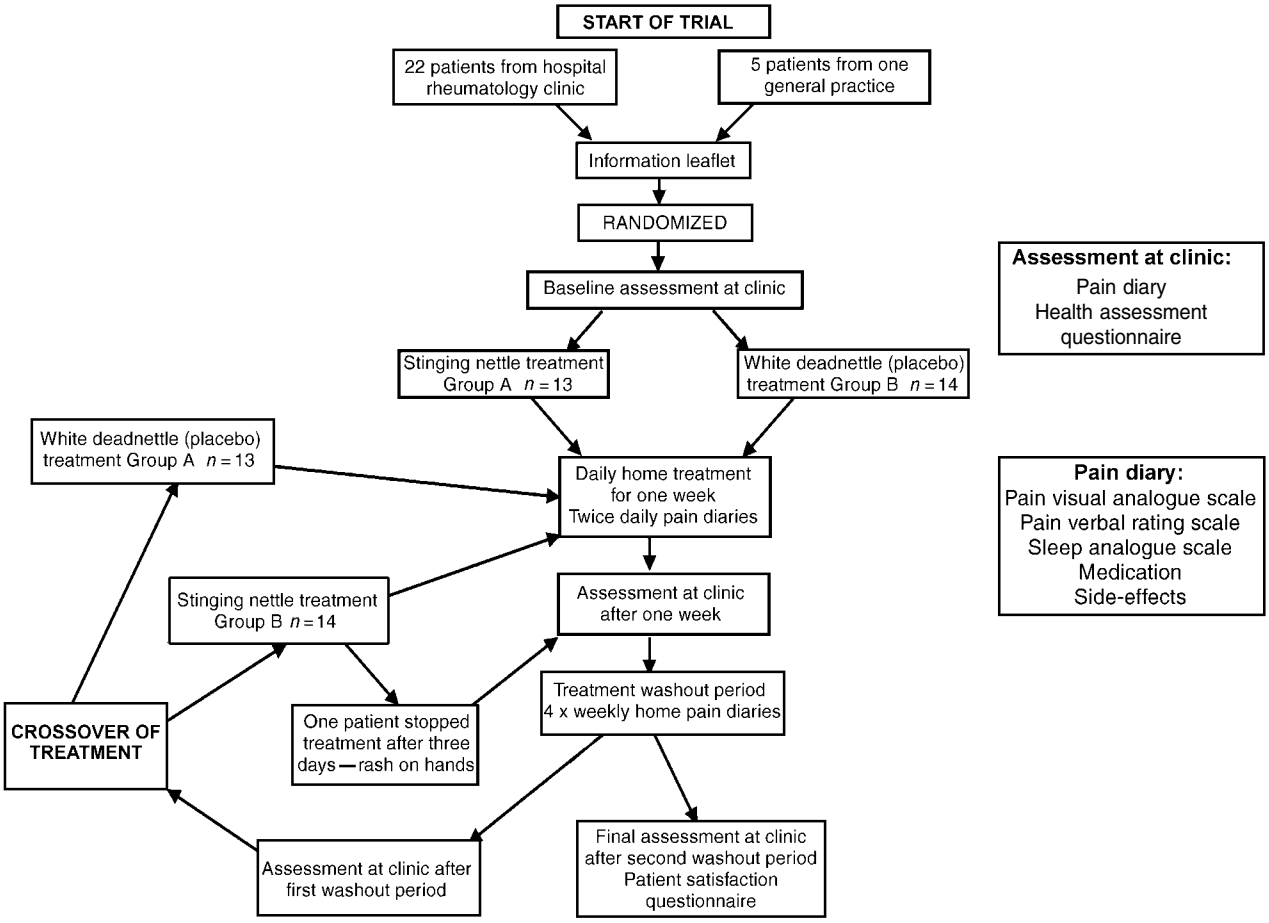

Figure 1 **Treatment and assessment protocol**

Table 1 **Results of outcome measures before and after one week's treatment**

	No. of patients	Pretreatment	After 1 week's treatment	Reduction	Reduction: stinging nettle–placebo	95% CI	P
Pain visual analogue scale							
Stinging nettle	27	38.30 (mean)	23.67 (mean)	14.63 (mean)			
Placebo	27	36.59 (mean)	37.04 (mean)	−0.45 (mean)	15.08 (mean)	−0.02, 30.72	0.026
Health assessment questionnaire							
Stinging nettle	27	1.53 (mean)	1.36 (mean)	0.17 (mean)			
Placebo	27	1.39 (mean)	1.43 (mean)	−0.04 (mean)	0.21 (mean)	0.07, 0.352	0.0027
Daily analgesic usage (non-anti-inflammatory)							
Stinging nettle	27	2.33 (mean)	1.44 (mean)	0.89 (mean)			
Placebo	27	2.04 (mean)	2.11 (mean)	−0.07 (mean)	0.96 (mean)		>0.05
Daily anti-inflammatory usage							
Stinging nettle	27	1.04 (mean)	0.70 (mean)	0.34 (mean)			
Placebo	27	0.93 (mean)	0.93 (mean)	0 (mean)	0.34 (mean)		>0.05
Pain verbal rating scale							
Group A:							
Stinging nettle	13	2 (median)	1 (median)	1 (median)			
Placebo	13	2 (median)	2 (median)	0 (median)	1.0 (median)		0.028
Group B:							
Placebo	14	2 (median)	2 (median)	0 (median)			
Stinging nettle	14	1 (median)	1 (median)	0 (median)	0 (median)		>0.05

pain experience. A visual analogue pain scale is more sensitive to treatment-related changes than are numerical and verbal rating scales[10]. It is an interval scale, thus parametric procedures (e.g. *t*-test) may be used to analyse responses[10]. The verbal rating scale used was a simplified five-category scale modified from the seven-category scale described by Bradley[10]: no pain; faint pain; moderate pain; strong pain; worst pain ever.

Analgesic and anti-inflammatory medication usage, sleep analogue scale scores and side-effects were also monitored. At the end of the study patients completed an eight-question satisfaction questionnaire.

Statistical analysis

Two-sample *t*-tests were applied to period I–period II differences calculated for each patient. Kolmogorov–Smirnov tests on these variables showed the assumption of Normality had a reasonable justification. Pain visual analogue scale and health assessment questionnaire scores were the two best-validated measures and were nominated as the key outcome measures. The mean reductions in visual analogue scale scores and health assessment questionnaire scores were compared for stinging nettle versus placebo, the 95% confidence interval being calculated for each.

The verbal rating scale was a categorical/ordinal score, thus non-parametric analysis was used (Wilcoxon paired-samples test). Reduction of analgesic and anti-inflammatory drug consumption was analysed with two-sample *t*-tests.

RESULTS

Completion rate of pain diaries was 99% and attendance rate at review clinics was 96%. At the end-of-trial final assessment clinic 6 patients did not attend, but 3 of these were interviewed by telephone and completed pain diaries/end-of-trial assessments.

Pain and disability scores are shown in Table 1. The visual analogue scale scores for stinging nettle treatment fell below those for placebo after day two and remained lower for the rest of the week (Figure 2).

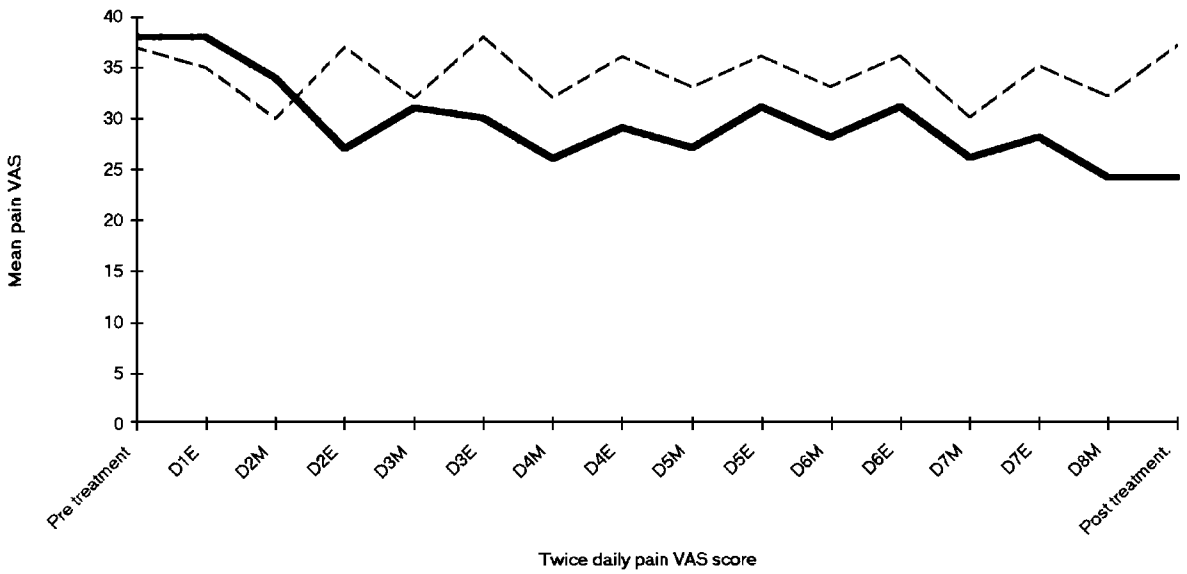

Figure 2 **Mean pain visual analogue scale (VAS) score during treatment week: nettle versus placebo. —** Mean nettle VAS; - - - mean placebo VAS

After one week's treatment the score reduction with stinging nettle was significantly greater than that with placebo. A week into the washout period there was still a difference in favour of stinging nettle, though no longer significant (P=0.11, see Figure 3).

Verbal rating scale scores showed greater pain reduction with stinging nettle but the difference was statistically significant only in the group who had stinging nettle first (see Table 1). The health assessment questionnaire scores showed a significant reduction for stinging nettle versus placebo after one week's treatment (see Table 1).

After one week's treatment daily use of analgesic and anti-inflammatory drugs showed a decline in the stinging nettle group but the difference versus placebo was not significant (at the start of the study only 19 were taking analgesics and 13 were taking anti-inflammatories).

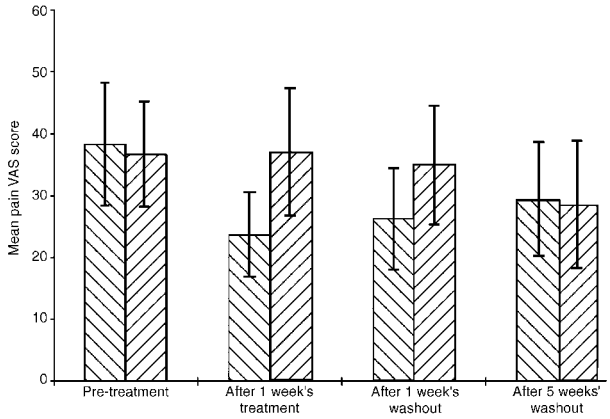

Figure 3 **Comparison of nettle/placebo mean pain visual analogue scale (VAS) scores with 95% confidence intervals. ▨ Nettle; ▨ placebo**

It became clear during the study that sleep was an unsatisfactory outcome measure. Only 6 of 27 patients considered their hand pain to be the predominant factor affecting sleep. There was a non-significant improvement in sleep with stinging nettle (3.8% versus 0.6%).

No serious side-effects were reported or observed. The localized rash and slight itching associated with stinging nettle was acceptable to 23 of 27 patients; 2 patients reported the sting as unpleasant but not distressing. 1 patient had a persistent rash on her forearms after treatment but this had occurred before and was not necessarily due to stinging nettle. The stinging nettle treatment caused a rash on the hand of one patient who discontinued treatment because he needed heavy gloves for his job.

On the measure of patient satisfaction, 14 patients out of 27 preferred nettle sting treatment to their usual treatment and 17 wished to use the treatment in the future.

DISCUSSION

The results of this trial demonstrate an analgesic effect and a reduction of disability after one week of daily treatment with stinging nettle. A weakness of the design was that the 'blinding' of both doctor and patients was incomplete; some patients reported stinging and a rash with the application of one plant treatment. Patients were not, however, given to understand that any benefit might be associated with the sting, and the patients did not seem to make this assumption. The sample size was small, but the crossover of treatment considerably increased the power of the results. Patient compliance was also high. Pain perception is

subjective and difficult to measure, which is why we used multiple validated indices of pain and function.

The stinging nettle is a freely available plant and its sting seems a safe treatment for musculoskeletal pain. Nettle sting contains serotonin, acetylcholine, histamine and leukotrienes, among other substances[14]. Serotonin and histamine are involved in the cascade of stimulation affecting levels of nerve growth factor, which in turn increases activation of nociceptive pain neurons[15–18]. The mechanism of nettle-sting analgesia could be hyperstimulation of the sensory nociceptors causing a TENS-like effect[19–21], a substance P depletion effect similar to that of capsaicin[22], an acupuncture-like effect[23,24] or a counter-irritant effect[25,26]. A stinging rash might also have a powerful effect on patients' cognitive perception of pain[27]. The potential of this treatment deserves further research.

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