smoking completely, a recommendation to avoid smoking after taking the night-time antisecretory tablet should be acceptable and, on the basis of our results, may prove to be clinically relevant and useful.

K. G. W. gratefully acknowledges a research grant from the Scottish Hospital Endowments Research Trust.

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REFERENCES

1. Doll R, Jones FA, Pygott F. Effect of smoking on the production and maintenance of gastric and duodenal ulcers. *Lancet* 1958; i: 657–62.
2. Elashoff JD, Grossman MI. Smoking and duodenal ulcer. *Gastroenterology* 1980; **79:** 181.
3. Valnes K, Wetterhus S, Ellekjaer E, et al. Trimpramine in the treatment of duodenal ulcer. A multicenter, open study. *Scand J Gastroenterol* 1980; **15,** suppl. 58: 65–70.
4. Korman MG, Shaw RG, Hansky J, et al. Influence of smoking on healing rate of duodenal ulcer in response to cimetidine or high-dose antacid. *Gastroenterology* 1981; **80:** 1451–53.
5. Boyd EJS, Wormsley KG. Inhibition of pentagastrin-stimulated and overnight gastric secretion by LM 24056, a new phenothiazine-derived antisecretory drug. *Lancet* 1981; i: 471–73.
6. Berstad A. A modified hemoglobin substrate method for the estimation of pepsin in gastric juice. *Scand J Gastroenterol* 1970; **5:** 343–48.
7. Wormsley KG. Smoking and duodenal ulcer. *Gastroenterology* 1978; **75:** 139–42.
8. Piper DW, Raine JM. Effect of smoking on gastric secretion. *Lancet* 1959; i: 696–98.
9. Cooper P, Knight JB. Effect of cigarette smoking on gastric secretion of patients with duodenal ulcer. *N Engl J Med* 1956; **255:** 17–21.
10. Debas HT, Cohen MM, Holubitsky IB, et al. Effect of cigarette smoking on human gastric secretion. *Gut* 1972; **12:** 93–96.
11. Wilkinson AR, Johnston D. Inhibitory effect of cigarette smoking on gastric secretion stimulated by pentagastrin in man. *Lancet* 1971; ii: 628–32.
12. Wormsley KG. The pathophysiology of duodenal ulceration. *Gut* 1974; **15:** 59–81.

# CONTROLLED TRIAL OF HOMOEOPATHIC TREATMENT OF OSTEOARTHRITIS

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***Summary*** In a double-blind, placebo-controlled cross-over study to compare the homoeopathic remedy *Rhus tox.* 6X with fenoprofen in osteoarthritis of the hip and knee, fenoprofen was shown to have beneficial analgesic and anti-inflammatory effects which differed significantly from those of placebo. The effects of *Rhus tox.* 6X and placebo did not differ significantly. Patient preference was for fenoprofen. Side-effects were not severe but were seen more frequently with fenoprofen. Similar results were seen in all patients regardless of whether they had been referred to and assessed by a homoeopathic physician or a rheumatologist.

## Introduction

THE joint pain of many patients with osteoarthritis (OA) can be satisfactorily controlled by drugs which are anti-inflammatory and analgesic. Sometimes, however, pain relief is incomplete and surgery may be indicated, or side-effects are sufficiently troublesome to preclude the effective use of these drugs. Many patients have thus turned to alternative forms of treatment and this has led to a considerable increase in interest in homoeopathic medicine.

Extracts of the poison oak *(Rhus toxicodendron)* produce many toxic effects, a few of which are said to mimic symptoms experienced by some patients with osteoarthritic joints. For this reason homoeopathic physicians frequently use a preparation of *Rhus tox.* in such patients. Although homoeopathic physicians will often combine several remedies, the use of *Rhus tox.* is sufficiently widespread to justify testing it against a standard anti-inflammatory analgesic (fenoprofen).

## Patients and Methods

Patients between the ages of 18 and 85 years were entered into the trial if they satisfied the clinical and radiological criteria for OA of one or more hips or knees. Exclusion criteria were those defined by the Helsinki Convention. Any patient who had previously received either *Rhus tox.* or fenoprofen was also excluded.

36 patients entered the trial, 15 in group I and 21 in group II. There were 24 women and 12 men. The mean age was 65 years (37–82 yr). 17 patients had OA of one or both knees, 15 had OA of one or both hips, and 4 had involvement of three joints. In these respects both group I and group II were comparable. Before entry 7 patients were taking no regular medication, 16 were using simple analgesics, and 14 were taking non-steroidal anti-inflammatory drugs. Group I included a greater proportion who were taking either no drugs or minimal medication.

Group I patients were specifically referred for homoeopathic advice to the Royal Homoeopathic Hospital, London, and group II were referred to the departments of rheumatology at the Kent and Sussex Hospital, Tunbridge Wells, and at King's College Hospital, London. Patients in each group were assessed by the same observer throughout the study, and the same protocol was adhered to and the same assessment forms were used by both. The results were analysed both separately and together.

The study was a double-blind, double-dummy, placebo-controlled crossover comparison of fenoprofen (600 mg three times a day), *Rhus tox.* (6X; 1/1 000 000 dilution), and placebo. No washout period was included in the design. Patients were randomly allocated to one of three treatment regimens. All other non-steroidal anti-inflammatory drugs were stopped. Paracetamol was permitted as the "escape" analgesic and its consumption during each treatment period was measured by counting the tablets returned. Two capsules each containing either 300 mg fenoprofen or placebo were given three times a day after meals. *Rhus tox.* 6X was a colourless solution and five drops were given three times a day, not within half an hour of food or strong beverages (this includes alcohol, tea, and coffee); matching dummy drops were provided. All patients received the three treatments, each for two weeks.

The following symptom patterns, which indicate to the homoeopathic physician that the patient is likely to respond to *Rhus tox.*, had to be satisfied for inclusion in the study. a) The pain in the affected joints is made worse by immobility and exacerbated on initial weight bearing and movement from rest, but partly relieved by further motion. b) The pain is made worse by cold and damp and relieved by warmth.

Patients were assessed on entry to the trial and at the end of each treatment period. Measurements were of pain at rest, pain on movement, and night pain using both 10 cm visual analogue scales and four point pain scores. A preference was sought from each patient at the end of the second and third treatment periods and between the first and second treatment periods, and an overall preference was sought at the end of the third period.

To determine side-effects patients were asked, "Has the treatment upset you in any way?" Return capsule counts and drop measurements were checked for compliance. Analysis of the results was statistically validated.

## Results

33 patients completed the trial (13 in group I and 20 in group II). 2 patients dropped out (1 in each group) because of

an apparent aggravation of symptoms while on *Rhus tox.* and a third was admitted from the waiting list for total hip replacement. The means and standard deviations for the values obtained in all patients are shown in table I. Independent comparison of the results in groups I and II shows that they did not differ significantly on entry. Analysis of results by a paired *t* test (table II) indicates that there was no significant difference between the effects of *Rhus tox.* and placebo. Fenoprofen produced highly significant pain relief compared with *Rhus tox.* and placebo.

In order to detect any differences between the results in the two groups, visual analogue scores were analysed separately (table III). Individually the results follow the trend seen so clearly in the combined results; the effect does not appear to differ, regardless of whether the patient was actively seeking homoeopathic advice (group I) or being offered a homoeopathic remedy as part of a trial in an allopathic clinic (group II).

When fenoprofen was compared with either placebo or *Rhus tox.* it was clearly preferred to either. When *Rhus tox.* and placebo were compared with each other, each was equally preferred. Overall, patients preferred fenoprofen (21 patients) to *Rhus tox.* (5 patients) and placebo (5 patients). Results between the two groups are comparable. Side-effects were few in general, the most common being mild gastrointestinal disturbances in patients on fenoprofen.

## Discussion

We have shown that, under the conditions of this study, treatment with five drops of *Rhus tox.* 6X three times a day does not differ significantly from placebo in its effects on the pain of osteoarthritic hips and knees. Fenoprofen is a useful anti-inflammatory analgesic but causes a relatively high incidence of minor side-effects. Compared with both placebo and *Rhus tox.* its beneficial effects were highly significant and, despite its side-effects, fenoprofen was still preferred by most patients.

5 patients experienced exacerbation of their symptoms while on *Rhus tox.* and 2 were withdrawn from the trial, both during the first treatment period (one had been taking piroxicam 20 mg daily and dihydrocodeine 30 mg four times a day, and the other 'Equagesic' [Wyeth] when necessary). This exacerbation might be explained by the homoeopathic phenomenon of aggravation or may simply reflect the removal of effective treatment. According to classic homoeopathic theory, after such an aggravation and subsequent withdrawal of treatment, the patient may experience relief of symptoms after a delay of four to six weeks. We did not maintain follow-up on either patient and do not know the outcome.

Only two previous controlled trials comparing homoeopathic remedies and conventional treatment have been reported[1,2] and both concerned patients with rheumatoid arthritis. The first was a preliminary communication, the design of which was severely criticised.[3] The second set out to answer these criticisms, permitting the patients to continue their conventional treatment unaltered and allowing the homoeopathic physician to recommend alteration of the homoeopathic treatment as he saw fit during the three months of the study. The patients were then given either placebo or the recommended remedies in a double-blind fashion which reflected the normal practice of multiple and varied prescription. Small but significant improvements were reported in subjective pain, articular index, morning stiffness, and grip strength in patients receiving homoeopathic treatment, but no significant changes were seen in those on placebo. Neither group showed any change in routine laboratory measurements. Evidence from our study leads us to conclude that *Rhus tox.* 6X alone had no greater effect than placebo on the pain of osteoarthritic hips and knees.

TABLE I—MEAN VALUES (±STANDARD DEVIATION) FOR VISUAL ANALOGUE SCALES (VAS) AND FOUR POINT PAIN SCORES OF ALL PATIENTS ON ADMISSION TO TRIAL AND AFTER TWO WEEKS ON EACH TREATMENT (n = 33)

| — | Admission | Placebo | *Rhus tox.* | Fenoprofen |
|---|---|---|---|---|
| *Pain on movement* | | | | |
| VAS | 53·4 ±25·1 | 61·0 ±27·6 | 58·2 ±25·5 | 41·5 ±29·0 |
| Pain | 2·09± 0·72 | 2·30± 0·88 | 2·27± 0·63 | 1·70± 0·85 |
| *Pain at rest* | | | | |
| VAS | 26·9 ±25·4 | 34·7 ±27·4 | 34·5 ±26·0 | 22·3 ±23·6 |
| Pain | 1·45± 0·90 | 1·64± 0·96 | 1·58± 0·87 | 1·18± 0·82 |
| *Night pain* | | | | |
| VAS | 40·2 ±30·5 | 48·3 ±31·1 | 46·5 ±30·2 | 35·1 ±34·5 |
| Pain | 1·55± 1·0 | 1·91± 0·95 | 1·91± 0·80 | 1·27± 1·04 |
| *Paracetamol* | | | | |
| Returns | .. .. | 61·8 ±30·1 | 59·0 ±33·0 | 70·1 ±30·6 |

TABLE II—ANALYSIS OF RESULTS BY PAIRED *t* TEST

| — | Placebo *vs.* *Rhus tox.* | | Placebo *vs.* fenoprofen | | *Rhus tox. vs.* fenoprofen | |
|---|---|---|---|---|---|---|
| | *t* | p | *t* | p | *t* | p |
| *Pain on movement* | | | | | | |
| VAS | 1·08 | NS | −5·7 | <0·001 | −6·27 | <0·001 |
| Pain | 0·47 | NS | −4·7 | <0·001 | −4·18 | <0·001 |
| *Pain at rest* | | | | | | |
| VAS | 0·01 | NS | −4·04 | <0·001 | −3·61 | <0·005 |
| Pain | 0·53 | NS | −4·23 | <0·001 | −3·21 | <0·005 |
| *Night pain* | | | | | | |
| VAS | 0·45 | NS | −3·7 | <0·001 | −3·09 | <0·005 |
| Pain | 0·53 | NS | −4·9 | <0·001 | −4·67 | <0·001 |
| *Paracetamol* | | | | | | |
| Returns | 0·13 | NS | 2·05 | <0·05 | 2·12 | <0·05 |

NS = not significant. VAS = visual analogue scales.

TABLE III—ANALYSIS OF RESULTS BY GROUPS WITH PAIRED *t* TEST

| Visual analogue scales | Placebo *vs.* *Rhus tox.* | | Placebo *vs.* fenoprofen | | *Rhus tox. vs.* fenoprofen | |
|---|---|---|---|---|---|---|
| | *t* | p | *t* | p | *t* | p |
| *Pain on movement* | | | | | | |
| Group I | 1·19 | NS | −3·41 | <0·005 | −5·22 | <0·001 |
| Group II | 0·63 | NS | −4·16 | <0·001 | −4·06 | <0·001 |
| *Pain at rest* | | | | | | |
| Group I | 1·94 | NS | −3·32 | <0·01 | −3·67 | <0·005 |
| Group II | −1·15 | NS | −2·8 | <0·02 | −2·74 | <0·02 |
| *Night pain* | | | | | | |
| Group I | 0·87 | NS | −1·50 | NS | −1·01 | NS |
| Group II | 0·2 | NS | −3·6 | <0·005 | −3·63 | <0·005 |

We thank A. Nelson & Co. Ltd for *Rhus tox.* 6X and dummy controls, and Dista Products Ltd for plain capsules of fenoprofen and matched dummy controls. We acknowledge the help of Mrs B. Bloom, Sister A. Moon, Miss M. Keep, and Miss J. Jones. Mrs C. Stede gave valuable statistical advice.

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REFERENCES

1. Gibson RG, Gibson SLM, MacNeil AD, Gray GH, Dick WC, Buchanan WW. Salicylates and homoeopathy in rheumatoid arthritis: preliminary observations. *Br J Clin Pharmacol* 1978; **6**: 391–95.
2. Gibson RG, Gibson SLM, MacNeil AD, Buchanan WW. Homoeopathic therapy in rheumatoid arthritis: evaluation by double-blind clinical therapeutic trial. *Br J Clin Pharmacol* 1980; **9**: 453–59.
3. Huston G. Salicylates and homoeopathy. *Br J Clin Pharmacol* 1979; **7**: 529–30.