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# HOMOEOPATHIC THERAPY IN RHEUMATOID ARTHRITIS: EVALUATION BY DOUBLE-BLIND CLINICAL THERAPEUTIC TRIAL

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**1** Twenty-three patients with rheumatoid arthritis on orthodox first-line anti-inflammatory treatment plus homoeopathy were compared with a similar group of twenty-three patients on orthodox first-line treatment plus an inert preparation.

**2** There was a significant improvement in subjective pain, articular index, stiffness and grip strength in those patients receiving homoeopathic remedies whereas there was no significant change in the patients who received placebo.

**3** Two physicians were involved in prescribing for the patients and there were no significant differences in the results which they obtained.

**4** No side effects were observed with the homoeopathic remedies.

## Introduction

A pilot study comparing the relative values of homoeopathic treatment and salicylate therapy in rheumatoid arthritis has been previously described (Gibson, Gibson, MacNeill, Gray, Dick & Buchanan, 1978). There were, however, two main criticisms of this study. Firstly, the patients who received homoeopathic treatment were allowed to continue their previous orthodox anti-inflammatory therapy whereas the patients who received salicylates had to discontinue all other previous anti-inflammatory drugs. Secondly, since the patients who received homoeopathic treatment were seen by different doctors from those being given salicylate, it could be argued that the better response of the patients on homoeopathy was due to the doctor and not the drug.

In order to evaluate the importance of these two points a second, more rigidly controlled trial was designed and is reported in this paper.

## Methods

### *Patients studied*

All the patients selected for the trial satisfied the diagnostic criteria of the American Rheumatism Association for definite rheumatoid arthritis (Ropes, Bennett, Cobb, Jacox & Jessar, 1959). They were seen in the outpatient department of the Centre for Rheumatic Diseases by the two physicians from the Glasgow Homoeopathic Hospital who were involved in the previous study (Gibson *et al.*, 1978). Because in homoeopathic practice the selection of the appropriate remedy depends on the patient's symptoms and signs and his reaction to his total exterior and interior environment, the patients were divided into two groups: those with good prescribing symptoms, R patients, and those with poor prescribing symptoms, U patients, (Dhawale, 1976; Mitchell, 1975; Clarke, 1978).

Good prescribing symptoms are onset of symptoms following a sudden fright, bereavement, physical injury or other profound emotional or physical trauma; complaint affected by climatic conditions, for instance damp or dry weather, heat, frost or wind; complaint markedly affected by other factors such as movement, rest or time of day; outstanding factors affecting the patient, not necessarily associated with the disease, such as marked craving or aversion for certain foods.

In the case of a female patient, emotional, mental and physical changes before, during or after the menstrual period may be of importance. Weighting is given to marked mental or emotional peculiarities such as extreme tidyness, fear of heights or unusual reactions to sympathy. Any patient with three or more of these marked characteristics would be classed as showing good prescribing symptoms, whereas a patient who showed less than three, or who was

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**Table 1** Clinical and laboratory features in 46 patients with rheumatoid arthritis (mean + range)

| *Clinical and laboratory feature* | | *Homoeopathy* | *Placebo* |
|---|---|---|---|
| Number | | 23 | 23 |
| Age (years) | mean | 54.0 | 52.1 |
| | range | 32–76 | 24–77 |
| Sex | male | 7 (30.4%) | 8 (34.8%) |
| | female | 16 (69.6%) | 15 (65.2%) |
| Duration of disease (years) | mean | 7.2 | 8.8 |
| | range | 1–25 | 0.5–36 |
| Articular index of joint tenderness | mean | 16.6 | 16.1 |
| | range | 6–38 | 4–44 |
| Functional index | mean | 7.9 | 8.4 |
| | range | 0–19 | 0–26 |
| Haemoglobin (g%) | mean | 12.5 | 12.9 |
| | range | 10.0–16.4 | 9.4–17.8 |
| Erythrocyte sedimentation rate (mm/first hour) | mean | 38.6 | 46.7 |
| | range | 3–214 | 5–120 |
| Rheumatoid factor (reciprocal of titre) | mean | 128 | 256 |
| | range | 32–2048 | 16–2048 |
| Antinuclear factor (reciprocal of titre) | mean | 64 | 64 |
| | range | neg – 256 | neg – 1000 |

uncertain in his reactions, would be classed as having poor prescribing symptoms.

This assessment into these two categories was made by the two homoeopathic physicians. The patients were then assigned to two groups so that as far as possible there were equal numbers of R and U patients in each group. In addition an attempt was made to match patients for drug therapy so that again, as far as possible, both groups contained the same proportion of patients receiving the different non-steroidal anti-inflammatory drugs. An attempt was also made to match the patients for clinical severity of disease, but this proved difficult. The allocation into the two treatment groups was made entirely independently by a third physician (SG) who otherwise took no part in the clinical assessment. This physician also dispensed the remedies: one group receiving placebo and the other active homoeopathic therapy. All the preparations were dispensed in identical powder papers and were indistinguishable from each other. Both the group receiving the placebo and the group receiving the active homoeopathic remedies continued their previous orthodox therapy unaltered. The patients were not told that they were to be treated with homoeopathic remedies but they were told that they were taking part in a double-blind trial and might receive inactive substances. All were willing to take part. As half the subjects were to receive placebo for a period of 3 months it was considered ethically unjustifiable to discontinue their current non-steroidal anti-inflammatory drug therapy (El-Ghobarey, Mavrikakis, MacLeod, Reynolds, Capell, Spencer, Balint, Mathieu, McAllister, Cooney & Dick, 1978).

Current therapy consisted of one or other or the following:— salicylate, either soluble or enteric coated, dextropropoxyphene hydrochloride, indomethacin, naproxen, ibuprofen, ketoprofen, fenoprofen, flurbiprofen, benorylate and sulindac. No patient was on more than one of these anti-inflammatory agents and each was maintained on the maximum tolerated therapeutic dose. Treatment had

**Table 2** The homoeopathic remedies most commonly used in the trial

| | |
|---|---|
| Arnica | Nux vomica |
| Arsenicum album | Opium |
| Bryonia alba | Pulsatilla* |
| Calcarea carbonica | Rhododendron |
| Causticum | Rhus toxicodendron* |
| Ignatia | Ruta* |
| Lachesis | Sepia* |
| Lycopodium | Sulphur* |
| Morgan | Sycotic co |
| Natrum muriaticum | Thuja |

*Remedies of wide action in rheumatoid arthritis used more often in patients with poor prescribing symptoms.

been administered for periods ranging from 2 to 6 months. Although in most cases there had been some initial benefit from these anti-inflammatory drugs, the patients had either ceased to improve or were deteriorating when they were admitted to the trial.

The clinical and laboratory features in the placebo and homoeopathic groups are summarized in Table 1.

A variety of homoeopathic remedies was prescribed (Table 2). Both the remedies and the placebo were manufactured and supplied by A. Nelson & Co., London. The patients in both the placebo and homoeopathic groups were seen twice in the first month and monthly thereafter. The physicians changed the homoeopathic treatment if they felt that this was indicated, but no alteration was made in conventional therapy. The doctors of course did not know whether the patients were receiving active homoeopathy or placebo. They therefore did not know whether a failure of the patient to respond to their prescription was due to their inability to select the appropriate remedy or to the fact that the patient was on placebo.

All the patients were mobile and none had advanced or 'burnt out' rheumatoid arthritis. Apart from one patient who had received gold several years previously, none of them had received cortico-steroids, chrysotherapy, D-penicillamine or levamisole.

*Clinical and laboratory parameters*

The age and sex of the patients were recorded and the length of time for which the disease had been present. Their progress was assessed by means of the following tests: pain on a visual analogue scale (Huskisson, 1974; Scott & Huskisson, 1976), articular index of joint tenderness (Ritchie, Boyle, McInnes, Jasani, Dalakos, Grieveson & Buchanan, 1968), grip strength in each hand (Deodhar, Dick, Hodgkinson & Buchanan, 1973; Lee, Baxter, Dick & Webb, 1974), digital joint circumference (Webb, Downie, Dick & Lee, 1973), duration of morning stiffness (limbering up time) and functional index (Lee, Jasani, Dick & Buchanan, 1973).

These assessments were made by an independent assessor (MM) who routinely did the assessments of all patients at the Rheumatic Centre, and were made at the initial visit and thereafter at monthly intervals for the 3 months of the trial. In addition both the patient and the physician made their own assessments of whether improvement had taken place or not.

Laboratory tests included full blood counts, serum biochemistries and serology. These parameters were measured at the initial visit and at the end of the 3 month period.

The codes were broken at the end of 3 months. Before this was done each prescribing physician was asked to state whether he thought the patient had been on active remedy or placebo. This assessment was made after careful review of all the data on the patient's progress over the preceding three months and included the independent observer's data which was not available to the prescribing physicians until that time. The patients who had received placebo were then put on to active therapy and assessed over a further 3 month period. (The results of this part of the trial will be reported later.) It was not possible to conduct a complete double-blind crossover because homoeopathic remedies, once given, may continue to act in the body for several months. No clear-cut information could therefore be gained by putting the patients who had received active remedy first on to placebo for a further three month period.

*Statistics*

The results were analysed by the $\chi^2$ test, the Wilcoxon matched-pairs signed-ranks test (Wilcoxon, 1945), and the Mann-Whitney U-test (Mann & Whitney, 1947).

## Results

The two prescribing physicians were AM and RG. AM had 20 patients, 10 on active remedy and 10 on placebo, while RG had 26 patients, 13 on active remedy and 13 on placebo. The drop-out rate and the patients' own assessment of how they felt at the end of the three month period compared with how they felt at the start of it are summarised in Table 3. This table shows that there were two drop-outs from the placebo group and one from the active group. One of these patients had moved to another part of the country. The other two gave no reason. There was a significant improvement in those patients on active therapy over those on placebo ($P = 0.001$ on $\chi^2$ test).

AM made two errors in assessing his patients on active homoeopathy and two in assessing his placebo patients, while RG made one error in assessing his patients on active therapy and four in assessing his placebo patients. The patients on active therapy who were assessed wrongly by both physicians had not improved and had therefore been assessed as being on

**Table 3** Drop-out and improvement rates in patients on homoeopathy and placebo.

| *Patient's assessment* | *Homoeopathy* | *Placebo* |
|---|---|---|
| Drop-out | 1 | 2 |
| Worse | 1 | 3 |
| No change | 2 | 13 |
| Slightly better | 15 | 5 |
| Much better | 4 | 0 |
| Total | 23 | 23 |

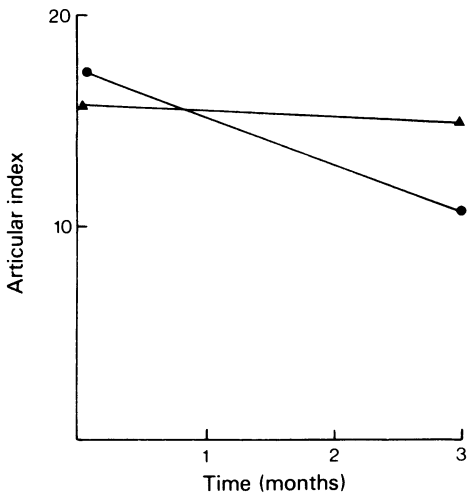


**Figure 1** Comparison of articular index before and after treatment in patients on first-line anti-inflammatory therapy plus homoeopathy (●), and in patients on first-line anti-inflammatory therapy plus placebo (▲).

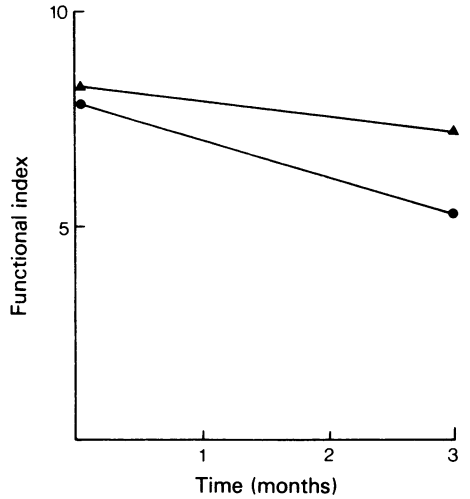


**Figure 2** Comparison of limbering up time before and after treatment in patients on first-line anti-inflammatory therapy plus homoeopathy (●), and in patients on first-line anti-inflammatory therapy plus placebo (▲).

placebo, while the placebo patients who were wrongly assessed had shown clinical improvement.

Table 4 summarises the data for articular index, limbering up time, grip strength in each hand, pain on the visual analogue scale and functional index for the patients on both active remedy and placebo, at the beginning of the trial and at the end of the three month period. All these measurements improved significantly in the active group but not in the placebo group. The most obvious changes were in the various assessments of pain and in the degree of stiffness. Grip strengths and functional index, although significantly altered, improved less. The results for these parameters for the active and placebo groups are presented diagrammatically in Figures 1, 2, 3, 4 and 5.

The results for the digital joint circumference have not been tabulated as these showed no changes in either group. No change was observed in this parameter in the previous trial (Gibson *et al.*, 1978) and this has also been the experience of other workers (Deodhar *et al.*, 1973).

Table 5 compares the data for articular index, limbering up time, grip strength in each hand and pain as assessed by the visual analogue scale for the R patients and the U patients. While it can be seen that the R patients improved more than the U patients, the differences between these groups are not statistically significant.

*Laboratory indices*

There were no obvious changes in haemoglobin, white cell count, ESR, serum biochemistry or serology over the 3 month period of the trial in either the patients on active homoeopathy or in the patients on placebo.

## Discussion

The results of this trial confirm the impression obtained from the preliminary study that homoeopathic treatment is effective in the control of

**Table 4** Mean indices before and after treatment

| | *Articular index* | | *Limbering up time (min)* | | *Grip strength (mmHg) Right* | | *Left* | | *Visual analogue scale* | | *Functional index* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Before* | *After* | *Before* | *After* | *Before* | *After* | *Before* | *After* | *Before* | *After* | *Before* | *After* |
| Homoeopathy | 17.3 | 10.9 ** | 114.6 | 73.8 ** | 104.3 | 121.2 * | 96.7 | 112.7 ** | 45.6 | 31.1 ** | 7.9 | 5.4 ** |
| Placebo | 15.7 | 15.2 | 80.2 | 72.3 | 147.4 | 152.1 | 140.5 | 151.4 | 42.3 | 41.9 | 8.4 | 7.3 |

** Difference significant $P < 0.005$.
* Difference significant $P < 0.01$.

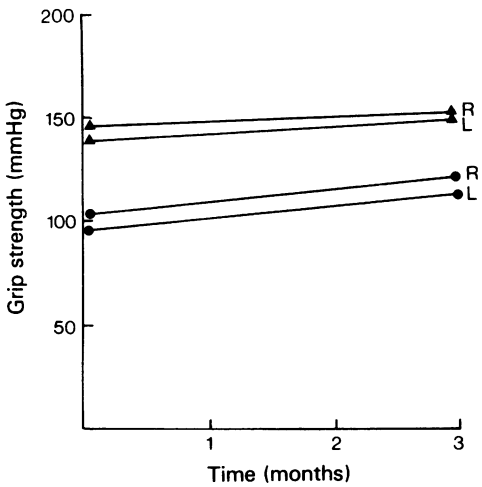


**Figure 3** Comparison of grip strength in both hands before and after treatment in patients on first-line anti-inflammatory therapy plus homoeopathy (●), and in patients on first-line anti-inflammatory therapy plus placebo (▲).

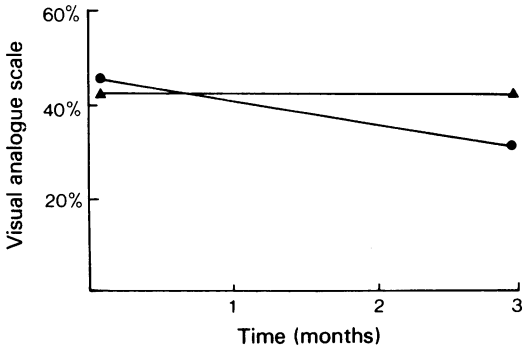


**Figure 4** Comparison of pain on the visual analogue scale before and after treatment in patients on orthodox first-line anti-inflammatory therapy plus homoeopathy (●), and in patients on first-line anti-inflammatory therapy plus placebo (▲).

patients with rheumatoid arthritis. The design of the trial was such that differences in orthodox anti-inflammatory therapy and in the doctor treating the patient were eliminated. Both AM and RG obtained significant improvements in pain scores, stiffness, grip strength and functional index in their patients on active homoeopathy whereas their patients on placebo did not vary significantly. There were no statistical differences in the results obtained by the two doctors. It would therefore seem that the differences observed were due to the remedies administered and not to any psychological inter-relationship between patient and physician or to placebo response to the homoeopathic substances. The fact that neither placebo group improved significantly is strong evidence that it is the drug and not the doctor which is effective.

It might be argued that the changes in the various parameters assessed, though statistically significant on rank testing, were small and of no clinical importance. However, similar changes in articular index and smaller changes in grip strength were obtained by Deodhar *et al.* (1973), when comparing the relative merits of four anti-inflammatory drugs.

The improvements obtained in the present trial were of a similar order of magnitude to those obtained in the pilot study (Gibson *et al.*, 1978). The

**Table 5** Mean indices for R and U groups before and after treatment

| | *Articular index* | *Limbering up time (min)* | *Grip strength (mm Hg)* | | *Pain on visual analogue scale* |
|---|---|---|---|---|---|
| | | | *Right* | *Left* | |
| R group before | 18.9 | 110.9 | 122.5 | 110.1 | 41.6 |
| after | 11.7 | 58.8 | 142.4 | 130.3 | 26.4 |
| difference | −7.2 | −52.1 | +19.9 | +20.2 | −15.2 |
| U group before | 16.2 | 118.5 | 86.2 | 82.4 | 47.5 |
| after | 9.9 | 88.9 | 102.2 | 95.3 | 34.9 |
| difference | −6.3 | −29.6 | +16.0 | +12.9 | −12.6 |
| Placebo group | | | | | |
| before | 15.7 | 80.2 | 147.4 | 140.5 | 42.3 |
| after | 15.2 | 72.3 | 152.1 | 151.4 | 41.9 |
| difference | −0.5 | −7.9 | +4.7 | +10.9 | −0.4 |

**Table 6.** Comparison of drop-out rates and toxic effects in patients on gold and levamisole (El Ghobarey *et al.*, 1978) and homoeopathy, salicylate and placebo (Gibson *et al.*, 1978)

| | *Levamisole* | *Gold* | *Homoeopathy* | *Salicylate* | *Placebo* |
|---|---|---|---|---|---|
| % Drop-out | 60% | 55% | 26% | 85% | 100% |
| % Side effects | 45% | 35% | 0% | 39% | 0% |

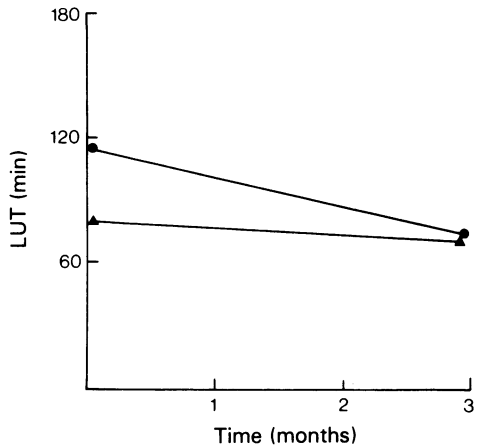


**Figure 5** Comparison of functional index before and after treatment in patients on orthodox first-line anti-inflammatory therapy plus homoeopathy (●), and in patients on orthodox first-line anti-inflammatory therapy plus placebo (▲).

pilot study, however, was conducted over a period of a year, and it was possible to discontinue all orthodox therapy in 42% of the patients. In the present trial patients were on homoeopathic treatment for 3 months only, and no attempt was made to reduce or discontinue orthodox therapy. All patients were actively encouraged to continue their orthodox drugs unchanged as any alterations might have made evaluation of the results misleading.

The enhanced response of those on conventional therapy plus homoeopathy over those on conventional therapy plus placebo is a measure of the value of this addition to therapy in the management of the patient with rheumatoid arthritis.

Since the selection of a homoeopathic remedy depends on the patient's symptoms and on his reaction to his environment as a whole, treatment should be more effective in patients with good prescribing symptoms than in those with poor prescribing symptoms. While the differences in the two groups are not statistically significant, Table 5 shows that the R patients did improve more than the U patients with respect to their pain indices, stiffness and grip strength. Both groups of patients on homoeopathic remedies improved and significant differences in degrees of improvement in a small number of patients (23) over a short period of time (3 months) are difficult to demonstrate. With a larger group of patients over a longer period of time, it is likely that the difference in response in the R and U groups would have become more obvious. The present results are encouraging in that they indicate that it may well be possible to predict which patients are most likely to respond to this form of therapy.

Another important point in the discussion of homoeopathic treatment is the lack of toxic effects observed. Out of 23 patients on active treatment, only one dropped out. The reason for this is not known. None of the other 22 patients reported any toxic side effects over the 3 month period. In the previous study, conducted over a year, no patient experienced toxic side effects. In the present trial improvements in pain scores, stiffness and grip strength produced with homoeopathy over 3 months compare favourably with those produced by gold and levamisole over 1 year (El-Ghobarey *et al.*, 1978).

It is noteworthy that more than one third of the patients dropped out from both the gold and the levamisole series because of toxic side effects while no toxic effects were reported with homoeopathy. A comparison of drop-out rates and toxic effects is presented in Table 6. From the data it therefore appears that homoeopathy is a safer and probably no less effective alternative to present-day second-line drugs. Since approximately half of all side effects reported annually are due to anti-rheumatic therapy (Girdwood, 1974), this in itself is a very important consideration.

It is not known at present how homoeopathic remedies work in the body. However the efficacy of his form of therapy in reducing pain may suggest that at least part of the effect might be endomorphin mediated, and further research to investigate this possibility would be of value. The response of patients given naloxone, to subsequent treatment with homoeopathy, might help to elucidate this point.

The possibility that the use of homoeopathy might become more widespread leads to the question of whether or not orthodox doctors would obtain such good results as their homoeopathically trained colleagues. To become an expert homoeopathic prescriber requires years of practice, and few conventional physicians are willing to undertake the additional training.

It therefore seems important to find some means of making homoeopathic knowledge more accessible to the medical profession, and work on this problem is currently in progress.

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