The place for non-pharmaceutical therapy in chronic rheumatoid arthritis: A critical study of homœopathy

ROBIN G. GIBSON, MRCP, FFHOM,
SHEILA L. M. GIBSON, MD, BSC, MFHOM,
ALISTAIR D. MACNEILL, MB, CHB, MFHOM and
W. WATSON BUCHANAN, MD, FRCP

Department of Clinical Pharmacognosy, The Glasgow Homœopathic Hospital, and
The Centre for Rheumatic Diseases, University Department of Medicine, Royal Infirmary, Glasgow, Scotland

SUMMARY

A two-part trial is reported in which patients with rheumatoid arthritis were treated with homœopathy. In the first part of the trial, 54 patients on homœopathy were compared with 41 patients on salicylate over the course of a year. 66 per cent. of the patients on homœopathy improved, as compared with 14.6 per cent. of the patients on salicylate.

In the second part of the trial, 46 patients took part in a double-blind study in which homœopathy was compared with placebo for a period of three months. The patients on homœopathy improved significantly while those on placebo did not.

It was also shown that it may well be possible to predict which patients are most likely to respond to homœopathic treatment.

No toxic effects were observed in any patient on homœopathy whereas 39 per cent. of the patients on salicylate experienced toxic effects.

Introduction

The homœopathic approach to medicine has been known for nearly 200 years and has been a part of the National Health Service since its inception in 1948. However, despite its long history, to our knowledge no properly controlled therapeutic trials have been carried out by other groups to evaluate its efficacy.

The field of rheumatology presents an interesting challenge to the homœopathic prescriber. Rheumatoid arthritis is a systemic disease affecting connective tissue throughout the body, and running a remittent but usually progressive course over many years. Many well-controlled therapeutic trials have been carried out on this problem and for this reason rheumatoid arthritis was chosen as an appropriate and challenging field in which to test the efficacy of this aspect of therapeutics.

The study was planned in two parts. Firstly a pilot trial was carried out comparing homœopathy with salicylate therapy and placebo.[1] As the results were encouraging, this was then followed by a more rigidly controlled double-blind trial in which homœopathy was compared with placebo.[2] The present paper compares these two parts of the study and reports the results of the cross-over extension of the double-blind trial.

Materials and methods

PILOT STUDY

Patients

Ninety-five patients took part in the trial. They were seen at the Centre for Rheumatic Diseases, and all satisfied the American Rheumatism Association diagnostic criteria for "definite" or "classical" rheumatoid arthritis.[3] All had previously been given various anti-inflammatory treatments, but the majority were not adequately controlled. None of the patients had previously had crysotherapy, corticosteroid, D-penicillamine, cyclophosphamide or levamisole. All had received salicylates in the past and none had shown intolerance.

The patients were seen in adjoining rooms in the same clinic. Those in the homœopathic group were treated by two physicians from the Glasgow Homœopathic Hospital and those in the salicylate group by a physician from the Centre for Rheumatic Diseases. After being seen by an independent consultant, they had been allocated to the homœopathic and salicylate groups by the clinic nursing staff. Due to the absence for three weeks of the physician in charge of the salicylate group, 54 patients were allocated to the homœopathic group and 41 to the salicylate group. The numbers were left as they were, as some form of selection might well have ensued in discarding patients to equalize the groups.

The two treated groups were compared with a group of 100 similarly affected patients, who were seen by other physicians at the Centre for Rheumatic Diseases over the same period of time, and who were given placebo only.

All patients freely accepted participation in the study. They were told that should they have side effects, or should they deteriorate, they would be free to withdraw from the study. Since the homœopathic remedies were administered as powders, the patients on salicylate were given inert powders. The patients on salicylate therapy had to discontinue all previous anti-inflammatory drugs whereas the patients on homœopathy were allowed to continue their previous anti-inflammatory therapy unchanged. The patients were seen fortnightly for the first month and monthly thereafter. The trial was continued for a year.

Drug treatment

The salicylate preparation was enteric-coated aspirin (Nu-seals, Lilly, 325 mg tablets). This preparation was used because it had been found in previous trials to be more satisfactory in terms of patient acceptability than soluble aspirin[4] and because it was not immediately recognizable as aspirin. The dose was tailored to the patient's individual needs and ranged from 1.95 to 5.85 g/day (6–18 tablets/day) with a mode of 3.9 g/day (12 tablets).

The homœopathic remedies were selected for each patient on the basis of his symptomatology, according to homœopathic principles.[5,6] They were supplied by A. Nelson & Co., London. The remedies which were most commonly used are shown in Table 1. The inert powders were sucrose.

Table 1. The homœopathic 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*

DOUBLE-BLIND STUDY

Patients

Forty-six patients took part in the double-blind trial. They were seen at the same clinic by the two physicians from the Glasgow Homœopathic Hospital. All satisfied the same criteria for "definite" rheumatoid arthritis. They were assigned to the active and placebo groups by a third physician who otherwise took no part in the management of the patients.

Since the selection of the appropriate homœopathic remedy depends on the patient's symptoms and signs, and his total reaction to his environment,[5,6] the patients were divided into two groups, those with good prescribing symptoms, Group R, and those with poor prescribing symptoms, Group U.* This assessment was made by the prescribing physicians.

The patients were then assigned to the active and placebo groups so that as far as possible each group contained equal numbers of R and U patients. No change was made in the patients' previous orthodox anti-inflammatory therapy. An attempt was made to match patients for drug therapy so that as far as possible each group contained equal proportions of patients receiving the different non-steroidal anti-inflammatory drugs. These were dextropropoxyphene hydrochloride, naproxen, indomethacin, ketoprofen, ibuprofen, fenoprofen, flurbiprofen, benorylate and sulindac. No patient was on more than one of these anti-inflammatory agents.

The patients were told that they would be taking part in a double-blind trial with a safe addition to therapy and all were willing to participate. They were seen fortnightly for the first month, and monthly thereafter. The closed part of the trial was conducted for three months.

At the end of three months, the code was broken and the patients who had been on placebo were changed to active homœopathic therapy for a further three-month period. It was not possible to conduct a complete cross-over trial since

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

homœopathic remedies may work for several months after being administered. No clear-cut information could therefore be obtained by putting the patients who had been given homœopathy first, onto placebo for a further three months.

CLINICAL AND LABORATORY PARAMETERS

Progress in both trials was assessed by means of the articular index of joint tenderness,[7] duration of morning stiffness (limbering-up time), grip strength in each hand,[8] digital joint circumference,[9] pain on a visual analogue scale[10,11] and, in the double-blind trial only, functional index.[12] These parameters were assessed by an independent assessor who routinely did the assessments on all the patients coming to the clinic, and were carried out monthly.

An assessment was also made of the patient's overall well-being and of any toxic effects. These latter were assessed by asking the patients if they had experienced any unpleasant symptoms which they had not had previously. Improvement was considered to have occurred when both the patient's and the physician's opinion agreed, and there was objective supporting evidence.

Laboratory tests included full blood counts, serum biochemistry, serology and salicylate levels.[13] The tests were carried out at the initial visit and at three-monthly intervals thereafter.

STATISTICS

The results were analysed by the χ^2 test, the Wilcoxon matched-pairs signed-ranks test[14] and the Mann-Whitney U-test.[15]

Results

Pilot Study

The mean age, duration of disease, articular index, limbering-up time, grip strength in each hand and digital joint circumference in each hand for the 41 patients in the salicylate group and the 54 patients in the homœopathic group are shown in Table 2. It can be seen that apart from the duration of disease which was greater in the homœopathic group, the two groups did not differ significantly.

Thirty-five of the 41 patients in the salicylate group (85.4 per cent.) dropped out of the trial before the end of the year, the majority doing so in the first four

Table 2. Mean data of 95 patients with rheumatoid arthritis treated with salicylate and homœopathy at start of pilot trial

		SALICYLATE	HOMŒOPATHY
Number		41	54
Age (years)		47.0	49.7
Duration of disease (years)		5.0	8.6
Articular index		15.3	15.1
Limbering-up time (minutes)		81.3	76.7
Grip strength (mmHg)	Right	137.2	133.1
	Left	133.5	133.6
Digital joint circumference (mm)	Right	296.4	287.9
	Left	287.7	283.6
Male:female ratio		1:2.4	1:2.4

months, while 14 of the 54 patients in the homœopathic group (26 per cent.) dropped out, again in most cases by the first four months. Of the 100 patients on placebo, 60 had dropped out after three weeks and all had discontinued placebo by six weeks (Figure 1).

Six of the 41 patients in the salicylate group (14.6 per cent.) were still on this therapy after one year and clinically felt no worse than they had done at the commencement of the trial, although in fact the group as a whole had deteriorated according to the assessments of articular index, limbering-up time and grip strength (Table 3). Of the 40 patients in the homœopathic group who remained in the trial for one year, 23 (42.6 per cent. of the whole group) were clinically better and were maintained on homœopathic therapy alone, having discontinued their previous non-steroidal anti-inflammatory drugs (Group I). A further 13 (24 per cent. of the whole group, Group II), were clinically better but still had to take some orthodox therapy as well as their homœopathic treatment. Four (7.4 per

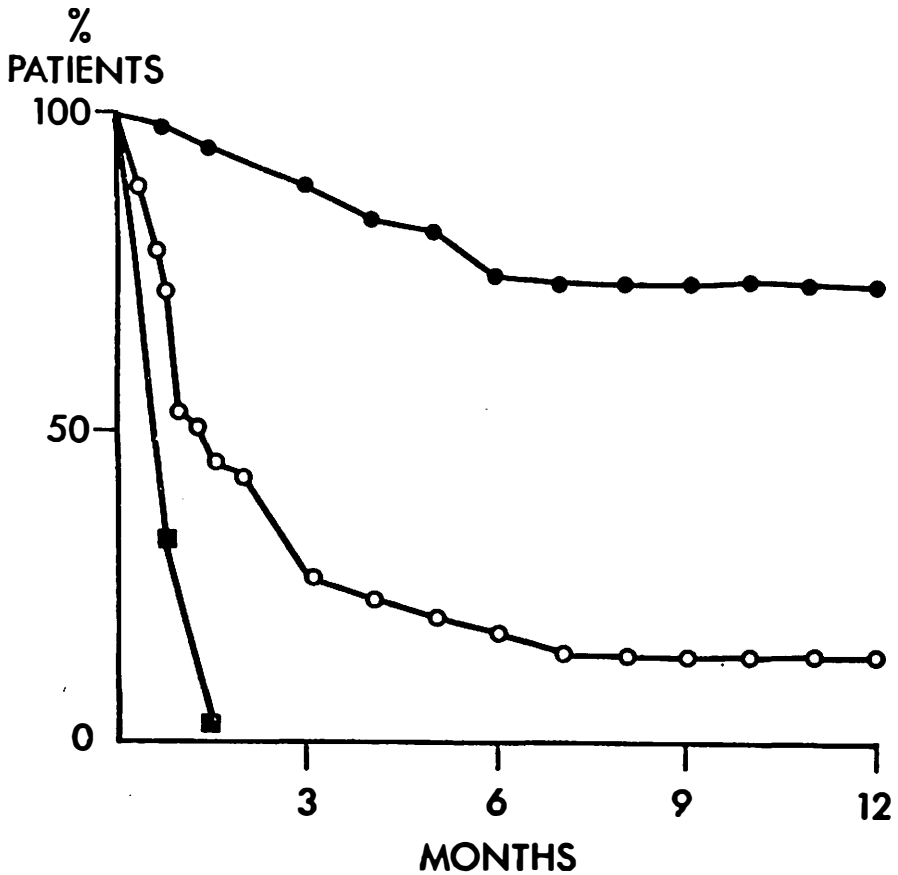

Figure 1. Comparison of drop-out rates of patients on homœopathy ●, salicylate ○, and placebo ■.

Table 3. Mean data for the three groups of patients on homœopathy and the group on salicylate who continued treatment for a year, before treatment and at the end of the year.

		ARTICULAR INDEX	LIMBERING-UP TIME (min)	GRIP STRENGTH (mmHg) Right hand	Left hand
Group I	before	12.1	67.0	140.0	143.0
(23 patients)	after	7.8	24.0	162.0	156.0
	difference	−4.3*	−43.0*	+22.0	+13.0
Group II	before	17.8	89.5	145.0	136.0
(13 patients)	after	11.2	51.6	128.0	124.0
	difference	−6.6*	−37.9*	−13.0	−12.0
Group III	before	17.0	55.0	174.5	166.8
(4 patients)	after	15.3	82.5	143.0	114.3
	difference	−1.7	+27.5	−31.5	−52.5
Salicylate	before	8.7	34.2	179.8	171.8
(6 patients)	after	9.7	76.7	137.2	148.5
	difference	+1.0	+42.5	−42.6	−23.3

*Difference significant $p<0.05$

cent.) had experienced no benefit (Group III). The mean values for articular index, limbering-up time and grip strength in each hand are tabulated in Table 3 for the three homœopathic groups and the six patients on salicylate who did not drop out of the trial, at the beginning of the trial and at the end of the year. Obviously after-treatment data are not available for the patients who dropped out. The table shows that while homœopathic Groups I and II improved with regard to pain, stiffness and grip strength, Group III and the salicylate group showed no overall improvement. It was found that the digital joint circumference did not change significantly in any group.

Toxic effects

Of the 35 patients who dropped out of the salicylate group, 16 (39 per cent. of the whole group) did so because of unacceptable side effects. These included tinnitus, dizziness, nausea, vomiting and in one case haematemesis. The other 19 dropped out because they were experiencing no benefit.

Of the 14 patients who dropped out of the homœopathic group, all did so because they were experiencing no benefit. None reported toxic effects.

Double-blind study

The mean indices for the homœopathic and placebo groups at the start of the trial are shown in Table 4. There were no significant differences between the two groups.

Mean values for articular index, limbering-up time, grip strength in each hand, pain by the visual analogue method and functional index, before and after treatment, for the homœopathic and placebo groups, are shown in Table 5. Significant improvements were obtained in all parameters in the active group while there were no significant changes in the placebo group (Figure 2).

Table 4. Mean data of 46 patients with rheumatoid arthritis at start of double-blind trial

	HOMŒOPATHY	PLACEBO
Number	23	23
Age (years)	54.0	52.1
Duration of disease (years)	7.2	8.8
Articular index	16.6	16.1
Limbering-up time (minutes)	112.2	84.7
Grip strength (mmHg) Right	118.0	140.9
Left	110.8	134.4
Pain on visual analogue scale	44.1	43.2
Functional index	7.6	8.3
Hæmoglobin (g/dl)	12.5	12.9
Antinuclear factor (reciprocal of titre)	64	64
Rheumatoid factor (reciprocal of titre)	128	256
Male:female ratio	1:2.3	1:1.9

Table 5. Mean values for the homœopathic and placebo groups before and after treatment

		ARTICULAR INDEX	LIMBERING-UP TIME (min)	GRIP STRENGTH (mmHg) Right	Left	PAIN ON VISUAL ANALOGUE	FUNCTIONAL INDEX
Homœo-	before	17.3	114.6	104.3	96.7	45.6	7.9
pathic	after	10.9	73.8	121.2	112.7	31.1	5.4
group	difference	−6.4**	−40.8**	+16.9*	+16.0*	−14.5**	−2.5**
Placebo	before	15.7	80.2	147.4	140.5	42.3	8.4
group	after	15.2	72.3	152.1	151.4	41.9	7.3
	difference	−0.5	−7.9	+4.7	+10.9	−0.4	−1.1

** Difference significant $p<0.005$
* Difference significant $p<0.01$

Table 6. Mean values before and after treatment for 19 patients firstly on placebo and then on homœopathy

		ARTICULAR INDEX	LIMBERING-UP TIME (min)	GRIP STRENGTH (mmHg) Right	Left	PAIN ON VISUAL ANALOGUE SCALE	FUNCTIONAL INDEX
Placebo	before	15.8	74.9	153.5	146.3	43.7	8.2
(first 3	after	14.9	68.9	159.4	158.8	41.1	7.6
months)	difference	−0.9	−6.0	+5.9	+12.5	−2.6	−0.6
Homœo-	before	14.9	68.9	159.4	158.8	41.1	7.6
pathy	after	9.4	37.9	177.3	166.7	25.3	5.4
(second 3	difference	−5.5*	−31.0*	+17.9	+7.9	−15.8*	−2.2*
months)							

* Difference significant $p<0.005$

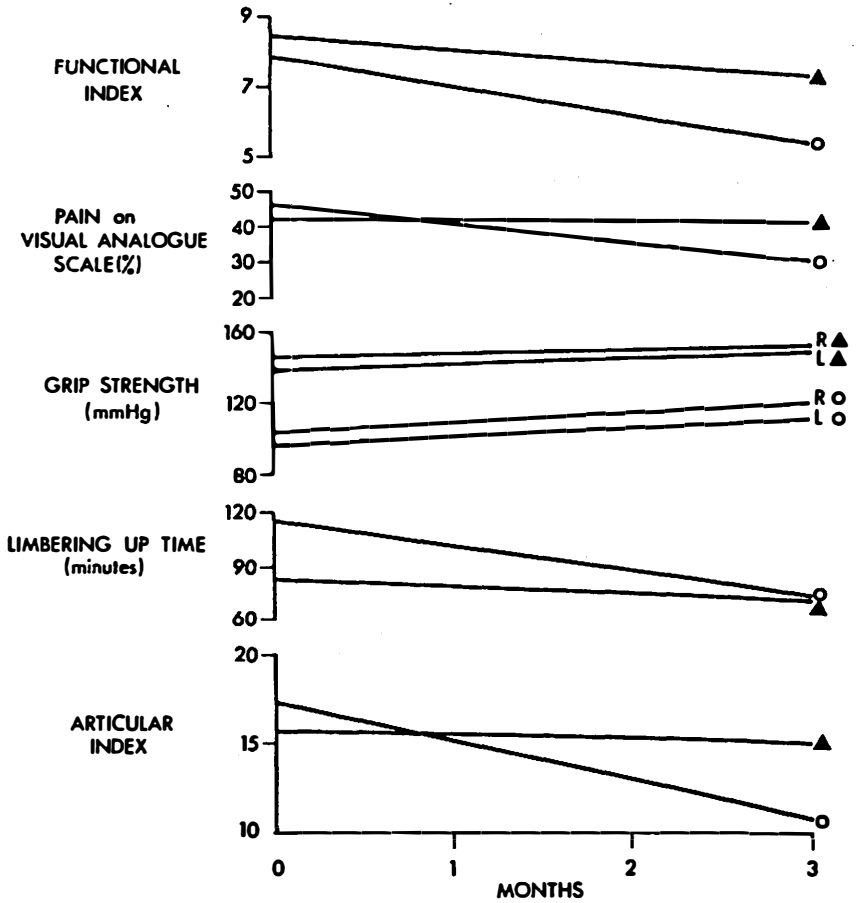

Figure 2. Mean values for parameters at the beginning and end of three months in patients on homœopathy O, and placebo ▲.

There was one drop-out from the active group and two from the placebo group. Of these, one had moved from Glasgow. The others gave no reason.

Two of the patients in the placebo group who completed the three months of the double-blind part of the trial had deteriorated considerably, although they had not changed their orthodox anti-inflammatory treatment in any way. They required hospitalization and were unable to continue in the trial. The remaining 19 patients in the placebo group were given active homœopathic treatment for a further three-month period. The mean values for their pain, stiffness, grip strength and functional index parameters before and after three months on placebo and three months on homœopathy are summarized in Table 6 and Figure 3. With the exception of grip strength, the improvement in parameters was of a similar order to that obtained with the first group of patients in the first three months of the study (Table 5).

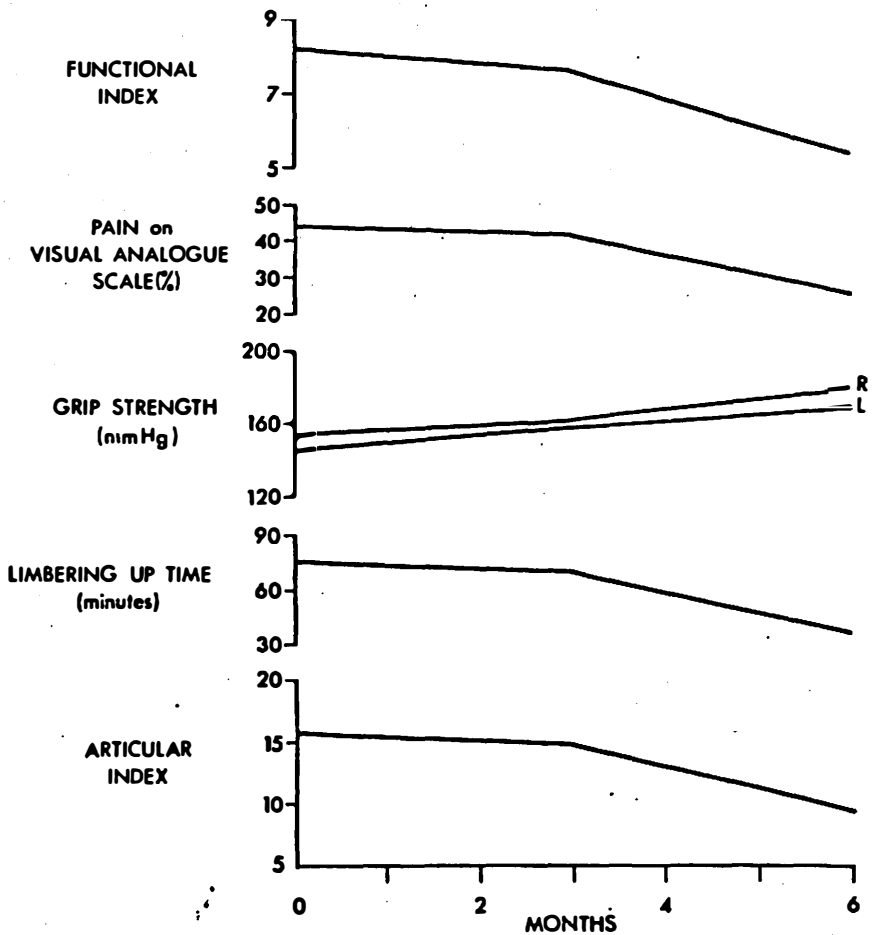

Figure 3. Mean values for parameters in patients firstly on placebo for three months and then on homœopathy for three months.

Table 7. Mean values for R and U patients before and after treatment

		ARTICULAR INDEX	LIMBERING-UP TIME (min)	GRIP STRENGTH (mmHg)		PAIN ON VISUAL ANALOGUE SCALE
				Right	Left	
R patients	before	17.3	97.7	150.1	142.0	40.5
	after	9.9	45.6	180.7	158.8	22.0
	difference	−7.4	−52.1	+29.8	+16.8	−18.5
U patients	before	15.2	86.4	110.6	109.8	45.0
	after	10.4	68.2	122.9	117.8	33.1
	difference	−4.8	−18.2	+12.3	+8.0	−11.9

A comparison of the relative improvements of the R and U patients is shown in Table 7. While it can be seen that all parameters improved to a greater extent in the R patients than in the U patients, the differences between the two groups are not statistically significant.

On reviewing the data at the end of the trial, it was noted that two weeks after the start of the trial, four of the 23 patients in the placebo group had experienced a slight improvement, whereas 12 of the 23 patients on active therapy had improved. At the end of the three-month period five of the patients on placebo had improved, compared with 19 of the patients on the active remedy. These differences were significant on χ^2 testing.

No toxic effects were reported by any patients in either part of the double-blind study.

Discussion

The results of the pilot trial were encouraging in that they showed that homœopathy appeared to be more effective than salicylate in the control of rheumatoid arthritis. Fewer patients dropped out of the homœopathic group (26 per cent.) than the salicylate group (85.4 per cent.). Of the patients on homœopathy, 42.6 per cent. were able to discontinue all other therapy over the course of the year and were both subjectively and objectively improved, while a further 24 per cent., while not able to discontinue all other orthodox therapy, felt better and showed objective improvement. Although 14.6 per cent. of the patients on salicylate continued this therapy for a year, pain, stiffness and grip strength parameters were actually worse in most cases than at the start of the trial. It is interesting that the patients who stayed on salicylate were the least severely affected of the group. Those who responded best to homœopathy were on the whole less severely affected than the rest of the homœopathic group, while those who did not respond were the most severely affected.

No side effects were reported by any of the patients on homœopathy, whereas 39 per cent. of the patients on salicylate dropped out of the trial because of unacceptable side effects. The conclusion reached from this trial was therefore that homœopathy may prove to be a safe and effective alternative to salicylate in the management of rheumatoid arthritis.

There were however two main criticisms of the trial. In the first place the patients on salicylate had to discontinue all previous anti-inflammatory therapy whereas the patients on homœopathy were not required to do this. This was necessary because homœopathic remedies tend not to act immediately in chronic progressive conditions. The patients were therefore allowed to continue their previous therapy and only reduced this if they felt that it was possible to do so. However it could be argued that the patients in the homœopathic group had an unfair advantage over those in the salicylate group.

The second major criticism was that different doctors treated the groups on homœopathy and salicylate, and it might have been the doctors and not the drugs that were operative. The double-blind study was therefore designed to eliminate both these possibilities, the same doctor managing patients on both active remedy and placebo, and both groups being matched with respect to first-line anti-

inflammatory therapy. Since this trial was of short duration, three months, no attempt was made to discontinue the previous anti-inflammatory regime.

The results of the trial clearly show that homœopathy added to first-line anti-inflammatory therapy was superior to placebo added to similar therapy, in the management of rheumatoid arthritis. There was a significant improvement in pain, stiffness, grip strength and functional index in the group given homœopathic treatment, whereas there was no significant change in the placebo group. Similar results were obtained in the second part of the trial when the patients who had been given placebo in the first three months were used as their own controls. Their improvement in pain, stiffness and function was of a similar order to the improvement experienced by the first group. Interestingly, however, grip strengths did not improve significantly. There had been some improvement, though not significant, in this parameter during the three months on placebo, and this increase in grip strength was maintained though not accelerated, on the active treatment. It is felt that an increase in grip strength may be in part a learning phenomenon as the patient becomes more familiar with the grip-strength apparatus. If this is so, it might explain the anomalous grip strength results obtained in the second three months of the trial.

The improvements obtained with homœopathic treatment were of a similar order to those obtained in previous trials using various first-line non-steroidal anti-inflammatory treatments[16] and gold and levamisole,[17] although in the latter instance the patients were more severely affected. Significantly no toxic effects were observed with homœopathy, whereas toxic effects were reported by more than one third of the patients in the gold and levamisole series. This fact emphasizes the safety as well as the efficacy of this form of treatment as compared with other anti-inflammatory therapies.

Only two thirds of the patients in the pilot study responded to homœopathic treatment. This observation raised the question of whether or not it might be possible to predict which patients are most likely to benefit from this form of therapy. The patients in the double-blind trial were therefore classed as either R (good prescribing symptoms) or U (poor prescribing symptoms) at the beginning of the study. On these considerations one would expect greater success in treating the R patients than the U patients.

The R patients as a whole did improve more than the U patients (Table 7) in all the parameters tested, although the differences are not significant statistically. The group of patients was small, however, and they were assessed over a relatively short period of time. Had they been followed up for a year, as was the case with the pilot study, the differences between the R and the U patients might well have reached significant levels. Six out of a total of 41 patients treated with homœopathy (14.6 per cent.) experienced no improvement, three in the double-blind part of the trial, and three in the cross-over section. These had all been classed as U. These results therefore suggest that it may be possible to predict, at least to some extent, which patients are likely to do well and which may not. Obviously the better the remedy matches the patient, the greater the likelihood of treating that patient successfully.

The suggestion has been made that homœopathy merely acts by producing a

placebo effect, or that it may reduce pain through a mechanism similar to the endorphin pathway. The results of the double-blind section of the study, however, suggest that this is not the case. When the patients were seen at the first return visit, two weeks after the start of the trial, four of the patients who were receiving placebo felt some improvement, compared with 12 of the patients receiving homœopathy. At the end of three months five of the patients on placebo were improved, compared with 19 on homœopathy. If homœopathy were merely exerting a placebo effect one would expect equal numbers of patients to improve in both the active and placebo groups. Even in the early part of the trial, when placebo is known to produce at least a 30 per cent effect,[18] the improvements in the placebo group did not match those in the active group, so that a mechanism other than placebo effect must be postulated.

The mechanism of action of homœopathic remedies may well be much more complex than would be suggested by a single final common pathway. It could even be that the different homœopathic remedies each work at different points in intermediary metabolism. The patient's symptomatology is thought to occur as a result of an imbalance or block in one or other of the numerous enzyme systems, causing disharmony in the internal environment through build-up of some intermediary metabolites. Since it is likely that all of the elements occur in some quantity, however small, in the body, and since many metabolic processes and intermediary substances are widespread in the vegetable and animal kingdoms as well as occurring in man, it could be that the appropriate homœopathic remedy is related to the metabolic defect in question. By preparing the remedy according to the Hahnemannian principles of dilution and succussion, it may be enabled to become the key to unlock that particular metabolic block. Studies on dielectric strength,[19] NMR patterns[20] and viscosity[21] suggest that during the succussion process, long chain water polymers are built up which may be analagous to the formation of antibody in response to antigen. The effect of the remedy on the metabolic block or defect may therefore be analogous to a lock and key, or antigen-antibody type reaction. Much work, however, remains to be done on the elucidation of this aspect of homœopathic therapy.

In this study homœopathic therapy was used to treat patients with chronic rheumatoid arthritis. It is however, not limited in its scope to this condition, but can be applied equally successfully to other clinical problems. Further study and evaluation of this system of therapeutics would therefore be of value.

ACKNOWLEDGEMENT

The authors wish to thank Mrs Marion MacLeod for help with the patients' assessments.

REFERENCES

1 Gibson RG, Gibson SLM, MacNeill AD, Gray GH, Dick WC, Buchanan WW. Salicylates and homœopathy in rheumatoid arthritis: preliminary observations. *Br J Clin Pharmacol* 1978; 6: 319–95.
2 Gibson RG, Gibson SLM, MacNeill AD, Buchanan WW. Homœopathic therapy in rheumatoid arthritis: evaluation by double-blind clinical therapeutic trial. *Br J Clin Pharmacol* 1980; 9: 453-9.
3 Ropes MW, Bennett GA, Cobb S, Jacox R, Jessar RA. 1958 Revision of diagnostic criteria for rheumatoid arthritis. *Bull Rheum Dis* 1959; 9: 175.
4 Lee P, Anderson JA, Miller J, Webb J, Buchanan WW. Evaluation of analgesic action and efficacy of anti-rheumatic drugs. Study of 10 drugs in 684 patients with rheumatoid arthritis. *J Rheum* 1976; 3: 283–94.
5 Dhawale ML. *Principles and practice of Homœopathy*. Bombay: Karnatak Publishing House, 1967.
6 Mitchell GR. *Homœopathy*. London: WH Allen, 1975.
7 Ritchie DM, Boyle JA, McInnes JM *et al.* Clinical studies with an articular index for assessment of joint tenderness in patients with rheumatoid arthritis. *Quart J Med NS* 1968; 37: 393–406.
8 Lee P, Baxter A, Dick WC, Webb J. An assessment of grip strength measurements in rheumatoid arthritis. *Scand J Rheum* 1974; 3: 17–23.
9 Webb J, Downie WW, Dick WC, Lee P. Evaluation of digital joint circumference measurements in rheumatoid arthritis. *Scand J Rheum* 1973; 2: 127–31.
10 Huskisson EC. Measurement of pain. *Lancet* 1974; II: 1127–31.
11 Scott PJ, Huskisson EC. Graphic representation of pain. *Pain* 1976; 2: 127–31.
12 Lee P, Jasani MK, Dick, WC, Buchanan WW. Evaluation of a functional index in rheumatoid arthritis. *Scand J Rheum* 1973; 2: 71–7.
13 Trinder P. Rapid determination of salicylate in biological fluids. *Biochem J* 1954; 57: 301–9.
14 Wilcoxon F. Individual comparisons by ranking methods. *Biometrics Bull* 1945; 1: 80–3.
15 Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. *Ann Math Statist* 1947; 18: 52–4.
16 Deodhar SD, Dick WC, Hodgkinson R, Buchanan WW. Measurement of clinical response to anti-inflammatory drug therapy in rheumatoid arthritis. *Quart J Med NS* 1973; 42: 387–401.
17 El-Ghobarey A, Mavrikakis ME, MacLeod M *et al.* Clinical and laboratory studies of levamisole in patients with rheumatoid arthritis. *Quart J Med NS* 1978; 47: 385–400.
18 Rooney PJ, Capel HA, Paterson S, Buchanan WW, Dick WC. Continued use of non-steroidal anti-inflammatory drugs: an index of clinical efficacy. *Brit J Clin Pharmacol* 1978; 5: 453–5.
19 Brucato A, Stephenson J. Dielectric strength testing of homœopathic dilutions of $HgCl_2$. *J Am Inst Hom* 1966; 59: 281–6.
20 Smith RB, Boericke GW. Modern instrumentation for the evaluation of homœopathic drug structure. *J Am Inst Hom* 1966; 59: 263–80.
21 Barnard GP. Microdose paradox: a new concept. *J Am Inst Hom* 1965; 58: 205–12.