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SALICYLATES AND HOMOEOPATHY IN RHEUMATOID ARTHRITIS: PRELIMINARY OBSERVATIONS

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1 This paper reports the results of a pilot study in which 41 patients with rheumatoid arthritis were treated with high doses of salicylate, 3.9 g per day, and the results compared with a further 54 similar patients treated with homoeopathy. Both groups were compared with 100 patients who received placebo.

2 The patients who received homoeopathy did better than those who received salicylate. The design of the trial was such, however, that it was not possible to distinguish between the effects due to the physicians and the effects due to the drugs and a further trial is planned to elucidate this point.

3 Patients on homoeopathic treatment did not experience toxic effects.

Introduction

Homoeopathy has been practised under the National Health Service since 1948. However, to our knowledge, no properly controlled study on the efficacy of this method of treatment in rheumatoid arthritis has been published.

Rheumatoid arthritis is a constitutional disease in which there are inflammatory changes throughout the connective tissues of the body. It is usually a long-standing, progressive disorder, often running a remittent course, and patients, once on therapy, are likely to remain on treatment for many years. A number of drugs have been tried with varying degrees of success, but the first line treatment of this disease is still salicylate.

It was felt that it would be of interest to compare the relative values of homoeopathy and salicylate in rheumatoid arthritis and this paper describes the results of the preliminary study.

Methods

Subjects

Ninety-five patients with rheumatoid arthritis took part in the study. All satisfied the American Rheumatism Association diagnostic criteria for 'definite' or 'classical' rheumatoid arthritis (Ropes, Bennett, Cobb, Jacox & Jessar, 1959) and all were either seropositive or had X-ray evidence of rheumatoid arthritis. All the patients had been attending the Centre for Rheumatic Diseases for periods extending from 4 months to 10 years. All had previously had varying anti-inflammatory treatments but the majority had not been adequately controlled by any of their previous therapies. It was, therefore, felt that enteric coated aspirin in a high dose which was tailored to suit the patient's needs was a justifiable form of therapy. Enteric coated aspirin was used since this preparation was not immediately recognisable as aspirin by the patients, and because it had been used in previous clinical trials (Lee, Baxter, Dick & Webb, 1976) and had been found to be more satisfactory than soluble aspirin. Patients who had previously had corticosteroid, gold, D-penicillamine, azathioprine, cyclophosphamide or levamisole were excluded from the trial. All the patients had received salicylates in the past and had shown no intolerance.

The patients were allocated alternately to the two treatment groups, salicylate and homoeopathy, by the clinic nursing staff, after having first been seen by a consultant. There were 41 patients in the aspirin group and 54 in the group receiving homoeopathy. The inequality in numbers arose inadvertently when the physician in charge of the aspirin group was absent for 3 weeks, and all new patients seen over this period of time were allocated to the homoeopathic group rather than having to be brought back later. Since some form of selection may well have ensued in discarding patients at a later date, it was decided to leave the numbers as they were. A further 100 consecutive seropositive rheumatoid patients, attending the same clinic for the first time over the same period, but seen on a different day of the week by an orthodox physician, were given an inert preparation only. Their allocation differed from the two treatment groups in that the first 100 consecutive new rheumatoid patients to attend on that day of the week were placed in the placebo group and there was no alternative allocation.

None of these patients had received, or was receiving, corticosteroid therapy, gold, D-penicillamine, azathioprine, cyclophosphamide or levamisole.

All the patients were seen in the same clinic, the physicians in charge of the two treated groups being in adjoining rooms. The patients in the homoeopathic group were treated by two physicians from the Glasgow Homoeopathic Hospital, both of whom had had many years of experience in this field of medicine. The patients in the salicylate group, and the placebo group, were treated by two physicians at the Centre for Rheumatic Diseases. The patients were told that they would be treated by different drug preparations and that their progress would be assessed regularly. They were not, however, told that they would be treated by homoeopathy since it was felt that they may have been favourably, or unfavourably biased towards this method of treatment. They were seen every 2 weeks for the first 2-3 visits, and thereafter at monthly intervals.

Because the homoeopathic remedies were administered as powders, the patients on salicylate were also given inert powders. All patients were told that, should they have side effects, or should their arthritis deteriorate, they would be free to withdraw from the study. All the patients freely accepted participation in the study and it was planned that they be kept on their respective therapies for 1 year.

The patients receiving homoeopathy were allowed to continue their previous orthodox therapy for as long as they felt it necessary. All those who discontinued their orthodox therapy had done so by the time they had been in the trial for 4 months. The patients on salicylate on the other hand, had to discontinue all previous orthodox therapy.

The aspirin preparation used was Nu-seals (Lilly) 325 mg tablets. The mean daily dose was 3.67 g. The range was 1.95 g - 5.85 g (6-18 tablets) mode 3.9 g (12 tablets) and s.d. 1.01 g.

The homoeopathic remedies were manufactured and supplied by A. Nelson & Co., London. Approximately 200 different remedies were used over the period of the trial. The appropriate remedy was selected for each patient on the basis of the patient's symptomatology, according to homoeopathic principles (Dhawale, 1967; Mitchell, 1975) and there were no differences in the prescribing methods of the two homoeopathic physicians. The same patient might receive different remedies at different times. Six of the most commonly used remedies were bryonia, calcarea carbonica, lycopodium, natrum muriaticum, pulsatilla and rhus toxicodendron. The inert powders used were sucrose.

Clinical and laboratory indices

The age and sex of the patients were recorded and the length of time for which the disease had been present. A clinical assessment of the degrees of pain, stiffness and swelling of joints was made by the following methods: 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 (Lee *et al.*, 1974), digital joint circumferences (Webb, Downie, Dick & Lee, 1973) and the duration of morning stiffness (limbering up time). These parameters were assessed both by the physicians seeing the patients and by an independent assessor who routinely assessed all patients coming to the clinic and, who, consequently, did not know which physician was in charge of which patient or what therapy had been given.

Improvement was considered to have occurred when both the patient's and the physician's opinion agreed and there was objective evidence supporting this. This definition is clearly arbitrary.

An assessment was also made of the overall well-being of the patient and of any toxic effects. These latter were assessed by asking the patients if they had experienced any unpleasant symptoms which they had not previously experienced.

Laboratory tests included: full blood counts, serum biochemistries, serology and salicylate levels (Trinder, 1954). The clinical and biochemical parameters were reassessed three-monthly.

Statistical methods

The data were analyzed by means of the Mann-Whitney U test (Mann & Whitney, 1947).

Results

There were 41 patients in the salicylate group and 54 in the group receiving homoeopathy.

The average duration of the disease prior to the trial was 5 years in the salicylate group and 8.8 years in the homoeopathic group ($P < 0.05$). Sex distribution and mean ages, articular indices, limbering up times (L.U.T.), grip strengths and digital joint circumferences did not differ significantly between the two groups (Table 1).

Drop-out rate (Figure 1 and Table 2)

Before the end of the year, 35 of the 41 patients in the salicylate group (85.4%) had dropped out of the trial (Subgroup B, Table 2). Of these 35, 16 (39% of the patients in the total group) discontinued therapy because of unacceptable toxic effects and 19 (46.4%) because they were experiencing no relief of symptoms. Toxic effects included tinnitus, dizziness, deafness, nausea, vomiting and in one patient, haematemesis. Most of those who dropped out did so in the first 4 months of the trial.

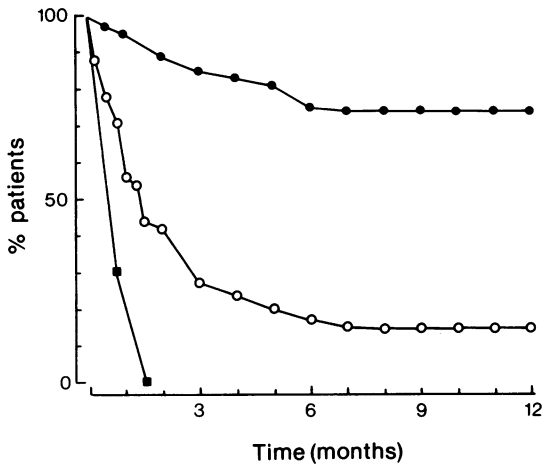

Figure 1 Comparison of the drop-out rate of patients. ● homoeopathy; ○ salicylate; ■ placebo

Fourteen of the 54 patients in the homoeopathic groups had dropped out of the trial before the end of the year, in most instances again by the first 4 months. None of these patients defaulted because of toxic effects.

It can be seen from Figure 1 that although approximately 30% of patients who were given placebo were still on this therapy at 3 weeks, all had discontinued by 6 weeks.

At the end of 1 year, 6 of the 41 patients in the salicylate group (14.6%) were still on their therapy and were doing well (Subgroup A). Clinically they were better than they had been at the commencement of the trial.

Of the 54 patients in the homoeopathic group, 23 (42.6%) were being maintained solely on homoeopathic treatment at the end of 1 year and were clinically better than they had been one year earlier (Subgroup C). A further 13 (24%, Subgroup D) were still on homoeopathy and doing well at the end of the year but had found that to maintain clinical well-being the homoeopathic treatment had to be supplemented with some orthodox therapy, in most cases either aspirin or indomethacin, but at dose levels significantly lower than they had been taking when entering the trial. A further 4 patients completed the year but were not helped clinically. These with the 14 patients who dropped out of the trial constitute Subgroup E.

Table 1 shows that although the salicylate and homoeopathic groups as a whole were fairly equally matched with respect to the mean severity of the disease, those patients who responded to salicylate had a milder degree of the disease than those who did not respond (Table 2). They had lower articular indices of joint tenderness and limbering up time, and greater grip strength, although because of the large standard deviations the means do not actually differ significantly.

Patients who reponded to homoeopathy (Subgroup C) were almost as severely affected as those who did not respond to salicylate (Subgroup B). The patients who did not respond to homoeopathy had on average been affected for twice as long as those who did respond ($P < 0.05$) and had weaker grip strength. This latter difference, however, was not significant.

Table 3 summarizes the data for articular index of joint tenderness, limbering up time, grip strength and digital joint circumference in the two homoeopathic subgroups who responded to treatment, before treatment began, and at the end of the year. Since follow-up assessments were made at 3 monthly intervals, after-treatment data is not available for the salicylate group or for the group on homoeopathy who did not respond to treatment, since many of these patients had left the trial before follow-up assessments could be made. The data suggests that homoeopathic treatment, either alone or in combination with some orthodox therapy improved pain as assessed by the articular index of joint tenderness and joint stiffness (limbering up time) of the patients in both Subgroup C ($P = 0.05$ and $P < 0.05$ respectively) and D ($P < 0.05$ and $P = 0.05$ respectively). The grip strength of patients in Subgroup C also improved, but not signifi-

Table 1 Data of patients with rheumatoid arthritis treated with salicylate and homoeopathy (mean ± s.d.) at start of trial

Clinical treatment groups	*Salicylate*	*Homoeopathy*
Age (years)	47.0 ± 13.6	49.7 ± 11.6
Duration of disease (years)	5.0 ± 5.2	8.6 ± 7.3
Articular index	15.3 ± 10.9	15.1 ± 8.2
Limbering up time (min)	81.3 ± 76.1	76.7 ± 76.4
Grip strength (mm Hg): Right hand	137.2 ± 58.6	133.1 ± 71.8
Left hand	133.5 ± 62.9	133.6 ± 62.8
Digital joint circumference (mm):		
Right hand	296.4 ± 23.4	287.9 ± 25.8
Left hand	287.7 ± 25.5	283.6 ± 24.4
Male : Female ratio	1 : 2.4	1 : 2.4

Table 2 Data of subgroups of patients with rheumatoid arthritis treated by salicylate and homoeopathy (mean ± s.d.) at start of trial

		n	Duration of disease years	Articular Index of joint tenderness	Limbering up time (min)	(Grip strength) (mm/hg) Right	Left	Digital joint circumference (mm) Right	Left
Salicylate subgroup	A	6	5.3± 4.7	8.7± 5.6	33.0±35.2	180±46.1	172±64.1	302±33.5	291±37.6
	B	35	5.0± 5.4	16.6±11.3	90.4±78.5	129±57.8	127±61.1	295±21.6	287±23.4
Mean			5.0± 5.2	15.3±10.9	81.3±76.1	137±58.6	133±62.9	296±23.4	288±25.5
Homoeopathic subgroup	C	23	6.4± 5.4	12.1± 6.5	67.0±76.4	140±65.7	145±59.6	285±25.2	276±22.4
	D	13	6.3± 7.4	17.8± 7.1	89.5±75.5	143±86.6	136±71.3	239±27.3	290±21.7
	E	18	14.1± 7.2	16.6±10.3	84.6±78.8	112±66.5	113±58.9	291±26.9	290±28.0
Mean			8.6± 7.3	15.1± 8.2	76.7±76.4	133±71.8	134±62.8	288±25.8	284±24.4

Subgroups
Salicylates
A remained on salicylates for 1 year.
B dropped out.
Homoeopathy
C remained solely on homoeopathy.
D remained on homoeopathy, but supplemented with orthodox therapy.
E dropped out or remained on homoeopathy, but not helped clinically.

Table 3 Data of homoeopathic groups C and D before and after treatment (mean ± s.d.)

	Group	Before	After	P value
Articular index of joint tenderness	C	12.1± 6.5	7.8± 5.2	0.05
	D	17.8± 7.1	11.2± 6.3	<0.05
Limbering up time (min)	C	67.0±76.4	24.0±22.5	<0.05
	D	89.5±75.5	51.6±43.2	0.05
Grip strength: Right hand (mm/Hg)	C	140 ±65.7	162 ±62.1	—
	D	145 ±59.6	128 ±67.0	—
Left hand	C	143 ±86.6	156 ±62.3	—
	D	136 ±71.3	124 ±67.1	—
Digital joint circumference: Right hand (mm)	C	285 ±25.2	281 ±28.6	—
	D	289 ±27.3	297 ±14.5	—
Left hand	C	276 ±22.4	273 ±25.1	—
	D	290 ±21.7	284 ±21.9	—

Table 4 Improvement and toxic effects in the three groups studied

	n	Improvement	Toxic effects
Placebo	100	0 (0%)	0 (0%)
Salicylate	41	6 (14.6%)	16 (39%)
Homeopathy	54	23 (42.6%)	0 (0%)

cantly. Treatment had no apparent effect on the digital joint circumference.

Table 4 summarizes the percentage improvement and the percentage of toxic effects in the three groups of patients, those on an inert preparation only, those on salicylate and those on homoeopathy.

Discussion

In this trial, the patients who received homoeopathic treatment did considerably better than the patients who received salicylate in the form of enteric coated aspirin. 42.6% of the patients in the homoeopathic group were maintained on homoeopathy alone compared with 14.6% maintained on salicylate. If we include the 24% of patients who were maintained on homoeopathy plus some orthodox therapy, then 66.6% of this group was improved at the end of one year. The failure and drop-out rate was 33.4% compared with 85.4% in the salicylate group.

The patients on homoeopathy, however, had an advantage over those on salicylate because they were allowed to continue with their previous orthodox therapy, whereas the patients on salicylate had to discontinue their previous therapies when starting salicylate. Although none of the patients were well maintained on their previous therapies, this could have biased the drop-out rate in favour of those receiving homoeopathy.

There is a further point which could have influenced the results. In a trial of this nature, there are two variables involved, the drug and the physician who gives it (Balint, 1973). The patients in the homoeopathic group were treated by different physicians from the patients in the salicylate group. It could be that the differences in response in the two groups of patients were due to the different physicians rather than to differences in the drugs. A further trial is therefore being planned to eliminate this factor. The advantage to the homoeopathic patients of continuing their previous orthodox therapy, will also be eliminated in this further trial. It is of interest, however, that placebo had little effect.

Perhaps one of the most interesting aspects of this preliminary study is that none of the patients on homoeopathy experienced toxic effects whereas 39% of patients treated with salicylates dropped out from the study because of toxic effects (Table 4). Modern medicines have been criticised for their unacceptable toxic effects (Illich, 1975), and the finding that homoeopathy could maintain a proportion of patients with rheumatoid arthritis in a satisfactory state for a period of a year seems important. Approximately half the side effects reported to the Committee on Safety of Medicines are due to antirheumatic drugs (Girdwood, 1974), and a recent review of deaths in patients with rheumatoid arthritis in Glasgow has shown that a surprising number were due to drug therapy, especially corticosteroids (Brooks, Stephens, Stephens & Buchanan, 1975).

References

BALINT, M. (1973). *The doctor, his patient and the illness*, 2nd edition. London: Pitman Medical.

BROOKS, P.M., STEPHENS, W.H., STEPHENS, M.E.B. & BUCHANAN, W.W. (1975). How safe are antirheumatic drugs? A study of possible iatrogenic deaths in patients with rheumatoid arthritis. *Health Bulletin (S.H.H.D.)*, **33**, 108–111.

DHAWALE, M.L. (1967). *Principles and Practice of Homoeopathy*. Bombay: Karnatak Publishing House.

GIRDWOOD, R.H. (1974). Death after taking medicament. *Br. med. J.*, **1**, 501–504.

HUSKISSON, E.C. (1974). Measurement of pain, *Lancet*, **ii**, 1127–1131.

ILLICH, I. (1975). *Medical Nemesis. The Expropriation of Health*. London: Calder and Boyars.

LEE, P., BAXTER, A., DICK, W.C. & WEBB, J. (1974). An assessment of grip strength measurements in rheumatoid arthritis. *Scand. J. Rheum.*, **3**, 17–23.

LEE, P., ANDERSON, J.A., MILLER, J., WEBB, J. & BUCHANAN, W.W. (1976). Evaluation of analgesic action and efficacy of antirheumatic drugs. Study of 10 drugs in 684 patients with rheumatoid arthritis. *J. Rheum.*, **3**, 283–294.

MANN, H.B. & WHITNEY, D.R. (1947). On a test of whether one of two random variables is stochastically larger than the other. *Ann. Math. Statist.*, **18**, 52–54.

MITCHELL, G. (1975). *Homoeopathy*. London: W. H. Allen.

RITCHIE, D.M., BOYLE, J.A., McINNES, J.M., JASANI, M.K., DALAKOS, T.G., GRIEVESON, P. & BUCHANAN, W.W. (1968). Clinical studies with an articular index for assessment of joint tenderness in patients with rheumatoid arthritis. *Quart. J. med. N.S.*, **37**, 393–406.

ROPES, M.W., BENNETT, G.A., COBB, S., JACOX, R. & JESSAR, R.A. (1959). 1958 revision of diagnostic criteria for rheumatoid arthritis. *Bull. Rheum. Dis.*, **9**, 175.

SCOTT, P.J. & HUSKISSON, E.C. (1976). Graphic representation of pain. *Pain*, **2**, 175–184.

TRINDER, P. (1954). Rapid determination of salicylate in biological fluids. *Biochem. J.*, **57**, 301–309.

WEBB, J., DOWNIE, W.W., DICK, W.C. & LEE, P. (1973). Evaluation of digital joint circumference measurements in rheumatoid arthritis. *Scand. J. Rheum.*, **2**, 127–131.

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