New Zealand

PURE GREEN LIPPED MUSSEL EXTRACT

Abstract

Perna canaliculus in the treatment of arthritis

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This was a double blind study into the use of Biolane extract (Seatone) in the treatment of osteo and rheumatoid arthritis. 66 patients were involved with 28 suffering classical rheumatoid arthritis and 38 with radiological evidence of osteo arthritis. The mean ages of the patients were 68.8 and 57.0 years respectively for osteoarthritis and rheumatoid, and the mean duration of the disease 12.9 and 17.8 year, respectively.

All patients were severely affected and all had deteriorated to the stage where they were on the waiting list for joint surgery for the relief of pain and disability.

The daily dosage was 1050mg (Seatone) with a subsequent reduction for continued long term treatment after two months to 700mg in those patients who seemed to be well maintained for a total of 6 months.

The patients were seen monthly and full clinical assessments were made each visit (except joint movement, which was measured at 0, 3 and 6 months).

This trial was a landmark paper for Seatone as the patients were all old and very severe cases. At the end of six months, 76% of the rheumatoid and 45% of the osteoarthritis patients improved.

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GYNAECOLOGY

TENDER SPOTS

MANAGEMENT OF ANGINA PECTORIS

IN GENERAL PRACTICE

Perna canaliculus in the treatment of arthritis

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Arthritis in one or other of its several forms continues to be a major cause of disability in the UK. Although many non-steroidal anti-inflammatory drugs are now available, none is wholly effective, and side effects remain a problem. The search for a safer and more effective anti-inflammatory agent therefore continues.

Five years ago, a preparation of the New Zealand green lipped mussel, *Perna canaliculus* (see figure), came to our notice, and a preliminary therapeutic trial was carried out in 86 patients, 55 with rheumatoid arthritis and 31 with osteoarthritis. The patients were treated for periods ranging from six months to 4.5 years: 67% of those with rheumatoid arthritis and 35% of those with osteoarthritis benefited. Toxic effects were uncommon and generally mild.

In order to evaluate the efficacy of this preparation more fully, it was decided to carry out a carefully controlled double-blind trial on a similar group of patients. This second trial was also designed to include a greater number of patients suffering from osteoarthritis to obtain a more accurate assessment of the effect of the agent in this condition.

Patients and methods

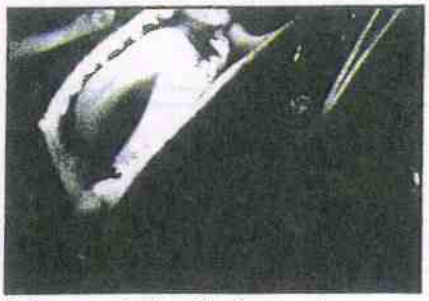
Sixty-six patients took part in the trial. Twenty-eight suffered from classical rheumatoid arthritis (Ropes *et al.*, 1959) and 38 had clinical and radiological evidence of osteoarthritis.

All the patients were on the waiting list of the orthopaedic unit of the Victoria Infirmary, Glasgow, for joint surgery. All were taking some form of non-steroidal anti-inflammatory therapy. They were told that they would be taking part in a double-blind trial to assess the value of a new anti-inflammatory preparation, and all were willing to co-operate. Inquiry was made regarding any known allergy to fish or shell-fish. The patients were requested to continue all previous therapy unchanged and to take the trial materials as an additional treatment.

Therapeutic preparations

The mussel extract was prepared in capsule form, 350mg per capsule. The placebo was a pharmacologically inactive preparation of fish that was identical in appearance, taste and smell to the active preparation. Both were prepared by McFarlane Laboratories, New Zealand. The initial dose was three capsules per day (1050 mg). Both materials were given to the hospital pharmacy department where a random code was produced.

Experience during the preliminary study indicated that the effects of the mussel preparation could last



Perna canaliculus *feeding under laboratory conditions.*

for two to three weeks after cessation of the therapy if this had been taken for more than two months. It was therefore not possible to conduct a full double-blind cross-over trial. The patients were accordingly kept on their randomly allocated double-blind therapy for a period of three months after which they were fully reassessed. They were then given the active preparation for a further three months, thus giving all the patients the opportunity of taking the test material. Since the codes were not broken until the patients had been in the trial for six months, neither the patients nor the physicians conducting the trial knew whether there had been any change of therapy in the second three-month period. The patients were then again reassessed and the codes broken.

Clinical assessments

The patients were seen at monthly intervals in the orthopaedic outpatient department. With the exception of joint movements which were measured at the initial visit, at three months and at six months, full clinical assessments were made at each visit. Any previously unnoticed side effects were also recorded.

Rheumatoid patients.—The following measures were used to assess the progress of the patients with rheumatoid arthritis: articular index of joint tenderness (Ritchie *et al.*, 1968), morning stiffness (limbering up time), grip strength in each hand (Lee *et al.*, 1974), pain as assessed by the visual analogue scale (Huskisson, 1974; Scott and Huskisson, 1976), functional index (Lee *et al.*, 1973), and the time taken to walk a measured distance of 50 feet (15.24m). The patient and the physician also made their own assessments of whether or not there had been an improvement. The patient was considered to have improved when both the patient's and the physician's opinion agreed and there was objective supporting evidence.

Patients with osteoarthritis.—The progress of the patients with osteoarthritis was assessed by means of the following measures: degree of morning stiffness (limbering up time), pain as assessed by the visual analogue scale, functional index, time taken to walk 50 feet (15.24m), the range of movements of hip and knee joints, and the patient's and physician's own assessments of improvement. Again improvement was judged to have occurred when both the patient and the physician agreed and there was objective supporting evidence.

Laboratory indices

In the four-year pilot study, haemoglobin, white-cell count, ESR, serum biochemistry, rheumatoid serology and urine analysis were performed at regular intervals. No statistically significant changes were observed in any of these parameters although haemoglobin levels tended to rise and in one case a positive R_3 value became negative. In view of these largely negative results over four years, laboratory tests were not performed routinely in the six-month trial, although individual tests were done when clinically indicated.

Statistics

The results were analysed by the Wilcoxon matched-pairs signed-ranks test (Wilcoxon, 1945).

Results

The age and sex of the patients, the time for which they had been affected and the severity of their disease are presented for the active and placebo groups of both rheumatoid and osteoarthritic patients in table I. The groups were comparable.

Of the 66 patients in the trial, eight dropped out before the end of the first three months— three had rheumatoid arthritis and five had osteoarthritis. Three of these patients were admitted to hospital for reasons unrelated to their arthritis, two had difficulties with transport, one had previous dyspepsia and felt the capsules disagreed with her, and two gave no reason.

Ten of the 17 rheumatoid patients on the active preparation improved during the first three months compared with three of the 11 patients on the inert preparation. In the osteoarthritic group six of the 16 patients on the active and three of the 22 patients on the inert preparation, improved. During the second three months of the trial, a further six rheumatoid and six osteoarthritic patients improved. At the end of six months, therefore, 19 of the 28 rheumatoid patients (67.9%) and 15 of the 38 osteoarthritic patients (39.5%) felt that they had benefited from being included in the trial. If the patients who dropped out are disregarded, as in most instances the reason for drop-out was unrelated to the arthritis, then 76% of the rheumatoid and 45% of the osteoarthritic patients improved.

The mean results for the measurements of pain, stiffness and function in the various groups of patients before and after treatment are presented in tables II and III.

Night pain

Of the 66 patients in the trial, 46 suffered from night pain. This was relieved in 17 patients on active treatment and in two on placebo—a 37% response to the active preparation.

Apart from the patients who improved when assessed objectively, seven patients, four on placebo and three on the active material, showed a temporary response lasting less than two months. Since previous experience with rheumatoid patients in Glasgow has suggested that a placebo effect is not maintained for longer than six weeks (Rooney *et al.*, 1978), these patients were classed as placebo responders.

Exacerbation

Six patients experienced an increase in the severity of their symptoms two to four weeks after starting active treatment. This exacerbation lasted for one to two weeks, after which they made good progress. It is interesting that a similar flare-up

has been observed in other patients one to five weeks after beginning treatment with this extract (Croft, 1979).

Side effects

Apart from the exacerbation of symptoms nine of the 66 patients in the trial experienced side effects, eight on the active preparation and one on the inert material. Two patients experienced increased stiffness which disappeared within two to three weeks. One patient had epigastric discomfort, one suffered from increased flatulence and four, of whom one was on placebo, had nausea. One patient retained fluid which was reversed by stopping the treatment for a week and recommencing at a lower dose level.

Dose adjustment

When patients were seen to be well-maintained on the active preparation for two months or more, an attempt was made to reduce the dose. It was found that several patients could be satisfactorily maintained on two capsules (700mg) per day.

TABLE I.—Comparison of active and placebo groups for both rheumatoid arthritis and osteoarthritis at the start of the trial

Group	Number	Age (years)	Duration of disease (years)	Articular index	Limbering up time (min)	Visual analogue	Functional index	Time for 50ft (sec)	Sex (no.)
Rheumatoid arthritis									
Active drug	17	54.1	15.1	15.5	93.8	55.9	16.2	37.5	M (0) F (17)
Placebo	11	60.6	19.2	13.4	106.4	52.3	12.4	31.7	M (1) F (10)
Osteoarthritis									
Active drug	16	69.6	11.2	—	28.3	58.8	5.9	28.0	M (0) F (16)
Placebo	22	68.6	13.7	—	24.0	52.5	6.0	26.8	M (1) F (21)

TABLE II.—Mean results (s.d.) of measures in osteoarthritic patients before and after treatment

Patient's category† (no.)	Age (years)	Duration of disease (years)	Limbering up time (min)		Visual analogue		Functional index		Time for 50ft (sec)	
			Before	After	Before	After	Before	After	Before	After
				*		*		*		*
Responders (15)	67.6 (8.9)	11.8 (5.8)	17.9 (10.9)	8.6 (9.4)	39.3 (24.4)	18.0 (15.0)	5.1 (2.7)	2.6 (2.7)	20.2 (6.9)	14.2 (2.7)
Non-responders (18)	69.8 (7.6)	12.9 (17.4)	22.4 (17.6)	22.4 (17.2)	65.0 (17.8)	65.0 (15.7)	5.7 (2.5)	5.3 (2.5)	28.4 (15.3)	25.4 (13.9)

*Difference significant: P<0.01
†There were 5 drop-outs, giving an initial total of 38 patients

TABLE III.—Mean results (s.d.) of measures in rheumatoid patients before and after treatment

Patient's category† (no.)	Age (years)	Duration of disease (years)	Articular index		Limbering up time (min)		Grip strength (mm Hg) Right		Grip strength (mm Hg) Left		Visual analogue		Functional index		Time for 50ft (sec)	
			Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
				*		*						*		*		*
Responders (19)	56.4 (12.6)	16.4 (8.7)	15.1 (9.3)	8.3 (8.1)	90.3 (60.5)	49.7 (43.9)	93.5 (33.0)	114.3 (39.6)	96.0 (38.7)	110.2 (56.6)	52.4 (18.3)	36.1 (19.8)	14.7 (7.8)	10.8 (7.8)	34.6 (19.9)	27.6 (14.8)
Non-responders (6)	58.8 (16.1)	20.2 (9.3)	11.3 (8.3)	9.5 (7.8)	110.0 (72.1)	116.7 (71.5)	92.7 (35.0)	88.0 (17.9)	90.3 (18.4)	87.0 (14.5)	57.5 (17.1)	67.5 (10.8)	14.8 (2.7)	14.5 (3.7)	34.0 (22.3)	30.8 (15.7)

*Difference significant: P<0.01
†There were 3 drop-outs, giving an initial total of 28 patients

Discussion

It was encouraging that the proportion of patients who responded to treatment with the mussel extract in the double-blind trial was similar to that obtained in the preliminary study, 67.9% of rheumatoid patients and 39.5% of osteoarthritic patients benefiting from this form of therapy. The measures of pain, stiffness and the ability to cope with the environment improved significantly in those patients who responded to the therapy. Grip strength did not improve significantly in the short-term double-blind trial although in the pilot study, which included a number of patients with less severe destruction of the joints of the hands, there was significant improvement in strength. Many of the rheumatoid patients in the double-blind trial had marked deformities of the hands and had difficulty in grasping the cuff of the grip-strength apparatus. It was therefore not surprising that no marked change was seen in this measure. There were no significant changes in joint function as assessed by measurement of the range of movement in the osteoarthritic group as a whole although individual patients did improve. This again was not surprising since gross destructive changes requiring joint surgery are unlikely to be reversible by drug therapy.

Most of the patients in the study were old and had suffered from their disease for many years. The mean ages were 68.8 and 57.0 years, respectively, for osteoarthritic and rheumatoid patients and the mean duration of disease 12.9 and 17.8 years, respectively. All patients were severely affected and all had deteriorated to the stage where they were on the waiting list for joint surgery for the relief of pain and disability. They were therefore patients who were nearing the end of the road as far as orthodox therapy was concerned. While it is unlikely that many will have been improved to the extent that joint surgery becomes unnecessary, nevertheless the quality of life for about half of them has been improved considerably. The encouraging fact that improvement could be obtained in such old and long-standing cases confirmed the impression gained from the preliminary four-year study that benefit was related neither to age of the patient nor to the extent or severity of the disease.

Toxic effects were uncommon and, with the exception of the one patient who retained fluid, were mild. The mussel extract used in the present trial was as effective as gold, though not as effective as levamisole (El-Ghobarey *et al.*, 1978) in improving pain, stiffness and grip strength. The drop-out and side-effect rates moreover were much lower with *Perna canaliculus* than with either gold or levamisole. These latter are both second-line drugs with a high incidence of toxic reactions (table IV). It is therefore suggested that *Perna canaliculus* may prove to be a safe alternative to second-line drugs when first-line treatment is failing to maintain the patient in a reasonably comfortable and functional state.

The dose of mussel extract required to maintained improvement varies from patient to patient. In the four-year pilot study it was possible to reduce the dose in a considerable number of patients to one capsule per day or less after they had been on the therapy for a period of several months. In the double-blind trial some patients managed to reduce their dosage from three capsules (1050mg) per day to two capsules (700mg) per day without experiencing any set-back. None has so far been able to reduce the dose further, but none has yet been on the therapy for longer than six months.

Table IV.—Comparison of drop-out and side-effect rates on treatment with Perna canaliculus *(present trial), and gold and levamisole (El-Ghobary* et al., *1978)*

	Treatment		
	Perna canaliculus	Gold	Levamisole
Drop-out rate	12%	55%	60%
Side-effect rate	13.6%	35%	45%

Conclusion

This trial suggests that the extract of the green lipped mussel, *Perna canaliculus* is an effective supplement or possible alternative to orthodox therapy in the treatment of both rheumatoid arthritis and osteoarthritis. It reduces the amount of pain and stiffness, improves the patient's ability to cope with life, and apparently enhances general health. Added to these benefits is the low incidence of side effects. It would therefore seem that this substance could be of considerable value to patients suffering from these two chronic and disabling conditions.

We wish to thank McFarlane Laboratories, Auckland, New Zealand, for supplying both the active and the inert preparations, and the pharmacy department of the Victoria Infirmary, Glasgow, for preparing the coding system.

References

Croft, J. E. (1979): 'Relief from Arthritis', Thorsons.

El-Ghobarey, A., Mavrikakis, M. E., MacLeod, M., Reynolds, P. M. G., Capell, H. A., Spencer, D. G., Balint, G., Mathieu, J. P., McAllister, T., Cooney, A., and Dick, W. C. (1978): *Quart. J. Med.*, **47**, 385.

Huskisson, E. C. (1974): *Lancet*, **2**, 1127.

Lee, P., Baxter, A., Dick, W. C., and Webb, J. (1974): *Scand. J. Rheumatol.*, **3**, 17.

———, Jasani, M. K., Dick, W. C., and Buchanan, W. W. (1973): ———, **2**, 71.

Ritchie, D. M., Boyle, J. A., McInnes, J. M., Jasani, M. K., Dalakos, T. G., Grieveson, P., and Buchanan, W. W. (1968): *Quart. J. Med.*, **37**, 393.

Rooney, P. J., Capell, H. A., Paterson, S., Buchanan, W. W., and Dick, W. C. (1978): *Brit. J. clin. Pharmacol.*, **5**, 453.

Ropes, M. W., Bennet, G. A., Cobb, S., Jacox, R., and Jessar, R. A. (1959): *Bull rheum. Dis.*, **9**, 175.

Scott, P. J., and Huskisson, E. C. (1976): *Pain*, **2**, 175.

Wilcoxon, F. (1945): *Biometrics Bull.*, **1**, 80.