PAPERS AND ORIGINALS

Manipulation in Treatment of Low Back Pain: A Multicentre Study

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Summary

In a multicentre trial 456 selected patients with low back pain were randomly allocated to one of four treatments—manipulation, definitive physiotherapy, corset, or analgesic tablets. Patients were reassessed clinically after three weeks' treatment and again after a further three weeks. Questionnaires were used to find out the patients' condition three months and one year after admission to the trial.

There were never any important differences among the four groups of patients. A few patients responded well and quickly to manipulation, but there was no way of identifying such patients in advance. The response to a corset was slow, but the long-term effects were at least as good as those of the other treatments. Patients treated only with analgesics fared marginally worse than those on the other three treatments. There is no strong reason, however, for recommending manipulation over physiotherapy or corset.

Introduction

In its second multicentre trial the British Association of Rheumatology and Rehabilitation (B.A.R.R.) undertook a trial of manipulation in comparison with definitive physiotherapy, corset, and placebo in the treatment of low back pain. As in the first trial[1] the protocol for the study was drawn up by a research committee of the B.A.R.R. To participate a hospital department had to provide two assessing doctors, an experienced manipulator and a relief (able to give at least two treatments per week), and a co-ordinating physiotherapist. Seven hospitals took part: Brook General Hospital, Woolwich; Cardiff Royal Infirmary; Dryburn Hospital, Durham; King's College Hospital; St. Thomas's Hospital; Watford and District Peace Memorial Hospital; and West Middlesex Hospital.

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Admission to Trial

SELECTION OF CASES

Though back pain is very common, we studied only patients who had been referred to a department of rheumatology with low back pain and who satisfied three criteria: they had to be aged 20-50 years; have painful limitation of movement in the lumbar spine; and be suitable for any of the four treatments. The latter requirement led to many patients being excluded because of (*a*) obvious psychological disturbance; (*b*) pregnancy; (*c*) a deviation of the lumbar spine from vertical of over 15°; (*d*) significant root pain in one or both legs; (*e*) straight-leg raising reduced to less than 30° on either side; (*f*) continuous paraesthesia or paraesthesia brought on by weight bearing; (*g*) associated disturbances of micturition; (*h*) abnormal reflexes, sensory loss, significant weakness, or wasting due to latest attack; (*i*) osteoarthrosis of the hip joint; (*j*) clinical evidence of sacroiliitis; (*k*) significant radiological osteoporosis; (*l*) previous manipulation, successful or not; (*m*) corset wearing; (*n*) radiological evidence of spondylolysis, spondylolisthesis, hemivertebra, or vertebral abnormalities including those associated with systemic disease.

INITIAL EXAMINATION

The first proforma for patients who satisfied the criteria gave details of the history of back pain, the characteristics of the present attack, and the results of the clinical examination. At the examination the presence of lumbar lordosis, deviation from the midline, and limitation of the four lumbar movements by pain were recorded, and lumbar flexion was measured by the distance from fingertip to floor at maximal comfortable flexion. For straight-leg raising the best of three attempts was recorded to the nearest 15°. The results of the femoral nerve stretch test, decrease in muscle power, knee, and ankle reflexes, and impaired sensation were noted, and, finally, the doctor assessed the clinical severity as mild, moderate, or severe.

Once accepted as suitable for the trial the patient was passed to the co-ordinating physiotherapist, who allocated the patient to a three-week course of one of the four treatments. The allocation was random

though stratified by hospital and also by time so that three out of each successive group of 12 patients admitted at each hospital would undergo each treatment.

PATIENTS

Altogether 456 patients (245 men and 211 women) entered the trial, with about equal numbers in the third, fourth, and fifth decades of age. For 36% of them it was a first attack, but 25% had had attacks for at least five years. A third of these earlier attacks had lasted less than a week and a third had lasted a month or more. The episodes which brought the patients into the trial were on average more severe than earlier attacks. Only 16% had lasted less than a week and 56% had lasted a month or more, including 14% which had lasted more than six months. The pain was sufficient to stop 40% of patients from working, and a further 40% said that it interfered with their work. In 59% the pain was central, 19% complained of tingling or numbness in the leg, and impulse pain was present in 49%. Altogether 63% of patients said that their pain was continuous rather than intermittent and 27% that it was getting worse at the time of entry.

On examination, deviation of the spine on standing erect was noted in 14% of patients, though patients with a deviation of more than 15° had been excluded. Straight-leg raising was limited in 30% of cases. There was no loss of lumbar lordosis in 68%. Pain limited extension in 60%, side bending in 40%, and flexion in 70% of patients. Lumbar flexion was recorded at only 58% of the initial examinations and may not have been measured in patients with the greatest pain or most limited flexion. The average distance was 23 cm (range 1-72 cm).

The Treatments

It was impossible to specify closely the details of each treatment, so our interpretation rests on the effect of referring a patient for a type of treatment rather than the specific kind. The trial was not large enough to analyse results separately for each hospital, where techniques would be uniform.

Manipulation.—The technique used was at the discretion of the manipulator. Ancillary osteopathic procedures, such as mobilizing and soft-tissue techniques, could be included. A minimum of two treatments were to be given each week unless complete relief was achieved. An average of 6·0 treatments per patient was actually given.

Definitive Physiotherapy.—This included any treatment within the usual practice of the department except manipulation. The therapist could vary the treatment in an attempt to give the patient maximum benefit with a planned minimum of two treatments each week. This resulted in an average of 7·3 physiotherapy treatments per patient.

Corset.—Any corset applied on the day of entry to the trial was acceptable. Each hospital decided in advance which type it would use throughout the trial.

Analgesics.—This was effectively a control treatment as it was recognized that most patients would seek some form of pain relief and placebo tablets could not be ethically justified. A course of two paracetamol (Panadol) tablets every four hours was given. Paracetamol was also given to patients in the other three treatment groups to be taken as required, and postural advice and a posture chart were also given to all patients.

All patients were told not to divulge to the assessing doctor which treatment they had received. Corsets were removed before examination to eliminate traces of pressure and examining doctors were urged to make their assessment "blind" and to state whether or not they had done so. In only 10% of cases did the assessing doctor inadvertently discover the treatment during his examination.

Comparability of Four Groups.—Statistical comparisons among the four groups of patients showed that there were no significant differences in 29 of the 31 variables recorded at the initial assessment (at the 5% level). If 31 independent measurements are taken on random groups one or two "significant" results are to be expected. Despite the fact that more patients in the "corset" group had their extension and left-side flexion limited by pain (and this persisted after treatment) the allocation was unbiassed and patients were fairly allotted to the four treatments by the randomization procedure.

Withdrawal from Treatment.—Sixty-eight patients (15%) failed to complete the course of treatment, though some attended follow-up examinations or replied to questionnaires. They were predominantly from one treatment group (see below).

Results after Three Weeks

The patients' own assessments of the change in their pain at three weeks is shown in table I. Though there was no significant difference between treatments only 12 patients receiving manipulation said their pain was unchanged, and there were correspondingly more in the "markedly improved" and "completely relieved" categories. On the other hand, only three patients treated with a corset were completely relieved.

TABLE I—*Patients' Assessments of Pain at Three Weeks*

	Manipulation	Physiotherapy	Corset	Analgesics
Worse	6	9	5	7
Unchanged	12	21	24	24
Slightly improved	17	20	18	20
Moderately improved	19	18	19	13
Markedly improved	30	26	24	23
Completely relieved	14	10	3	13
Total	98	104	93	100

$\chi^2 = 15{\cdot}5$; D.F. = 15; P = 0·5; not significant

On clinical examination spinal deviation was noted in only 6% of patients compared with 14% on entry. Lordosis was present in 81% compared with 68% originally. Flexion was limited by pain in only 46% compared with 70% initially, but in none of these improvements was there any significant difference between groups. Lumbar extension was limited in 60% of patients on entry but in only 37% at three weeks. For manipulation, however, this latter figure was only 29% whereas for those treated with a corset it was 52% (table II). But there were more patients with limited extension in the corset group originally than in any other group so these figures do not indicate differences in the effects of the treatments. The improvement in lumbar flexion as assessed by fingertip-to-floor measurement varied from 20 cm to 40 cm. The distance was measured in only 147 patients at three weeks, and there was no significant difference between treatments (table III).

There were no significant differences among treatments in any of the other clinical values or in patients' assessments of their condition. The patients' assessments concurred closely with those of the doctor (table IV), and both showed manipulation to be marginally, though insignificantly, better.

Failure to Complete Treatment.—A small group of patients failed to complete the three-week course of treatment. Many returned for assessment at three weeks and so contributed to the above results. Altogether 40 patients on manipulation, 18 on physiotherapy, eight wearing corsets, and only two on analgesics withdrew from treatment. The patients on manipulation included 26 who stopped treatment "because they were better." Careful examination of the 40 records showed that these patients did not differ appreciably from the others when they first presented, so we have no way of recognizing in

TABLE II—*Proportion of Patients in whom Extension was Limited by Pain Initially and at Three Weeks according to Treatment*

	Initially		At Three Weeks	
	No. (%) Limited	Total Assessed	No. (%) Limited	Total Assessed
Manipulation	66 (57)	116	28 (29)	98
Physiotherapy	68 (60)	114	35 (34)	104
Corset	78 (72)	109	47 (52)	91
Analgesics	61 (54)	113	33 (34)	97
Statistical comparison	$\chi^2 = 8{\cdot}2$; D.F. = 3; P<0·05		$\chi^2 = 12{\cdot}3$; D.F. = 3; P<0·01	

TABLE III—*Fingertip-to-floor Measurements Initially and at Three Weeks according to Treatment*

	Initially		At Three Weeks	
	No. of Patients	Mean Distance (cm)	No. of Patients	Mean Improvement (±S.E.) (cm)
Manipulation	68	26·1	41	4·4±1·9
Physiotherapy	67	21·0	40	4·8±2·1
Corset	61	23·4	31	5·4±2·2
Analgesics	58	22·9	35	4·1±1·6

TABLE IV—*Number (Percentage) of Patients "Better"* at Three Weeks*

	Manipulation	Physiotherapy	Corset	Analgesics	Total
Patients' assessments	63 (64)	54 (52)	46 (49)	49 (49)	212 (54)
Doctors' assessment	61 (62)	56 (54)	46 (49)	49 (49)	210 (53)

*Better consists of "Completely Relieved," "Markedly Improved," and "Moderately Improved" and excludes "Slightly Improved," "Unchanged," and "Worse."

advance which patients will benefit from manipulation. The good effects did not persist in all the patients: 12 of the 26 who returned at three weeks were completely or greatly improved; the other 14 were only "moderately relieved." No clinical differences persisted at the six-week assessment between these patients and the others on manipulation or other treatment, but the few with a good response to manipulation had not lost time from work.

Results after Six Weeks

At the six week follow-up examination 340 (75% of the original 456) patients attended. In the three weeks after the trial 153 patients had had more treatment (table V), in most cases a continuation of their original treatment, particularly if this had been manipulation or a corset.

TABLE V—*Numbers of Patients who Underwent Additional Treatment in Three Weeks after Treatment**

	Original Treatment Group			
	Manipulation	Physiotherapy	Corset	Analgesics
Manipulation	20	4	8	8
Physiotherapy:				
including traction	6	7	4	6
other	2	17	3	7
Corset	3	1	37	3
Analgesics only	1	1	0	15
None	61	52	29	45
Total attending at 6 weeks	93	82	81	84

*Several patients received combinations of treatments, but they have been entered only once, in the highest appropriate line; a patient who received manipulation and traction would be entered under manipulation.

Clinical examination at six weeks showed no overall reduction in the numbers still complaining of painful limitation of movement, and there were no significant differences among treatments except that left-side bending was limited by pain in 29% of the analgesic group but in only 14% of the three active-treatment groups.

The doctor's overall assessment at six weeks showed no significant differences between treatments, but the largest number of patients recorded as worse were among those treated with manipulation (table VI). The patients' own assessments gave very similar results (table VII). At six weeks, therefore, there was still nothing to choose between the three active treatments, but they were marginally better than analgesics on both the doctor's and, to a lesser extent, the patient's assessment. The corset took longer to achieve results but was equally effective.

Follow-up at Three Months

Patients were sent a questionnaire three months after the first assessment which asked them to state whether their pain was worse, unchanged, improved, or completely relieved. Altogether 335 (73%) patients replied. Overall 5% claimed to be worse, 21% unchanged,

TABLE VI—*Doctor's Assessment at Six Weeks*

	Initial Treatment Group			
	Manipulation	Physiotherapy	Corset	Analgesics
Worse	10	3	4	7
Unchanged	12	12	13	16
Slightly improved	5	12	8	14
Moderately improved	11	8	13	9
Markedly improved	28	26	21	19
Completely relieved	26	20	20	19
Total	92	81	79	84

TABLE VII—*Number (Percentage) of Patients "Better"* at Six Weeks*

	Manipulation	Physiotherapy	Corset	Analgesics	χ^2 between Treatments (3 D.F.)	χ^2 "active" *v.* "control" (1 D.F.)
Patients' assessments	60 (65)	54 (67)	61 (77)	49 (58)	5·41 (N.S.)	2·83 (N.S.)
Doctors' assessment	65 (71)	54 (67)	54 (68)	47 (56)	4·80 (N.S.)	4·49 ($P<0.05$)

*See footnote to table IV.

TABLE VIII—*Patients' Assessment of Pain at Three Months according to Original Treatment Group. Percentage who were "Better" are shown in parentheses*

	Manipulation	Physiotherapy	Corset	Analgesics
Worse	2	7	3	4
Unchanged	22	22	10	16
Improved	43 (74%)	43 (65%)	48 (83%)	46 (76%)
Completely relieved	26	11	16	16
No reply	24	33	33	31

54% improved, and 21% completely relieved (table VIII). There were no significant differences between the treatment groups but the corset achieved some degree of success in 83% of cases compared with 65% for physiotherapy. At three months 6% complained that they could still not work and 44% that pain interfered with their work. Further pain since the end of treatment was reported by 65%, and of these 39% had continuous pain and 20% five attacks or more, but these results showed no relation to the previous method of treatment.

There was no relation between the doctor's initial assessment and the patient's assessment of pain at three months, which illustrates the difficulty in predicting which patients are going to respond well to any treatment. The relation between the doctor's three-week assessment and the patient's three-month report yielded some interesting results (table IX). For those treated by manipulation the relation-

TABLE IX—*Patients' Assessment of Pain at Three Months related to Doctor's Assessment at Three Weeks*

Patients' Pain at Three Months	Doctor's Assessment at Three Weeks		
	Worse or Unchanged	Improved	Completely Relieved
Manipulation			
Worse or unchanged	15	6	1
Improved	2	31	4
Completely relieved	1	13	10
Physiotherapy			
Worse or unchanged	15	12	0
Improved	12	24	6
Completely relieved	0	7	4
Corset			
Worse or unchanged	5	6	0
Improved	19	21	4
Completely relieved	1	11	3
Analgesics			
Worse or unchanged	10	7	1
Improved	8	30	5
Completely relieved	4	5	5

ship was particularly close. Those worse or unchanged at three weeks were nearly all in the same category at three months. Those who had improved and those completely relieved at three weeks were likely to remain so. For physiotherapy, the relationship was not so close: nearly half of those unchanged or worse at three weeks had improved at three months. Those who had improved at three weeks were likely to remain so at three months but those completely relieved were more likely to have slipped back than to have remained symptom free. In the corset group patients were more likely to remain unchanged after three weeks, but by three months were very likely to have improved. In the analgesic group there was less association between the three-week assessment and their own assessment at three months.

When the patients' own assessments of pain at three weeks were compared with their three-month report the results were very similar, especially in the analgesic group. This general agreement was to be expected since the patient's and the doctor's assessment agreed completely in 60% of cases and the remainder were largely only one category apart. The close agreement of results in manipulation may indicate that there is little point in continuing this form of treatment if there is no improvement after three weeks.

Follow-up at One Year

A further postal follow-up was carried out after one year. Only 262 (57%) of the original entrants to the trial returned their forms, and 66% of those who replied said that they were still having backache. The highest proportion (79%) was in the physiotherapy group but the differences between treatments were not significant. This backache was not equally severe in all patients, and 49% reported that no attack had prevented them from working in the year since treatment. Twenty-one per cent. reported continuous pain which prevented them from working, and the others reported varying numbers of episodes. There were no important differences between treatments though the analgesic group had rather more patients with continuous pain and fewer with acute attacks than the other groups. Of 151 patients who had more pain 62% reported episodes lasting less than a week, 11% reported episodes of one to four weeks, and 27% reported episodes lasting over a month. There were no significant differences among the treatment groups.

Finally, those who had had more treatment during the year were asked to indicate which of the following were most helpful: none, tablets, traction, corset, manipulation, bed rest, heat, exercises, or any other treatment (to be specified). The replies covered nearly every possible combination. A quarter found tablets alone most helpful (to prevent confusion we had not asked which had been used). Twelve patients thought manipulation most helpful and another 12 found the corset (with or without tablets) best, but no other combination was mentioned by more than two patients. One patient originally treated by manipulation finally resorted to acupuncture.

Conclusion

Clearly, none of the methods of treating low back pain compared in this trial showed any great superiority. Patients treated with analgesics alone fared marginally worse than those on the other three treatments. In the long term the corset was as effective as the other treatments, and it is certainly less expensive than manipulation or physiotherapy and safer than drugs. Manipulation produced an early response in a few cases, but our results suggest that there is little point in continuing to manipulate patients who show no early improvement. Nothing found at the initial assessment enabled us to identify in advance the relatively small number of patients who benefited from manipulation.

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Reference

[1] British Association of Physical Medicine, *British Medical Journal*, 1961, **1**, 253.

Hydroxyproline Excretion in Patients with Breast Cancer and Response to Treatment

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Summary

The urinary excretion of hydroxyproline, measured as the hydroxyproline:creatinine ratio, was useful in monitoring the progression of metastatic cancer of the breast. After new treatment was started changes in the hydroxyproline excretion occurred earlier than other clinically observable responses. The test could therefore be used for predicting the response to treatment and early detection of the sensitivity of the tumour to hormone therapy.

Introduction

Hydroxyproline excretion is reported to be a sensitive index of bone metastases.[1 2] Most urinary hydroxyproline originates from bone,[3] mainly from degradation of newly synthesized collagen.[4 5]

Breast tumours break down bone in vitro by release of osteolytic substances,[6] and development of tumour deposits in bone may depend on this property, which may be reflected in hydroxyproline excretion. Therefore, successful treatment of metastatic breast cancer may be associated with a decrease in hydroxyproline owing to a decrease in bone destruction, whereas progression of tumour growth with unsuccessful treatment may be associated with increased hydroxyproline excretion. To examine this hypothesis we estimated hydroxyproline excretion in patients with metastatic breast cancer before, during, and after various treatments.

Patients and Methods

Thirty-one patients with metastatic breast carcinoma were admitted to the metabolic ward for full metabolic and biochemical assessment. This included thorough clinical evaluation; bone scan (Tc-polyphosphate); liver scan by isotopic methods and B-mode ultrasound; chest *x*-ray examination; modified skeletal survey; marrow aspiration; urinary and serum calcium, phosphorous, and magnesium estimation; and liver function tests. Evaluation of the patients' progress was made jointly by surgeon, physician, and radiotherapist and recorded in the patients' notes. Urinary hydroxyproline excretion was not estimated

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