CHYMOPAPAIN VERSUS CONVENTIONAL SURGERY FOR LUMBAR DISC HERNIATION

10-YEAR RESULTS OF TREATMENT

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We reviewed two comparable groups of patients who had been treated for lumbar disc herniation by chymopapain chemonucleolysis (145) or conventional surgical discectomy (91). They were reviewed 10 years after treatment by questionnaire, followed by a personal interview by an independent observer.

The results of the surgically treated groups were slightly better than those treated with chymopapain. In particular, there was significantly better early relief of leg and low back pain, and fewer patients needed a second procedure. Complications were few in both groups.

Over the years, the place of open partial discectomy in the treatment of lumbar disc herniations has been well defined and documented (Hakelius 1970; Spangfort 1972; Weber 1983; Lewis et al 1987). Chymopapain chemonucleolysis is a much more controversial method of treatment and it is only recently that its long-term effects have been assessed. Only two of the 10 papers reporting long-term results of chymopapain chemonucleolysis published in *Clinical Orthopaedics* (Volume 206, 1986) achieved greater than 60% follow-up (Dabezies, Beck and Shoji 1986; Dubuc et al 1986; Flanagan and Smith 1986; Jabaay 1986; Maciunas and Onofrio 1986; Mansfield et al 1986; Nordby 1986; Sutton 1986; Thomas et al 1986; Weinstein et al 1986) and all but one were

Table I. Criteria for diagnosis of lumbar disc herniation, the rule of 5 (McCulloch and Macnab 1983)

2 symptoms	1 Leg pain, greater than back pain
	2 Specific neurological symptoms (paraesthesia)
2 signs	3 Straight leg raising < 50% of normal
and/or	positive crossover test and/or positive bowstring test
	4 Two of four neurological signs (altered reflex, wasting, weakness, sensory loss)
1 investigation	5 Positive myelogram

based solely on the questionnaire assessment of patients. These deficiencies detract from the validity of these studies (Howe and Frymoyer 1985; Bloch 1987).

We decided to compare a group of patients treated by conventional surgery at a mean of 10 years follow-up with a comparable group treated by chymopapain chemonucleolysis, 10 years after their treatment.

PATIENTS AND METHODS

The documents of all patients with a diagnosis of lumbar disc herniation and treated as in-patients at St Michael's Hospital, Toronto, between 1975 and 1980, were reviewed.

The criteria for inclusion in the study were those used to make a diagnosis of lumbar disc herniation (McCulloch and Macnab 1983) (Table I). All patients were in the age group 18 to 65 years and had to have

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completed a minimum period of two months adequate conservative treatment.

The patients fell into two groups.

The chymopapain group. This group included all the patients treated by injection of chymopapain. They were all treated by one of the authors (JAM) over the 15-month period from September 1976 to December 1977. There were 417 patients documented, of whom 253 were excluded for various reasons (Table II). The largest group of exclusions (185) were those who lived outside the province of Ontario and could not therefore be readily followed up.

The chymopapain study group therefore comprised the 164 patients resident in Ontario who satisfied the criteria for entry into this study. The mean follow-up time in this group was 10.2 years.

The technique of chemonucleolysis has been described previously (Macnab et al 1971; McCulloch 1977, 1980; McCulloch and Macnab 1983). All the injections were performed under local neuroleptic anaesthesia using image intensifier control. Multiple levels were injected in 41%. Discometry was performed prior to injection of the chymopapain. The patients were discharged from hospital one to two days after the injection (McCulloch 1977; McCulloch and Macnab 1983).

The surgical group. There were insufficient numbers of patients treated surgically in the period 1976 to 1977 to allow an adequate comparison with the chymopapain group. Therefore, the study period for this group was extended to cover the period from 1975 to 1980. The mean follow-up time was 9.7 years.

There were 188 patients documented, of whom 84 were excluded for various reasons (Table II). This left a surgical study group of 104 patients who all satisfied the criteria for inclusion and who, in addition, all had a disc herniation demonstrated at operation.

At the time that these two groups of patients were treated there was much controversy about the efficacy of chymopapain and some surgeons preferred conventional surgery for lumbar disc rupture. The surgical group were the patients treated by these surgeons. There is therefore no reason to suppose that the patients treated surgically were pre-selected or were more severely incapacitated than the chymopapain group.

The surgical operations were performed by five different surgeons working in the Departments of Neurosurgery and Orthopaedic Surgery at St Michael's Hospital. Although their methods were not identical, there was a considerable conformity in the surgical procedures performed. They all practised fenestration or localised partial laminectomy and removed the extruded portions of disc material from under the nerve roots and from within the disc space. Conventional postoperative regimes were followed.

Assessment. The review of documents and patients was carried out by an independent observer (GDT) and involved a careful review of all available records and

Table II. Reasons for exclusion from the study

	Chymopapain group Aug 1976 to Dec 1977	Surgical group 1975 to 1980
Documented patients	417	188
Living outside Ontario	185	0
Previous lumbar disc surgery	27	23
Inadequate documentation	25	8
Outside age group (18 to 65)	10	6
Other spinal abnormality (spinal stenosis, spondylolisthesis)	6	13
Previous chymopapain injection	—	12
Spinal fusion in addition	—	15
Diabetes mellitus	—	6
Cauda equina syndrome	—	1
Total excluded	253	84
Number left in study	164	104

Table III. Final patient rating (Macnab et al 1971)

Excellent	Good	Fair	Poor
No pain, full activity	Occasional pain, not interfering with activities	Pain occasionally interfering with activities	Pain frequently interfering with activities

Table IV. Details of the follow-up study

	Group	
	Chymopapain	Surgical
Total entered	164	104
Replied to questionnaire	145 (90%)	91 (89%)
Physically examined	134	82
Not traced	19	13
Died	3	2

clinical examination of the back and lower limbs. The patients completed a detailed questionnaire. In the chymopapain group evaluation was facilitated because the clinical notes had been recorded on a specially designed pro forma.

The questionnaire was designed to assess three measures of outcome: pain, progress, and work and recreation capabilities. Pain measurement utilised visual analogue scales and pain drawings in addition to the 'components of pain' assessment criteria of Million et al (1982) and Roland and Morris (1983). The questionnaire answers were checked and clarified at a personal interview. This proved to be a very necessary part of the

Table V. Details of patients, follow-up and treatment

	Group	
	Chymopapain (n = 145)	Surgical (n = 91)
Sex (<i>per cent</i>)		
male	69	66
female	31	34
Age (years)		
mean	39.9	41.3
range	20 to 65	22 to 62
Height (m)		
mean	1.71	1.70
range	1.48 to 1.97	1.50 to 1.95
Weight (kg)		
mean	79.45	78.01
Work variables (<i>per cent</i>)		
Workmen's Compensation Board	32	20
Heavy workers	29	21
Length of follow-up (years)		
mean	10.2	9.7
range	10.0 to 10.6	5 to 12
Number of disc spaces treated (<i>per cent</i>)		
3 levels	4	0
2 levels	37	0
single level	59	100
Specified disc spaces treated (<i>per cent</i> of patients)		
L3/4	3	6
L4/5	62	51
L5/S1	73	43

Fig. 1

Ratings at final follow-up in all 236 patients.

assessment as many patients had misinterpreted the questionnaire despite its simple construction.

Clinical examination of the spine included measurement of the range and pattern of spinal motion, the presence or absence of signs of nerve root irritation, and a full neurological evaluation. It was originally intended to perform a full radiological assessment, but this was abandoned because comparable pre-treatment views were not available and many patients refused to have more radiological studies.

At final assessment the patients were graded into one of four categories (Macnab et al 1971), excellent, good, fair and poor, based on the degree of satisfaction

as assessed by the patient and by the independent observer (Table III).

RESULTS

Of the 268 questionnaires mailed, 236 were returned. Five patients had died from unrelated causes. This represents a total follow-up rate of 90%.

Of the 164 questionnaires mailed to the chymopapain group, 145 were returned. Three patients had died of unrelated causes. All 145 patients were interviewed and 134 were physically examined.

Of the 104 questionnaires mailed to the surgical group, 91 were returned. Two had died from unrelated causes. Of the 91 patients, 82 were physically examined (Table IV).

Details of the patients in the two groups are shown in Table V. Both groups are generally comparable except in the proportion of Workmen's Compensation Board patients; 33% in the chymopapain group compared with 20% in the surgical group ($p < 0.05$).

Long-term results. The results are shown in Figure 1. There were more excellent results in the surgical group ($p < 0.5$) and more poor results in the chymopapain group ($p < 0.1$).

Worker's compensation patients. The Workmen's Compensation Board patients were assessed separately (Fig. 2). They showed more unsatisfactory results in both groups, 80% in the chymopapain and 78% in the surgical

group. When the worker's compensation patients are taken out of both treatment groups, the non-compensation patients still reveal a slightly better result from surgical treatment (Fig. 3).

Early relief of leg and low back pain. The surgical group were more likely to obtain early pain relief (Table VI); 87 (96%) derived significant relief of sciatica compared with 78% of the chymopapain group ($p < 0.001$); 94% of the patients in the surgical group were relieved of low back pain compared with 75% of the chymopapain group ($p < 0.001$).

Recurrence of pain. Some low back and leg pain recurred after an initial pain free period in 66% of the chymopapain group and 59% of the surgical group ($p < 0.2$). The mean time to recurrence was 3.5 years in both groups.

Repeat surgery. In the chymopapain group, 33 of the 145 patients (23%) eventually required surgical treatment for the herniated disc. In the surgical group nine of the 91 patients (10%) required further surgery.

The 33 patients who required subsequent surgery after chymopapain treatment fell into three groups. Most (20 patients, 61%) required surgery within one year of their chymopapain injection. These were designated the 'early failure group'. The surgical findings after failed chymopapain injection are shown in Table VII; 14 (70%) patients had either sequestered discs or large disc prolapse.

Five patients had incomplete but definite relief of symptoms following the injection but the return of severe pain necessitated surgery. This group was designated the 'incomplete relief group'.

Finally there was a small group of eight patients who required surgical treatment for pain which recurred more than five years after the injection, the 'late recurrence group'.

Results of surgery after failed chymopapain injections. There was a high proportion of unsatisfactory results in those who underwent operation after failed chymopapain injection (60% fair and poor), though nothing was found at surgery to account for the high failure rate.

Failures of primary surgery. Nine (10%) of the 91 patients treated surgically required a second operation, seven of them at more than one year after the initial procedure. In six patients a recurrent disc herniation was found. In the other three patients there was scarring around nerve roots but no evidence of residual or recurrent disc herniation. The results of the second operation were satisfactory in five patients (56%).

Work and recreational activities. The time off work was similar following the two treatments. In the chymopapain group 90 patients (62%) and in the surgical group 62 patients (68%) were back at work within three months. In the chymopapain group 46 patients (32%) were still continuing in their original occupations at 10 years compared with 45 (49%) of the surgical group.

Complications. An outstanding feature of this study was the small number of serious complications in both groups.

Fig. 2

Ratings at final follow-up in 65 Workmen's Compensation Board cases.

Fig. 3

Ratings at final follow-up in 171 non-compensation cases.

Table VI. Results of early relief of leg pain and low back pain

	Group		Significance of difference
	Chymopapain (n = 145)	Surgical (n = 91)	
Relief of leg pain	113 (78%)	87 (96%)	$p < 0.001$
Relief of low back pain	109 (75%)	86 (94%)	$p < 0.001$

Table VII. Surgical findings after failed chymopapain injection

	Type of failure (see text)		
	Early (n = 20)	Incomplete relief (n = 5)	Late recurrence (n = 8)
Sequestered disc	7	3	3
Large non-sequestered disc	7	2	2
Lateral recess stenosis	2		1
Sequestered disc and stenosis	1		1
Wrong level injected	1		
No abnormality	2		1

In the chymopapain group there were four early allergic reactions, two of which were classical anaphylactic responses (1.5% incidence). All allergic reactions were promptly and successfully treated. There were no post-injection infections or discitis.

In the surgical group there was one pulmonary embolus, one disc infection and three superficial wound infections. All responded well to appropriate therapy.

DISCUSSION

In assessing the long-term results of lumbar disc herniation, an important consideration is the natural history of the condition. It has previously been shown that at 10 years there is no difference between the long-term results of disc prolapse treated by conventional conservative methods or by surgery (Weber 1983). The recovery rate in the chymopapain group in this study is not significantly different from the recovery rate in Weber's conservatively treated patients who were similarly chosen with demonstrable sciatica and disc herniation. The main advantage shown for surgery over conservative treatment is the earlier relief of symptoms within the first year (Ejeskär et al 1983). This was confirmed in our study.

We chose to assess the 10-year results of chymopapain treatment specifically to determine whether the method had any long-term deleterious effects compared with surgery. We have demonstrated no such effect.

There was a discrepancy between the two groups in respect to length of follow up. Insufficient numbers in the surgical group had been followed for 10 years to allow valid comparison, therefore this group was expanded to include patients reviewed between seven and 12 years after surgery. We believe that this discrepancy had a minimal effect on the long-term results. Weber (1983) has shown that the results of treatment for disc herniation are the same at 10 years as they are at four years. Indeed, he concluded that a period of four years after treatment is sufficient for final evaluation.

In such a retrospective comparative review it is of paramount importance to determine that the two study groups were as comparable as possible. One major difficulty arises from the fact that in the surgical group the disc hernia was confirmed at surgery, whereas, in the chymopapain group the diagnosis was based on indirect evidence, history, examination and investigations. The modern imaging techniques of CT and MRI were not available at that time; oil-based myelography was employed. Previous studies, and indeed our own, have suggested that the majority of failures of chymopapain occur either in sequestered discs or in massive contained herniations (Smith 1975; Cauchoix, Ficat and Girard 1978; Carruthers and Kousaie 1982; Brown 1983; McCulloch and Macnab 1983; Postacchini, Lami and Massobrio 1987). With the newer imaging techniques the selection of suitable patients may be more accurate.

When these patients were treated, the use of

chymopapain was as controversial as it is today, and in St Michael's Hospital there were two main schools of thought – those who believed in its efficacy and those who did not. One possible criticism of the comparability of the two groups is that pre-selection of the patients occurred, so that those with more classical indications for a lumbar disc herniation may have been referred for treatment by surgeons known to favour discectomy leaving those with lesser indications to be treated by chymopapain. It was the policy of the surgeon using chymopapain to treat all patients referred to him with herniated intervertebral discs by chymopapain injection as a first measure. The fact that 24 of the 33 patients who failed chymopapain therapy and subsequently came to surgery, had either large, non-sequestered or fully sequestered discs also suggests that no such pre-selection had occurred.

It should be noted that from 1977 to 1978, when the chymopapain was used, it was the policy of the treating surgeon (and indeed of many other surgeons using chymopapain) to inject more than one disc level at a time. Thus, 41% of the patients in this series had two or more discs injected compared with the surgical group in which all patients had a single disc level discectomy. It is possible that multiple disc injections had a deleterious effect on the long-term results of the chymopapain group, particularly in causing the higher incidence of low back pain. Our data neither confirm nor refute this possibility.

The main strengths of our study are that the patient assessment was carried out by an independent observer, and that a 90% follow-up was achieved at 10 years. We achieved this by restricting the study to those patients who lived in the province of Ontario. Both of these factors have largely been shown to enhance the validity of such retrospective studies (Howe and Frymoyer 1985; Bloch 1987). Previous studies of the long-term results of chymopapain treatment have largely been based on questionnaire assessment alone. The difficulties of questionnaire design and assessment have been described (Howe and Frymoyer 1985); we confirmed in our study that in many cases there were discrepancies between the answers to the questionnaire and the results of the personal interview.

Another notable feature of our study was the surprisingly low incidence of complications in both groups. In the chymopapain group there were no deaths and no iatrogenic neurological complications. Recent studies (Brown 1983; Weitz 1984; Agre 1985; Dyck 1985) have highlighted some of the potential dangers of this method of treatment. Our experience serves to emphasise that in expert hands these complications are few. In the surgical group, also, there were no deaths nor any permanent long-term complications, and the recurrent disc herniation rate of 7% matches the generally accepted figure for this complication (Hakelius 1970; Spangfort 1972; Cauchoix et al 1978; Weber 1983).

Among the patients in the chymopapain group who

came to subsequent surgery 75% were found to have either sequestered or very large contained disc protrusions. The majority of these failures were in the 'early failure group' and were operated within one year. There was an interesting group of eight patients, the 'late failures', who had enjoyed complete relief of pain for periods of up to five years before recurrence. Of these, five had either a sequestered or a large non-sequestered disc. This suggests that recurrent herniation can occur in a disc that has previously been injected with chymopapain. This finding has not previously been reported.

The overall results of our comparative study suggest that by whatever parameters the patients are assessed there is a superiority of surgery over chymopapain. In particular, the surgical group achieved better early relief of leg and low back pain and, as has been demonstrated in previous studies, they were less likely to require subsequent surgical treatment. Although there was a disparity in the relative proportions of workers compensation patients in the two study groups, non-compensation patients showed a similar trend towards better results for surgery than for chymopapain. In the compensation patients, regardless of which method of treatment was used, the overall results were unsatisfactory – 80% of

the chymopapain group and 78% of the surgical group had fair or poor results.

Conclusions. At the present time, removal of the disc hernia through a small laminotomy incision remains the treatment of choice for the patient with sciatica in whom conservative treatment has failed and in whom a herniation at the suspected side and level has been demonstrated by the appropriate imaging technique. However, this study also indicates that chymopapain is still an acceptable last step in the conservative care of the patient with herniated nucleus pulposus. The method proved safe with minimal serious complications, and we believe that with careful patient selection it can give acceptable results not much inferior to those achieved by surgery.

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