A 1- to 4-year follow-up review of treatment of sciatica using chemonucleolysis or laminectomy

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To help clarify the comparative effects of chemonucleolysis and discectomy, the author studied 178 consecutive patients with sciatica who did not respond to conservative treatment. None had previously undergone laminectomy or chemonucleolysis or had spinal stenosis. All received postmyelography computerized tomography (CT) and, if the radiological interpretation was that of an extruded migrated disc, a laminectomy was performed; otherwise, the patient was given a choice of the two procedures. Of the 178 patients, 106 underwent chemonucleolysis and 72 laminectomy. Workers' compensation was being paid to 21.6% of the chemonucleolysis patients and 20.8% of the laminectomy patients.

Postoperatively, substantial improvement was noted in 82.7% of the chemonucleolysis patients and 92.5% of the laminectomy patients at 6 weeks and in 92.8% of the chemonucleolysis patients and 89.7% of the laminectomy patients at 6 months. The majority of patients in both groups had improved neurological signs. Follow-up questionnaires at 1 to 4 years postoperatively revealed an overall success rate of 86.5% for chemonucleolysis patients and 83.8% for laminectomy patients. In patients not receiving workers' compensation, 90.1% of the chemonucleolysis patients and 88.6% of the laminectomy patients had a successful outcome; in those receiving workers' compensation, 69.6% of the chemonucleolysis patients and 60.0% of the laminectomy patients had a successful outcome. No statistically significant differences in improvement rate in neurological symptoms or signs were identified between the two procedures. Overall, 85.1% of the chemonucleolysis patients and 78.5% of the laminectomy patients were employed at follow-up review.

To achieve optimum results and eliminate noncandidates for chemonucleolysis, routine use of postmyelography CT is recommended. When properly used, chymopapain chemonucleolysis is an acceptable alternative to surgical discectomy.

Key Words • Intervertebral disc • Chemonucleolysis • Laminectomy

In 1934, Mixter and Barr\textsuperscript{14} introduced laminectomy for the removal of herniated lumbar disc. In 1964, Smith\textsuperscript{22} designed a new approach to treat herniated nucleus pulposus with chemical hydrolysis using chymopapain; he coined the term “chemonucleolysis.” On the basis of a double-blind study, chymopapain chemonucleolysis was approved by the Food and Drug Administration (FDA) in 1982.\textsuperscript{10} In 1983, 7000 neurological and orthopedic surgeons in the United States received 1 day of training in the performance of chemonucleolysis. In retrospect, this training time was inadequate. During the ensuing 2 to 3 years, inappropriate selection of patients and technically incorrect performance of the procedure by inexperienced surgeons resulted in an unsatisfactory outcome, and catastrophic neurological complications occurred in some cases. Consequently, the use of chemonucleolysis dropped off dramatically in the United States. By contrast, the procedure is being successfully performed with increasing frequency elsewhere, especially in Europe, primarily due to the fact that only experienced surgeons with proper training perform the procedure.

In the author's neurological service, a lumbar myelogram is routinely performed before surgical discectomy or chemonucleolysis. When chymopapain was used experimentally before 1975, many noncandidates with spinal stenosis, lateral recess stenosis, or migrated intervertebral disc were injected with chymopapain. The advent of computerized tomography (CT) facilitated diagnosis. In 1982, when chymopapain was released, CT was used before myelography; during the latter part of 1983, CT was used following myelography and was found to be of value in excluding inappropriate candidates for chemonucleolysis. The present study was initiated in 1984 to determine whether the routine use of postmyelography CT was of significant value in select-
Follow-up study of chemonucleolysis and laminectomy

ing patients for chemonucleolysis versus laminectomy. The 1- to 4-year follow-up results are reported here.

Clinical Material and Methods

Between January, 1984, and January, 1988, we studied the results of laminectomy compared to chemonucleolysis using Chymodiactin (chymopapain). To be eligible for either treatment, patients had to have intractable sciatica and be candidates for laminectomy, could not have previously undergone chemonucleolysis or laminectomy, and had had myelography-CT. On the basis of radiological findings, patients with spinal stenosis or a sequestered migrated disc were excluded from consideration for chemonucleolysis. After both procedures were discussed in detail with each patient, candidates eligible for both procedures were given a choice between chemonucleolysis and laminectomy.

During this period, 178 patients were treated; 106 patients (59.5%) underwent chemonucleolysis and 72 (40.5%) laminectomy. The ratio of men to women was 67:33% for chemonucleolysis and 58.3:41.7% for laminectomy. The average age for the chemonucleolysis group was 38.0 years for men and 37.9 years for women; the average age for the laminectomy group was 40.6 years for men and 45.5 years for women. The average duration of back pain was 54.9 months for the chemonucleolysis patients and 64.1 months for the laminectomy patients. The average duration of sciatica was 5.7 months for the chemonucleolysis patients and 6.9 months for the laminectomy patients. Workers’ compensation was being paid to 21.6% of the chemonucleolysis patients and 20.8% of the laminectomy patients.

All patients were treated with bed rest for an average of 3 weeks before either procedure was performed. All patients had back pain, sciatica, and limitation of straight-leg raising; all but four chemonucleolysis patients and two laminectomy patients had limited forward flexion. An average of two-thirds of the patients had sensory loss and half had motor loss; 36 chemonucleolysis patients and 31 laminectomy patients exhibited reflex changes.

All patients who underwent chemonucleolysis had a Chemofast (fluorallergosorbent) test to check for possible allergy to the enzyme; cimetidine (H₂ antagonist) and diphenhydramine (H₁ antagonist) were then administered in divided doses during the 24 hours before injection. All procedures were carried out in the neuroradiology suite, with a neuroradiologist present; local anesthesia was supplemented by intravenous sedation administered by an anesthesiologist. The needle was inserted into the nucleus pulposus via a lateral approach. The saline acceptance test was used. Discograms with metrizamide or iohexol were obtained in 30% of the patients, the majority of these during 1984. Then 1.5 ml of 3000 U Chymodiactin was injected into the disc over a period of 4 minutes. The needle was kept in place for 5 minutes then withdrawn. The patient was observed in the recovery room for 1 hour and was usually discharged the following day (average stay 1.4 days).

Discectomy was performed by a partial hemisemilaminectomy, removing disc fragments as thoroughly as possible. Foraminotomy was carried out routinely (average hospital stay 5.8 days).

Patients were examined at 6 weeks and 6 months postoperatively. A follow-up questionnaire was sent in January, 1989, 1 to 4 years after treatment; 104 (98.1%) of the 106 patients in the chemonucleolysis group and 68 (94.4%) of the 72 patients in the surgical discectomy group responded. A chi-squared test with a mini tab program was used to determine significance of differences.

Results

Eight criteria were used to evaluate patients postoperatively: back pain, including stiffness and spasm; sciatica; paresthesias; straight-leg raising; forward bending; sensory deficit; motor loss; and reflex changes. Based on improvement in pain, 82.7% of chemonucleolysis patients and 92.5% of laminectomy patients showed successful results 6 weeks postoperatively (Fig. 1). Clinical examination showed no statistically significant differences in improvement rate between the two procedures with the exception of forward bending and sensory improvement, which were better in the chemonucleolysis group (p = 0.0029 and p = 0.0039, respectively) (Fig. 2).

At 6 months postoperatively, 92.8% of the chemonucleolysis patients and 89.7% of the laminectomy patients showed successful results. No statistically significant differences were observed between the two procedures in any neurological symptom or sign (Figs. 3 and 4). At the 1- to 4-year follow-up review, complete relief of back and leg pain was comparable for the two procedures: 86.5% and 83.8% overall improvement for chemonucleolysis and laminectomy, respectively (Fig. 5). There is a statistically significant difference in outcome between patients receiving workers’ compensation and those not receiving compensation in both groups (chemonucleolysis (p = 0.0133 and laminectomy p = 0.0101).

Additional Postoperative Treatment

Since undergoing the procedure, six chemonucleolysis patients and four laminectomy patients have sustained a back injury. In the chemonucleolysis group, 11 patients (10.3%) required additional nonsurgical treatment; three received epidural injections, three chiropractic management, three physical therapy, and two bed rest. Nine patients (12.5%) in the laminectomy group had additional nonsurgical treatment. One received an epidural steroid injection, one chiropractic management, three physical therapy, and four bed rest.

Eight patients (7.6%) underwent laminectomy after failed chemonucleolysis. The interval between failed chemonucleolysis and laminectomy ranged from 1.4 to

50 months (average 21 months). Findings at operation were: extruded disc (two patients), protruded disc (three patients), protruded disc on the opposite side (one patient), cavitation (one patient), and spondylolisthesis (one patient). Postoperatively, two patients were asymptomatic, three exhibited marked improvement, two showed good improvement, and one was not improved.

Five patients underwent a repeat laminectomy after the first laminectomy failed. The interval between failed laminectomy and reoperation ranged from 2.5 to 25 months (average 17.5 months). Findings at operation were: extruded disc (one patient), protruded disc and scar (two patients), protruded disc on the opposite side (one patient), and protruded disc at another level (one patient). Postoperatively, one patient was asymptomatic, two had good improvement, and two showed slight improvement.

The results were successful in 87.5% of patients who underwent laminectomy after failed chemonucleolysis and 60% of patients who underwent a repeat laminectomy.
Follow-up study of chemonucleolysis and laminectomy

![Graphs showing improvement in pain at 6 months postoperatively in patients treated with chemonucleolysis (white columns, CNL) or laminectomy (black columns, Lami). A: Incidence of back pain in 101 chemonucleolysis and 60 laminectomy patients. B: Incidence of sciatica in 96 chemonucleolysis and 60 laminectomy patients. C: Incidence of paresthesias in 72 chemonucleolysis and 34 laminectomy patients. D: Results of evaluation of pain in 97 chemonucleolysis and 58 laminectomy patients.](image)

Fig. 3. Graphs showing improvement in pain at 6 months postoperatively in patients treated with chemonucleolysis (white columns, CNL) or laminectomy (black columns, Lami). A: Incidence of back pain in 101 chemonucleolysis and 60 laminectomy patients. B: Incidence of sciatica in 96 chemonucleolysis and 60 laminectomy patients. C: Incidence of paresthesias in 72 chemonucleolysis and 34 laminectomy patients. D: Results of evaluation of pain in 97 chemonucleolysis and 58 laminectomy patients.

ectomy after failed laminectomy. The difference is not statistically significant (p = 0.2483).

Employment Status

The majority (85.1%) of the chemonucleolysis patients were employed; 4.3% of these had to change jobs postoperatively. Similarly, 78.5% of the laminectomy patients were employed, with 12.5% changing jobs postoperatively.

Complications

Of the 106 chemonucleolysis patients, the only complication occurred in a patient who developed a rash 9 days after chemonucleolysis which cleared up within 24 hours. Of the 72 patients who underwent surgical dis-

![Graphs showing results of clinical examination at 6 months postoperatively in patients treated with chemonucleolysis (white columns, CNL) or laminectomy (black columns, Lami). A: Limitation of straight-leg raising in 87 chemonucleolysis and 56 laminectomy patients. B: Limitation of forward bending in 76 chemonucleolysis and 49 laminectomy patients. C: Incidence of sensory deficit in 87 chemonucleolysis and 56 laminectomy patients. D: Incidence of motor loss in 48 chemonucleolysis and 25 laminectomy patients. E: Incidence of reflex changes in 28 chemonucleolysis patients and 23 laminectomy patients.](image)

Fig. 4. Graphs showing results of clinical examination at 6 months postoperatively in patients treated with chemonucleolysis (white columns, CNL) or laminectomy (black columns, Lami). A: Limitation of straight-leg raising in 87 chemonucleolysis and 56 laminectomy patients. B: Limitation of forward bending in 76 chemonucleolysis and 49 laminectomy patients. C: Incidence of sensory deficit in 87 chemonucleolysis and 56 laminectomy patients. D: Incidence of motor loss in 48 chemonucleolysis and 25 laminectomy patients. E: Incidence of reflex changes in 28 chemonucleolysis patients and 23 laminectomy patients.
enzymatic dissolution of the nucleus pulposus. In the hands of surgeons experienced in the technique, it has proved to be a valuable alternative to surgical discectomy. Between 1963 and 1975, chymopapain (Discase) was used experimentally in the United States and Canada by 65 investigators in 17,000 patients; 72% of these had satisfactory results. Since approval of chymopapain by the FDA, chymopapain (Chymodectin) has been used in more than 270,000 patients. Results of published studies, especially from Europe, show an improvement rate of 80% to 85%.

Chemoneucleolysis vs. Laminectomy

In 1985, Nordby\textsuperscript{16} reported comparisons of laminectomy and chemoneucleolysis in eight published studies.\textsuperscript{1,2,4,5,6,19,20,26} In six of these, the composite result was a satisfactory outcome for 77.5% of chemoneucleolysis patients and 77% of discectomy patients; in two studies\textsuperscript{4,6} with randomized assignment of patients to receive surgery or chemoneucleolysis, the high percentage of failures after chemoneucleolysis raised a question of the potency of the enzyme Discase, which was obtained from the same source in Europe.\textsuperscript{16}

A comparison of laminectomy and chemoneucleolysis has been reported in six additional articles.\textsuperscript{1,2,9,10,18,24} In five of these,\textsuperscript{1,2,13,18,24} no statistically significant difference was found. In the study by van Alphen, \textit{et al}\textsuperscript{24} (a randomized study), laminectomy was found to be superior to chemoneucleolysis. In that study, posteriorography CT was not used as a criterion to exclude non-candidates and suspicion of a sequestered disc did not exclude a patient from the study (it is generally agreed that a sequestered disc is a definite contraindication to the performance of chemoneucleolysis). Failure to puncture the disc was given as a cause of unsatisfactory outcome, but should not have attributed to the ineffectiveness of chemoneucleolysis since no enzyme was injected. In addition, as noted by Keet,\textsuperscript{11} the authors' assessment of posttreatment failures and subsequent surgery was based primarily on physician opinion rather than patient input. During the first posttreatment year, the need for surgical intervention after failed chemoneucleolysis was inordinately high compared with that for failed laminectomy (25% vs. 3%). It should be noted that patient assessment 12 months after final treatment showed an unsuccessful result in 16 (20.8%) of 77 patients treated with open surgery and in 20 (27.3%) of 73 patients treated with chemoneucleolysis; yet, only two (3%) in the open-surgery group underwent reoperation, whereas 18 (25%) in the chemoneucleolysis group were subjected to surgery.

This discrepancy in the ratio of discectomy performed after failed chemoneucleolysis versus repeat discectomy after failed laminectomy is not in conformity with the experience of the majority of surgeons in the United States and abroad. Even when comparing patients treated before the advent of CT, 11 series published between 1961 and 1984 and encompassing 3485

\textbf{Stiffness and Spasm}

Immediately after injection of chymopapain, 50% of the patients complained of stiffness in their backs, 4% of spasm, and 31% of both; only 15% had neither stiffness nor spasm. The stiffness or spasm ranged from very mild to very severe. At 6 weeks after chemoneucleolysis, 28% of patients suffered from stiffness, 4% from spasm, and 2% from both; 66% were free of both stiffness and spasm. Six months after chemoneucleolysis, 6% had stiffness, 2% had spasm, and 2% had both; 90% of patients had neither stiffness nor spasm.

\textbf{Discussion}

Since the introduction of chemoneucleolysis in 1964 by Lyman Smith,\textsuperscript{25} chymopapain has been used and studied extensively in the United States and abroad for

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\caption{Graphs showing improvement in pain at 1 to 4 years postoperatively in patients treated with chemoneucleolysis (white columns, CNL) or laminectomy (black columns, Lami). A: Incidence of back pain in 104 chemoneucleolysis and 68 laminectomy patients. B: Incidence of leg pain in 104 chemoneucleolysis and 68 laminectomy patients. C: Incidence of paresthesias in 81 chemoneucleolysis and 55 laminectomy patients. D: Results of evaluation of pain in 104 chemoneucleolysis and 68 laminectomy patients.}
\end{figure}
Follow-up study of chemonucleolysis and laminectomy

patients who underwent chemonucleolysis (using Disease) reported a 12% frequency of laminectomy after unsuccessful chemonucleolysis, compared to 7% after unsuccessful laminectomy in 16 studies published during the same period and including 10,502 patients.10

In the present study, the percentage of patients undergoing surgery following chemonucleolysis or laminectomy during the 1st year after treatment is identical for both procedures (3%). After 1 to 4 years, the percentage was 7.6% for chemonucleolysis compared to 7.3% for laminectomy. This clearly shows how judicious use reduces the number of chemonucleolysis patients requiring subsequent surgery to a level similar to that after failed laminectomy and discectomy.

Neurological Complications

In the United States, serious neurological complications due to poor technique and consequent malpractice suits have prompted the majority of surgeons to abandon chemonucleolysis. In each malpractice case brought by a patient who had serious complications from chemonucleolysis, exhaustive investigation revealed that the operating surgeon had performed 10 or fewer chemonucleolysis procedures (Boots Pharmaceutical, personal communications, 1991).

Currently, the procedure is being performed primarily by experienced surgeons in the United States. Wright and Nordby11 have reported the following statistics: between 1982 and 1985, there were 57 serious neurological complications due to chymopapain injection; in 1986, there were five. Intrathecal injection was documented in many of these patients. Included in the neurological complications were six patients with alleged acute transverse myelitis; only two patients and possibly a third fit the criteria for acute transverse myelitis.12 Since April, 1984, no such case has been described. Only one patient with neurological complication has been reported since 1987; this was due to documented intrathecal injection of the enzyme by a surgeon with limited chemonucleolysis experience. Anaphylaxis is no longer a serious potential complication, with only one death reported since 1986. This improvement is due to the routine use of Chemofast and administration of H1 and H2 antagonists before the chemonucleolysis procedure which antagonizes histamine effects on H1 and H2 receptors.

Stiffness and Spasm

An undesirable side effect of chymopapain is stiffness and spasm, which differs from back discomfort after surgery. In the author’s experience, this was more severe when 2 ml (4000 U) chymopapain was used. Patients in the present study received 3000 U of Chymodiactin, resulting in less severe stiffness and spasm. Some surgeons have injected the low dose of 500 U with reported successful results. Further studies are underway to determine the optimum dosage. Stiffness and spasm occur with both Disease and Chymodiactin; however, in our experience these symptoms are more intense with Chymodiactin in an equal dose. The only difference between the two preparations is that Chymodiactin does not contain sodium bisulfite and edetic acid.10 However, Chymodiactin is more potent and more effective than Disease; the increased stability of Chymodiactin maintains its potency.15,23

When comparing chemonucleolysis with surgical discectomy, it is important to bear in mind that laminectomy is an open procedure. The majority of patients treated with laminectomy experience immediate relief of sciatica, whereas the effectiveness of chemonucleolysis may take longer. The effect of the enzyme, although immediate in the majority of patients, may not become evident in some patients for several days or a few weeks. In a small number of patients, sciatica may recur in about 2 weeks after chemonucleolysis, lasting a few days or longer. In discussions of both procedures with the patient, it is important to stress that pain relief is more prompt after laminectomy than after chemonucleolysis. At 6 weeks, although the improvement rate for sciatica is still better in laminectomy patients, the difference is not statistically significant. A major disadvantage of surgical discectomy is postoperative fibrosis, which may occur in a significant number of patients. This serious problem does not occur after chemonucleolysis.3,7,8,23

Morbidity and Mortality

The morbidity and mortality rates due to chemonucleolysis are well documented. However, comparable data are not available for surgical discectomy, and the majority of serious complications remain unreported in the United States. The only exception is the study by Ramirez and Thisted,20 which provided statistical data on death and complications due to laminectomies performed in the United States on 28,395 patients during 1980. These data indicate a morbidity rate of 1.57% and a mortality rate of 0.059% for surgical discectomy. The data for chemonucleolysis indicate a morbidity rate of 0.399% and a mortality rate of 0.02%.15

Diagnostic Value of Postmyelography CT

Before 1975, the author treated 124 patients with chymopapain (Disease) injection. One year after chemonucleolysis, 110 patients (patients with and without workers’ compensation with no previous back surgery) showed an overall improvement rate of 77.3%. In the present study using Chymodiactin, the overall improvement rate for comparable patients at 1 year is 89.5%; this difference is statistically significant (p = 0.0149).

The improvement in results is attributable to refinement in diagnostic technique, especially postmyelography CT, which led to more stringent patient selection. By routine employment of this diagnostic tool, the majority of noncandidates for chemonucleolysis can be eliminated, allowing a more accurate comparison of chemonucleolysis and laminectomy.
Conclusions

The results of this study demonstrate how stringent selection of patients through appropriate diagnostic screening makes chemonucleolysis an attractive alternative to surgical discectomy. Given more experience with chemonucleolysis and refinement of technique, magnetic resonance imaging will probably replace myelography-CT in most patients in the future. However, in the author's opinion, myelography-CT is currently the gold standard in eliminating noncandidates for chemonucleolysis.

Neither laminectomy nor chemonucleolysis is a panacea. Unfortunately, chemonucleolysis has undeservedly been given a bad reputation based on the results of inexperienced surgeons who performed the technique poorly and on patients selected inappropriately. However, chemonucleolysis should not be abandoned as it offers an effective, less invasive alternative to laminectomy when patients are appropriately selected and the surgeon is experienced in the technique. Because herniated disc management constitutes the major portion of neurosurgical practice in the United States, in the interest of expanding clinical options, additional research is warranted to further refine chymopapain or to find another effective agent that does not produce side effects.

References


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