Efficacy of chymopapain chemonucleolysis

A long-term review of 105 patients

MANUCHER J. JAVID, M.D.
Division of Neurological Surgery, University of Wisconsin Clinical Science Center, Madison, Wisconsin

A 9- to 12-year follow-up review was conducted in 105 of 124 patients who were treated with chymopapain chemonucleolysis for herniated lumbar disc. The data were obtained from responses to a questionnaire. Seventy-nine patients (75.2%) reported marked improvement, six (5.7%) had slight improvement, and 20 (19.0%) had no improvement. Of the 87 patients not receiving workman’s compensation, 70 patients (80.5%) had marked improvement; four (4.6%) had slight improvement; and 13 (14.9%) had no improvement. Of the 18 compensation cases, nine patients (50.0%) had marked improvement; two patients (11.1%) had slight improvement; and seven patients (38.9%) had no improvement. These results are comparable to those reported for surgical discectomy, and confirm that chymopapain chemonucleolysis is an alternative to surgery.

KEY WORDS • intervertebral disc • lumbar spine • chymopapain • chemonucleolysis • outcome

Between 1972 and 1975, 124 patients with a herniated nucleus pulposus and sciatica were injected intradiscally with chymopapain (Discase) at our institution. In 1978, a questionnaire was sent to these patients and 114 responded. The 3- to 6-year follow-up results were published in 1980. In November, 1982, the Food and Drug Administration (FDA) approved the intradiscal injection of chymopapain based on the result of a double-blind study with Chymodiactin performed in seven major medical centers throughout the United States. That study established the safety and efficacy of chymopapain chemonucleolysis.

Recently, another questionnaire (Fig. 1) was sent to the original 124 patients to obtain 9- to 12-year follow-up results of therapy. Responses were received from 105 patients, 85% of the total number. The results are reported here.

Clinical Material and Methods
Chemonucleolysis was performed in 124 patients, 77 men and 47 women, ranging in age from 17 to 64 years. The average age was 42.2 years. All patients had sciatica which had not responded to conservative therapy, and were prime candidates for surgery. Twenty patients were receiving workman’s compensation, and 14 had previously undergone a laminectomy. Of the 105 patients who returned the questionnaire, 69 were men and 36 were women. Twelve of these 105 patients had submitted to laminectomy before chemonucleolysis. Eighty-seven had not received workman’s compensation, including seven patients who had previously undergone laminectomy, and 18 received workman’s compensation, including five patients with previous laminectomy. The details of patient selection methods, drug preparation, intradiscal injection technique, and complications have been reported previously.

We define the term “marked improvement” to include patients who were freed of pain and those with excellent and with good results. This is the same terminology used in the protocol of the clinical trial by Travenol Laboratories.

Results
Table 1 shows the overall results. Of 105 patients, 79 (75.2%), including four who had had a previous laminectomy, had marked improvement; six patients (5.7%), including one with a previous laminectomy, had slight improvement; and 20 patients (19.0%), including six patients who had undergone a previous laminectomy, had no improvement. In noncompensa-
Chymopapain Information Request

With the approval of Chymodiactin® (chymopapain) by the Food and Drug Administration (FDA) in November, 1982, there is interest in determining the progress of those injected prior to 1975. Providing this information will be appreciated and will be a further contribution by you toward improving care of the back with leg pain.

Name: ______________________ Tel. No. __________(Res.) __________(Work)
Address: ______________________

1. Present occupation: ______________________________________________________

2. Did you change work because of back trouble since your injection? Yes____ No____
   If so, explain.

3. Are you now employed? Yes ____ No ____ If not, is it related to your back problem?

4. Have you hurt your back since your injection? Yes ____ No ____
   If so, explain.

5. Have you had additional treatment since chymopapain injection?
   Yes ____ No ____
   If surgery, diagnosis and date: __________________________________________
   If medical, diagnosis and type of treatment: ________________________________

6. How do you grade pain relief following your back injection?
   Excellent (More than 85% relief) ____    Good (50-85% relief) ____
   Fair (25-50% relief) ____    No relief ____

7. Do you have pain at present? Yes ____ No ____ If yes, sketch in pain pattern below.

8. How long have you had your present pain?
   ______________________________

9. What causes your pain?
   Forward bending ____
   Sitting or riding ____
   Lifting ____
   Arching of back ____
   Walking (How far?) ____
   Strenuous exercise ____

10. Would you agree to a lateral lumbar x-ray (side view) at no cost to you?
    Yes ____ No ____

11. Additional comments (use the back of this sheet, if necessary):

Please return this questionnaire in the envelope provided.
Thank you for your cooperation.

Fig. 1. Questionnaire sent to 124 patients 9 to 12 years after undergoing chymopapain chemonucleolysis for herniated lumbar disc.
TABLE 1
Outcome in 105 patients assessed 9 to 12 years after chemonucleolysis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Overall</th>
<th>Noncompensation</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>marked improvement</td>
<td>79</td>
<td>75.2</td>
<td>70</td>
</tr>
<tr>
<td>pain-free</td>
<td>53</td>
<td>50.5</td>
<td>48</td>
</tr>
<tr>
<td>excellent (&gt; 85%)</td>
<td>14</td>
<td>13.3</td>
<td>12</td>
</tr>
<tr>
<td>good (50%-85%)</td>
<td>12</td>
<td>11.4</td>
<td>10</td>
</tr>
<tr>
<td>slight improvement</td>
<td>6</td>
<td>5.7</td>
<td>4</td>
</tr>
<tr>
<td>no improvement</td>
<td>20</td>
<td>19.0</td>
<td>13</td>
</tr>
<tr>
<td>total cases</td>
<td>105</td>
<td>100.0</td>
<td>87</td>
</tr>
</tbody>
</table>

Table 2 shows overall results in the same patients 1 year post-chemonucleolysis at which time evaluation was performed in the physician’s office, and at 3 to 6 years and 9 to 12 years when patients were evaluated by questionnaire. At 1 year there was marked improvement in 81 patients (77.1%), at 3 to 6 years 76 patients (72.4%) had marked improvement, and at 9 to 12 years 79 patients (75.2%) reported marked improvement. Table 3 shows results in 87 noncompensation cases. Marked improvement was recorded in 73 patients (83.9%) after 1 year, in 71 (81.6%) at 3 to 6 years, and in 70 (80.5%) at 9 to 12 years. Table 4 shows results in 18 workman’s compensation cases. Marked improvement was reported after 1 year in eight patients (44.4%), at 3 to 6 years in six patients (33.3%), and at 9 to 12 years in nine patients (50.0%). Seventeen patients underwent laminectomy after failed chemonucleolysis, and all of them are listed under the “no improvement” category. Table 5 shows the results obtained at 9 to 12 years following laminectomy. Eleven patients had marked improvement, two had slight improvement, and four patients remained unimproved.

The answers to Questions 4 and 5 on the questionnaire showed that 27 patients had reinjured their backs since chymopapain injections. Eight received no treatment, six underwent subsequent laminectomy, and 13 were treated conservatively. Nineteen patients who did not reinjure their back required additional treatment. Of these, 11 had laminectomy and eight were treated conservatively.

Table 6 shows that, of the 105 patients, 61 (58.1%) are employed full-time, 13 (12.4%) have retired, 16 (15.2%) perform housework, and 12 (11.4%) are unemployed (unemployment is pain-related in six patients). The employment status of three patients is unknown. Table 7 shows the incidence of symptom-related occupation changes. Eighty-four patients (80%) were able to return to the same job. Fifteen (14.3%) had to change their occupation to less physically demanding jobs, and for six patients (5.7%) this information is not available.

**Discussion**

The safety and efficacy of chymopapain chemonucleolysis have been well established since its introduction by Lyman Smith in 1964 for the management of herniated lumbar disc syndrome. A number of orthopedic and a few neurological surgeons who were involved with the experimental use of this enzyme prior to 1975 have published reports of their experience, but few publications report long-term follow-up results. Parkinson has published his results with 33 patients 12
Long-term follow-up results of chemonucleolysis

years after chemonucleolysis. Seventy-five percent of these patients continue to maintain their improvement. The results of long-term follow-up review of the present series corroborates Parkinson's favorable results, with overall improvement maintained in 75.2% of 105 patients (80.5% in noncompensation cases; 50.0% in compensation cases). In differentiating between compensation and noncompensation cases, whether or not a claim was settled, we acknowledge the widely accepted view that compensation patients do not do as well as noncompensation patients, whatever procedure they undergo.

Although the purpose of this paper does not include a review of the risks and complications of chemonucleolysis, which are reviewed elsewhere, for the sake of thoroughness the major complications of this procedure will be briefly recapitulated. Early reports of anaphylaxis associated with this procedure have not been substantiated as a big risk by subsequent experience. Since 1982, when Chymodiactin was approved by the FDA for intradiscal injection of lumbar disc herniation, about 85,000 patients have been treated with this drug (K Agre, personal communication, 1984). The incidence of anaphylaxis in these patients has been 0.6% for those who underwent the procedure under general anesthetic, and 0.4% for those anesthetized locally. There were two anaphylaxis-related deaths in the Illinois experimental trials prior to FDA approval, and three deaths among the 85,000 patients injected since the FDA approval. We have injected 159 patients with Chymodiactin using a combination of local anesthesia and intravenous sedation: only one case of anaphylaxis occurred and this was mild and treated successfully. None of the original 124 patients injected with chymopapain had an anaphylactic reaction, despite the fact that all these patients had general endotracheal anesthesia. Three complications occurred in our series of 124 patients. One patient had numbness in the right leg and foot; a second patient developed paralytic ileus; and a third patient developed a partial radial nerve palsy from his positioning on the operating table.2

Among the 85,000 patients injected with Chymodiactin, there have been 40 cases of serious neurological complications including subarachnoid hemorrhage, cerebrovascular accidents, and paraplegia (K Agre, personal communication, 1984). As reported in two memoranda from Smith Laboratories, Inc., sent in June and July, 1984, to all orthopedic and neurological surgeons, most of these incidents are due to inappropriate patient selection and procedural and technical errors. Another serious complication, acute transverse myelitis, has occurred at the rate of one of every 17,000 patients injected with Chymodiactin. The cause of this complication is unknown. None of the chemonucleolysis patients in this series has suffered any of the above neurological complications as a result of the procedure.

For safety and success, it is imperative that strict criteria be employed in the selection of patients and in the performance of this procedure. Every patient who is a candidate for chemonucleolysis is also a candidate for surgery, but the reverse is not true. All of the patients reported in this study were treated with chemonucleolysis prior to the development of computerized tomography (CT). The results of chemonucleolysis can now be improved by using CT to eliminate patients who are not candidates for chemonucleolysis but who are candidates for surgery. These include patients with lateral recess syndrome, spinal stenosis, facet arthropathy, instability syndrome, and sequestered disc that has migrated. A differential diagnosis can be accomplished in

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TABLE 5
Results of laminectomy after failed chemonucleolysis*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Total Cases</th>
<th>Noncompensation Cases</th>
<th>Compensation Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>marked improvement</td>
<td>11</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>pain-free</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>good</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>slight improvement</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>no improvement</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>total cases</td>
<td>17</td>
<td>12</td>
<td>5</td>
</tr>
</tbody>
</table>

* Results at 9 to 12 years after laminectomy are given. "Laminectomy" includes all forms of operation (lateral recess stenosis, spinal stenosis, and discectomy at another level).

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TABLE 6
Patients' employment status 9 to 12 years after chemonucleolysis

<table>
<thead>
<tr>
<th>Employment Status</th>
<th>Overall</th>
<th>Noncompensation</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>employed</td>
<td>61</td>
<td>58.1</td>
<td>56.4</td>
</tr>
<tr>
<td>retired</td>
<td>13</td>
<td>12.4</td>
<td>12.6</td>
</tr>
<tr>
<td>housework</td>
<td>16</td>
<td>15.2</td>
<td>17.2</td>
</tr>
<tr>
<td>unemployed*</td>
<td>12</td>
<td>11.4</td>
<td>11.5</td>
</tr>
<tr>
<td>unknown</td>
<td>3</td>
<td>2.9</td>
<td>2.3</td>
</tr>
<tr>
<td>total cases</td>
<td>105</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

* In six patients (four noncompensation, two compensation) unemployment was related to pain.

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TABLE 7
Symptom-related occupation changes 9 to 12 years post-chemonucleolysis according to patient's employment categories

<table>
<thead>
<tr>
<th>Occupation Status</th>
<th>Overall</th>
<th>Noncompensation</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>same</td>
<td>84</td>
<td>80.0</td>
<td>72</td>
</tr>
<tr>
<td>changed</td>
<td>15</td>
<td>14.3</td>
<td>11</td>
</tr>
<tr>
<td>unknown</td>
<td>6</td>
<td>5.7</td>
<td>4</td>
</tr>
<tr>
<td>total cases</td>
<td>105</td>
<td>100</td>
<td>87</td>
</tr>
</tbody>
</table>
most patients, especially by a combination of metrizamide myelography and post-contrast CT scanning.

All candidates for chemonucleolysis must have low-back pain and sciatica which have not responded to conservative measures. Patients who have back pain without sciatica are not candidates for chemonucleolysis. Only the lateral injection approach introduced by Brown should be used. Other approaches are unacceptable. Under no circumstances is intrathecal insertion of the needle permissible.

When these guidelines are scrupulously followed, the results of long-term experience confirm what has been observed over the short term: namely, that chymopapain chemonucleolysis is an alternative to surgical discectomy with a comparable record of success.

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References


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