Efficacy and Safety of Chymopapain Versus Laminectomy

To the Editor: Dr. Javid is to be commended for the candid honest evaluation of his results in a long-term follow-up by questionnaire of a series of patients treated with chymopapain (Javid MJ: Efficacy of chymopapain chemonucleolysis. A long-term review of 105 patients. J Neurosurg 62:662-666, May, 1985). He has been one of the few surgeons who appears to demand specific indications for this technique, although 18 of the 105 patients treated received workman’s compensation — an inordinately high percentage, since very few significant disc ruptures follow trauma.

Dr. Javid also states that “every patient who is a candidate for chemonucleolysis is also a candidate for surgery, but the reverse is not true.” This is a refreshing change from the erroneous concept of most advocates of intradiscal therapy that the ideal candidate for chemonucleolysis is also the ideal candidate for surgery. He has apparently also limited the injection to one level, rather than performing the multilevel injection to which many thousands of patients have been subjected.

Dr. Javid’s forthright report gives further evidence, however, that this hazardous procedure has nothing to recommend it. His poor results should be interpreted in the same light as those of the collaborative study reported by Javid, et al., in 1983. Among the seven centers in which chymopapain was tested, there were three in which it proved no better than the placebo (in one of these the placebo was distinctly better). Furthermore, treatment was deemed a success if the result was excellent, good, or fair. Patients with a fair result reported that they were able to do only very light work and had pain requiring moderate or strong analgesics.

Taking the same liberties, Dr. Javid now tells us in the current article 2 years later that, among 79 patients who showed “marked” improvement, there were 12 classified as “good:” this means 50% to 85% relief of pain 9 to 12 years after chemonucleolysis. Excluding these 12 patients who fared no better in this period of time than they would have with no treatment at all actually leaves just 67 patients with “marked improvement” (his “pain-free” or “excellent” category), thus giving a 64% improvement rate, not 75%. In a group of 17 patients who had laminectomy after failed chemonucleolysis, only 11 (64%) were considered improved. Limiting this group also to “pain-free” or “excellent” (an outcome expected by many surgeons) leaves only five patients — a surgical improvement rate of 29%! Obviously these data raise serious concern about selection criteria, surgical methodology, or both. The other possibility, of course, is that the enzyme injection drastically reduces the chance of success from subsequent surgery.

To consider these results comparable to those of surgical discectomy totally ignores all of the significant advances that have been made in the selection of patients and in surgical technique during the past 50 years. Such unfavorable outcome as Javid has reported does not begin to compare with the results of Scoville and Corkill or my own review of the most complicated types of ruptured discs; in both of those series, excellent pain-free recovery was achieved in well over 90% of patients. This type of success is not unique and is experienced by most neurosurgeons.

As for morbidity and mortality due to chymopapain, we are still asked to accept statements that can only be considered misleading. In the initial publication from Smith Laboratories, there were 11 deaths and 11 cases of paraplegia supposedly among 60,000 patients, although data were actually available on only 29,075 patients. Now Dr. Javid tells us that, “among the 85,000 patients injected,” there have been 40 cases of serious neurological complications. There are, of course, no published data on all 85,000 patients. If such data were obtained, the number of serious and fatal complications could prove to be much higher. The questionnaire sent to neurosurgeons early this year disclosed that more than half of the neurosurgeons who had ever used chymopapain no longer perform chemonucleolysis. Among those responders who had experience with the procedure, 87% found it less efficacious than surgery and 60% found it less safe than surgery.

The prospective study planned by the Joint Section on Spinal Disorders of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons is long overdue and should confirm that appropriate surgery on those selected patients who require treatment is more effective and far safer.

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References
of chymopapain (Chymodiactin) in herniated nucleus pulposus with sciatica. Results of a randomized, double-blind study. JAMA 249:2489-2494, 1983

RESPONSE: Dr. Fager's kind opening remarks acknowledging the forthright nature of my paper appear to be a refreshing change from his usual unremitting criticism of chymopapain chemonucleolysis. However, the remainder of his letter is as condemnatory as ever. In it, he continues to ignore facts that do not confirm his bias, and skewes yet others to accommodate his preconceptions.

Dr. Fager begins with unsubstantiated criticism of my 9- to 12-year follow-up study of chemonucleolysis patients by stating his opinions as fact in comments such as “... his hazardous procedure” and “His poor results ...”. In addition, he takes to task the percentage of my patients who were receiving workman's compensation, termsing 18 (16%) of 105 patients “an inordinately high percentage.” According to Dr. Frank Mayfield, the percentage of workman's compensation cases requiring laminectomy is much higher than 16% (personal communication, June, 1985).

Dr. Fager also questions the validity of the patient questionnaire we used in compiling our follow-up data. Although our patients replied subjectively as to whether they considered their outcome to be excellent, good, or fair, a subjective assessment in a follow-up study such as this is a valid measure of improvement since the primary aim of treatment is the relief of pain. (This was a 9- to 12-year follow-up evaluation of a series of patients that had already been reported, with many details from the earlier report omitted.) Dr. Fager makes a point of singling out the 12 patients who were categorized as having “good” improvement and a priori discounts them as treatment failures. Despite the fact that two of them had undergone unsuccessful laminectomy prior to chymopapain injection (now considered a contraindication for performing chemonucleolysis), three had received workman's compensation, and four indicated on the questionnaire that they had hurt their backs since chemonucleolysis, all 12 have enjoyed substantial improvement that cannot be credited to time alone. None has had sciatica, six are working full-time, three are able to perform normal housework, and one worked until he retired. Only two patients are not working.

Next, Dr. Fager takes issue with the fact that 17 patients had laminectomy after chemonucleolysis. Five of these 17 patients had a failed laminectomy prior to chemonucleolysis and five received workman's compensation. It is well established that both of these factors decrease considerably the success rate of subsequent treatment. Therefore, by misrepresenting the criteria for good improvement, then discounting the patients in this category as experiencing no improvement, and then switching the focus from the larger sample of chemonucleolysis patients to the smaller group of 12 patients who had laminectomy following failed chemonucleolysis, he misleadingly concludes that the improvement rate was only 29%, as if this were a comparable patient base to the larger sample.

The very same “significant advances...in selection of patients and in surgical technique” that Fager mentions in relation to laminectomy are just as true for chemonucleolysis. At the time that the patients in our long-term follow-up study were injected, we did not have the benefit of today's refined selection criteria or pretreatment diagnostic tools. For instance, today we would not inject patients who have had previous failed laminectomy, or if there is any suggestion of disorders such as lateral recess stenosis, spinal stenosis, or migrated disc fragments.

Dr. Fager suggests that it is possible that “enzyme injection drastically reduces the chance of success from subsequent surgery.” Data from both the double-blind study upon which the Federal Drug Administration (FDA) based its approval of chymopapain and the report by McDermott, et al., indicate that quite the opposite is true. As reported in that double-blind study, six of eight chymopapain-failure patients underwent surgery. Follow-up information was available for four of the six, each of whom responded well to surgery. As reported in the study by McDermott, et al., within the 6-month time frame of their investigation only 4.1% of the patients underwent surgery and, of these, 61.3% had improved sufficiently by the time of their final examination for the physician to rate their outcome as either “good” or “excellent.” Moreover, half of the remaining 38.7% were patients whose surgery had occurred less than 6 weeks before their final study visit. Of the 46 patients who underwent surgery 3 months or more before their final evaluation (after a failed response to chymopapain), 38 (83%) had a “good” or “excellent” result.

I am hard-pressed to understand Dr. Fager's claim to “well over 90%” success rate for laminectomy when, in his own paper, he claims 85% recovery. As for the article by Scoville and Corkill which Fager also mentions, the only thing that they state regarding their results is that 95% of patients "so treated experienced good to excellent results, and 90% were able to return to their previous occupation." Although Dr. Fager extricates us for the criteria used to assign patients to the "good" category, nowhere in either his paper or that of Scoville and Corkill do we learn how or why their patients were rated. I suggest that Dr. Fager send a questionnaire to his patients similar to the one we used if he is interested in a truly equitable comparison between our results. There are no recent long-term follow-up studies after laminectomy similar to the 9- to 12-year Wisconsin follow-up after chemonucleolysis. The