The case for chemonucleolysis in discogenic sciatica
A review

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Is it possible that a new study will change the present view, that in the treatment of discogenic sciatica the results after ten years are pretty much the same whether any definite treatment is given or not (Hakelius 1970, Weber 1983, Nachemson and Rydevik 1988, Nordby 1989)?

In a double-blind study Gogan and Fraser (1992) evaluated the effects of chemonucleolysis at 10 years versus placebo/natural history of herniated discs. There were no code breaks or exclusions. 24 of the 30 chymopapain patients regarded the intradiscal injection as successful compared to 9 of 26 patients of the placebo (saline) group. The conclusion of this study was that at 10 years intradiscal chymopapain injection is superior to the natural history. So far, this superiority has not been shown for operative treatment (Hakelius 1970, Weber 1983). However, nearly 30 years after the first human disc was injected with chymopapain (Smith 1964), the treatment is still controversial (Nachemson and Rydevik 1988, Nordby 1989). In itself this tells something of the viability of the procedure.

It is well appreciated that intradiscal injection of chymopapain hydrolyzes the cementing protein of the nucleus pulposus (Stern 1985), reducing its water binding capacities with resultant disc narrowing and, temporarily, affecting its mechanical behavior (Wakano et al. 1983, Spencer et al. 1985). The effect on the nucleus pulposus occurs within the first 3 days (Dolan et al. 1987, Muralikuttan et al. 1991). Tissue digestion is dose-related (Stern 1985) and can be measured by the serum levels of keratan sulfate before and after injection (Muralikuttan et al. 1991, Williams et al. 1991). It is postulated that a reduction in nuclear size will reduce nerve root pressure, but in spite of many studies its mode of action in relieving sciatic pain remains unclear. In a prospective CT-study it has been shown that in two thirds of the patients the compression of the herniated disc was reduced at 3 months, and in nearly all patients at 12 months. The reduction in disc height was on average one quarter (Konings et al. 1984, 1986). However, in a substantial percentage effectiveness of chemonucleolysis is accomplished with minor initial changes in the size or appearance of the disc herniation (Gentry et al. 1985, van Leeuwen and Hoogland 1991). On MRI scanning a complete loss of nuclear signal due to the loss of water content takes at least 6 weeks and corresponds to a maximum reduction in disc height (Szypryt et al. 1987); a correlation between clinical success and decrease in the size of the hernia is doubtful (Masaryk et al. 1986, Huckman et al. 1987). CT and MRI examinations performed within several weeks of lumbar discectomy have shown a soft tissue mass on the operated side mimicking pre-operative findings in the majority as well (Ross et al. 1987, Ilkko et al. 1988).

Following chemonucleolysis and discectomy, neither CT or MRI examination in the (immediate) post-operative period provide information about the etiology of persistent pain.

In young animals, an injected, healthy disc may regenerate (Bradford et al. 1983, Nitobe et al. 1988) and result in disc reexpansion. On the contrary, under similar conditions surgical excision ultimately results in irreversible disc-space narrowing (Lipson and Muir 1980, 1981). Clinical reexpansion of a narrowed disc after chymopapain injection has not been recorded consistently. This probably depends on the degree of degeneration of the injected disc.

There is no question that, if used properly, chymopapain is indicated in the treatment of unremitting sciatica, caused by a herniated disc. The ideal patient for chymopapain chemonucleolysis is also the ideal candidate for surgical discectomy. Discussion about intradiscal injection of chymopapain can be related to the questions of safety, effectiveness and comparison of these with other definitive treatments used to relieve sciatica. Chymopapain, if used intradiscally, is a safe procedure.
drug. If injected intrathecally it causes a rapid rise in CSF pressure, probably because of capillary bleeding and in time the microcirculation of nerve tissue may be interrupted. Chymopapain in itself is not neurotoxic (Stern 1985, Nordby 1989). Complications in chemonucleolysis are short-term and limited to the operative and immediate postoperative period. There is no long term effect (Parkinson 1983, Nordby 1986a, Tregonning et al. 1991). In a personal series of more than 1200 patients treated with chymopapain, complications of any significance were recorded in 9 patients (0.8 percent). The most important were gastric bleeding because of NSAID use, pulmonary embolism, and discitis; no major anaphylactic reaction was recorded. Statistics for the complications in chemonucleolysis are perhaps more accurate than in any other disc-directed procedure (Nordby 1989). Complications are at least two to six times as frequent after lumbar discectomy (Rameriz and Thisted 1989, Bouillet 1990). Chymopapain does not cause epidural fibrosis (Nordby 1983, Konings et al. 1984). On exploring the lumbar canal after chemonucleolysis no abnormality is found in the epidural space, the dura, or around the nerve roots as a result of chymopapain (Carruthers and Kousaie 1982, Roggendef et al. 1984, Deburge et al. 1985, Burkus et al. 1988). Epidural fibrosis is a well known finding after operative treatment, although the clinical importance is questionable. However, if one accepts the axiom, that after surgery it is difficult to differentiate between symptomatic scarring and recurrent disc herniation (Wilminck and Roukema 1987, Ilkko et al. 1988), the implication is that scarring can be symptomatic.

It is claimed that surgery remains the scientifically proven treatment of choice (Nachemson and Rydevik 1988). However, probably no treatment for the herniated disc has been scientifically explored so thoroughly as chemonucleolysis. The scientific facts: At least two double-blind randomized prospective studies have shown the superiority of chymopapain in comparison with placebo (Fraser 1984, Javid et al. 1983). Presently, one of these studies has been extended to 10 years (Gogan and Fraser 1992). Numerous open clinical studies have shown the effectiveness of chemonucleolysis in the treatment of the symptomatic herniated lumbar disc.

A compilation of long-term results in 3130 patients showed satisfactory results in 77 (71-93) percent (Nordby 1986). Success rates of studies, performed in The Netherlands, were between 72 and 94 percent (Wilms et al. 1986, Dekker 1987, van Leeuwen 1989, Hofstra et al 1991). The best results were seen in the herniated adolescent disc and "when all criteria for a herniated disc were met" (Dekker 1987). Although some authors believe chymopapain is contraindicated in the elderly (Spencer 1990), two studies on lumbar disk herniation in patients over 60 years have shown a high rate of success (Deutman and Douma 1988, Benoist et al. 1992). Recently several investigators showed a low dose (2000 pKat units) of chymopapain to be as effective as the recommended standard dose (4000 pKat units), but with less serious side-effects (Bonneville 1991, Wardlaw 1991). The minimum concentration of chymopapain required to degrade proteoglycans in the nucleus pulposus is not known.

In comparison, a review of papers on patients treated by laminectomy reported a similar success rate of 77 percent (Rameriz and Javid 1985). In The Netherlands Habberman et al. (1989) compared, in a well designed prospective study (492 patients), the situation after a root decompressing operation with the situation before surgery at one year. About 75 percent of the patients reported satisfactory improvement. The best results were obtained in 361 patients in whom the preoperative diagnosis of lumbar disc herniation was highly probable (79 percent satisfactory improvement). Radiating pain persisted in 35 percent. Back-pain persisted in 36 percent and increased in 7 percent. About half of the patients who were on sick leave before operation resumed work afterwards.

There are some studies comparing the effect of chemonucleolysis with that of surgery. Two studies showed the superiority of surgery (Ejeskar et al. 1983, Crawshaw et al. 1984). Inactive enzyme could have been the reason (Nordby 1989); a possibility supported by the 50 percent failure rate in the study by Ejeskar et al. (1983). In contrast, 3 studies on chemonucleolysis in The Netherlands reported secondary operative treatment at one year in 3-12 percent (Dekker 1987, Van Leeuwen 1989, Konings 1990). In a randomized clinical trial the outcome of open discectomy was compared with that of chemonucleolysis (van Alphen et al. 1989). A comparison of the final results of the two modes of treatment 12 months after the last intervention (including second treatment) did not reveal any differences. However, within a follow-up period of one year, 18 of the 73 chemonucleolysis patients had had open discectomy and 2 of the 78 patients in the discectomy group. In analyzing this study, it becomes apparent that failure after chemonucleolysis was followed by operation much more often (16 of 27) than failure after surgery (2 of 18) (Keet 1988). Success of open surgery, following failed chemonucleolysis, was seen in only 7 of the 16 patients. In contrast to the above-mentioned studies, prospective studies by Lavignolle et al. (1987), Alexander et al. (1989) and Javid (1992) showed similar results after chemonucleolysis and open discectomy. The first of these three studies was randomized, and in the other two studies the choice between chemonucleolysis and
surgical discectomy was left to the patient. In many studies the final results of surgery in chymopapain failures are as good as first-time discectomy (Deburge et al. 1985, Alexander et al. 1989).

Konings (1990) reviewed long-term results of our first 200 cases. No patient was lost to follow-up. After a mean period of 7 (6–9) years, 76 percent of patients were in a satisfactory condition. Secondary procedures had been performed in 13 patients within 3 years of chemonucleolysis. In another 13 patients a secondary procedure was performed after a symptom-free interval of at least 3 years. The second procedure of these 26 patients was done 24 times at the same level and twice at a different level. Secondary procedures after chemonucleolysis with a follow-up period of 6–14 years are reported in 16–32 percent (Javid 1985, Maciunas and Onofrio 1986, Mansfield et al. 1986, Nordby 1986b, Sutton 1986a, Weinstein et al. 1986). Similar rates (10–39 percent) are reported after primary surgery (Weber 1983, Weinstein et al. 1986, Lewis et al. 1987, Dvorak et al. 1988).

Thus, recurrent herniation in a disc previously injected with chymopapain is possible (Tregonning et al. 1991). We have documented in some patients the disappearance of the hernia, the subsequent reexpansion of the injected disc in the years thereafter and the recurrence of herniation, sometimes contralateral. This widening of the disk may be taken as evidence that chondrocyte-mediated synthesis of new disc substance is not irreversibly impaired by chymopapain (Stern 1985). A second chymopapain injection is considered contraindicated because chymopapain is a foreign protein. Sutton (1986b) on the contrary reported success in repeat chemonucleolysis in 24 of 33 patients. There was not a single anaphylactic reaction, once he started pretreating the patients with histamine-1 and -2 antagonists for 3 days. Of the 1000 treated patients in the period 1980–89 Bolscher and Deutman (1991) reviewed 28 who had repeat chemonucleolysis with this pretreatment protocol. There were no anaphylactic reactions. The follow-up period was 3–4 years after the second treatment and on average 8 years after the first chymopapain injection. 19 of the 20 patients who received the injection at the same level as the primary injection had a satisfactory result.

It has been stated that a truly effective injection therapy would be most welcome (Editorial 1986). How to promote chymopapain even more: A subgroup of medical professionals confirmed a 3 out of 4 success rate and 98 percent satisfaction in favor of this therapeutic option for their own intractable sciatica which most of their colleagues in North America, trained to treat such disorders, have repudiated (LeBlanc 1991).

Based on the literature and on our own experience, the message is explicit: With the proper selection of patients, there are presently two proven treatments for patients with symptoms due to a herniated disc—open discectomy and chemonucleolysis. Neither treatment results in a normal intervertebral disc. Results and secondary procedures seem rather similar in both methods. In case of recurrence after chemonucleolysis a second injection again has a high rate of success. The occurrence of epidural fibrosis and the higher rate of complications in open discectomy make chemonucleolysis an attractive alternative.

References


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