The Current Status of Chymopapain

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Chymopapain is the only minimally invasive technique that has withstood extensive study and validation with techniques of evidenced based medicine (EBM). Four prospective, randomized, double blind, placebo controlled studies and at least 32 cohort studies demonstrate that it is safe and effective for soft, contained, and protruded disc herniations contiguous with the disc space. Each year, continued reports of its benefits and efficacy continue to be presented at the annual meetings of the International Intradiscal Therapy Society (IITS). Reports continue in the form of scientific clinical papers presented as recent as the 19th annual meeting held in Phoenix , Arizona, April 2006. The manufacturer of the FDA approved Chymopapain, Boots Pharmaceutical, sold its rights to German manufacturer Knoll Pharmaceutical who then sold the product to Abbott, who decided discontinue selling it world wide in 2001. The FDA has confirmed that Chymodiactin was not discontinued for reasons of safety or effectiveness.
A Korean Company continues to manufacture the enzyme under the name of Disken, but it has not been approved by the USFDA or any other country's drug regulatory body. In 2002, Spinal Therapies LLC was formed to bring Chymopapain back to the US and the world markets by going through a new FDA application process.

From the first year of FDA approval in the US and especially from 1991-2005, I have utilized chymopapain both as a stand alone procedure and as an adjunct to Endoscopic disc excision. I reviewed my visually documented endoscopic results on 63 consecutive cases from Oct 1995-Feb 1998. The results were presented at the 11th annual meeting of Iits May, 1998.

Summary of Observations and clinical experience with Chymopapain used in conjunction with endoscopic disc removal (YESS Technique).

Chymopapain softens the nucleus pulposus, making it slippery and more easily removed by endoscopic suction- shaver techniques. There is evidence of partial endoscopic enzymatic digestion in the specimen removed manually. Chymopapain is immediately bound only to the chondromuchoprotein of the nucleus and is inactivated by the serum outside the disc space. When combined with the endoscopic discectomy technique, nuclectomy is easier.

No symptoms of allergic reactions, ie. rash, itching, breathing difficulty, anaphylactic reaction, have been encountered when chymopapain is used in conjunction with endoscopic nuclectomy. Tests for antibodies to Chymopapain are not performed routinely if there is not history of allergy to papaya. Chymopapain is safe, even if it extravasates

into the epidural space and around myelinated spinal nerves as demonstrated by chromo-discography intra-operatively. It is also inactivated by cystine in the blood stream. Following discectomy, bleeding can be seen coming from the epidural veins and the discectomy site, but intra-operative bleeding is always self-limiting, due to the absence of soft tissue dissection when the endoscopic transforaminal technique is utilized. If there is any post-operative concerns about bleeding, a hemovac catheter inserted down the access cannula will evacuate any potential hematoma formation until the bleeding stops. This will occur in the recovery room. Post-operative back spasms, a concern with 15-20% of stand alone chymopapain treated patients is dramatically reduced, if it occurs, when used in conjunction with endoscopic disc excision. All procedures are performed outpatient and only one patient in the entire series was hospitalized for back spasm when the primary care physician admitted the patient without consulting or notifying the surgeon.

The last update on Chymopapain summarized in 1998 in Http:// www.sciatica.com/presentations/002/chymopapain/html reviewed the literature on chymopapain as an adjunct to lumbar discectomy. In that article John Jane, et.al concluded that the rate of recurrence was reduced 50% (4.8% vs 9.6%) SPINE: Vol 20, #17, 1995.

OBSERVATIONS AND RATIONALE FOR CHYMOPAPAIN AS AN ADJUNCT TO ENDOSCOPIC DISCECTOMY

- The nucleus pulposus is hydrolyzed almost immediately with low dose chymopapain
- The mechanical extraction of hard, collagenized disc fragments is aided by having the nucleus partially digested prior to mechanical extraction.
- Any remaining degenerated nucleus pulposus may be altered biochemically to decrease the production of cytokines responsible for chemical sciatica
- Recurrent herniations are ideal for the combined endoscopic fragmenctomy technique since epidural fibrosus will limit the migration of the recurrent fragment.and treatment of the remaining nucleus may mitigate a third recurrence.
- Future indications and applications for chymopapain may include using it to aid nuclectomy for nucleus replacement

CLINICAL STUDY

From 19/95-2/98 , 47 consecutive patients with narrow based extruded herniations (height greater than width) and 16 consecutive patients with recurrent disc herniations following conventional transcanal discectomy underwent endoscopic percutaneous discectomy aided by low dose chymopapain.

RESULTS

Using MacNab criteria, 59/63 (93%) were good/excellent, 3/63 (5%) fair, and 1/63 (2%) poor. 16/63 were for for recurrent herniations after previous successful laminectomy/discectomy or microdiscectomy. 14/16 (88%) of the recurrent herniations

were good to excellent and 1/16 (6%) was fair. 1/16 (6%) was poor due to unrecognized lateral recess stenosis, but converted to good after lateral recess foraminoplasty. There were no complications even when chymopapain was ovserved to extravasate into the epidural space at the time of chromodiscography or when the annulus was fenestrated.

DISCUSSION

Hoogland, et.al. compared his results of lumbar and cervical percutaneous nuclectomy combined with low dose chymopapain versus nuclectomy alone, and found 10% better good/excellent results compared with discectomy without chymopapain. In this series, only the more difficult extruded herniations were selected for the combined technique. The overall results of 93% good/excellent were slightly better than a similar group demonstrating a 89% good / excellent result in 119 consecutive patients reported in the Spine Journal.

CONCLUSION

Chymopapain as an adjunct to endoscopic discectomy for HNP may improve endoscopic discectomy results, decrease recurrence rate, and is safe, even when the enzyme is used for extruded herniations. Future applications may include its use in nuclectomy for nucleus replacement implants where a more throrough nuclectomy is desired. As a stand alone procedure, it is still the first line treatment of choice in young patients with painful bulging discs with or without annular tears.

Current Recommendations for the use of Chymopapain

1. **Patient Selection**

Complete history and physical
Diagnostic testing
Discogram is mandatory either prior to the procedure (recommended) or during the procedure **(This is for the rare occasion where there is communication of the disc with the subarachnoid space (thecal sac) Another reason is to confirm concordant pain from the disc.**
AP Oblique and Lateral spine x-rays
CAT scan, myelo/CAT or
MRI
Allergy screening (if history warrants it)

2. Inclusion Criteria

Sciatica as a result of contained and non contained disc herniations
Annular tears/disruption by discography
Young patients where there is concern about the paradoxical effects with surgical discectomy

- Patient Clinical Inclusion

Inadequate response to appropriate non-surgical care
Persistent radicular pain dominates over back pain
Straight leg raising reproducing radicular pain
One or more of the following; muscle weakness, hypalgesia with appropriate dermatomal distribution, muscle wasting, diminished ankle or knee reflex
Contained or non-contained HNP.
Oswestry, SF-36, SF -12, VAS indicating significant impairment
Diagnostic Tests- X-ray, CAT Scan, 3D CAT scan, MRI, Myelogram documenting disc protrusion consistent with the clinical findings.
Discogram- if discogram done at time of procedure and there is any extravasations of contrast medium into the sub-arachnoid space **(thecal sac)** chymopapain should not be injected
Anaphylaxis Screening Tests- such as the chymopapain IgE FAST test

3. Relative patient exclusion criteria (Individual patient considerations may allow for inclusion of the patient with full disclosure, informed consent, and shared surgical decision)

Sequestrated disc fragment
Prior surgery at the same disc level, with poor result and or scarring
Spinal stenosis
Spondylolisthesis, isthmus or degenerative
Significant end stage DDD or end stage lumbar spondylosis
Obesity when it compromises needle placement

4. **Exclusion Criteria**

Rapidly progressing neurological deficit, neurological deficit producing bowel or bladder symptoms
Pregnancy
Sensitivity to chymopapain, papain, papaya or other papaya derivatives.
Back pain with out sciatica

2. Patient Education

- Thorough discussion of informed consent-

Anaphylaxis occurs in about 5 per thousand patients much more frequent in black females (about 3%). Other complications to include death, while rare, occurs three times more often following discectomy. Serious complications after discectomy occur nine times more often.

- The possibility of post op back pain-treatable with analgesics, muscle relaxant, and therapeutic injections. Symptoms are almost always self limiting, and usually do not require further surgical intervention for back pain.

3. The Procedure

Out-patient/same day, or over night stay

- Patient preparation- H2-H1 blockers, well hydrated with oral fluids and administer100% oxygen prior to the procedure
- Recognition and treatment of possible anaphylaxis, have anesthesiologist present
- OR equipment- needles, translucent table, C-arm, crash cart, 2 large bore IV lines
- Enzyme prep-wipe stopper with alcohol, inject 2ccs of sterile water for injection into the vial containing the chymopapain, use time, within two hours of reconstitution
- Anesthesia- general or local. Local anesthesia RECOMMENDED
- Needle technique- Posterolateral approach- Single Needle- 4-8 inch, 18 gauge. Double Needle- 6-10 inch, 22 gauge (bent) and 4-8 inch 18 gauge. Single needle bent tip. Reduce tissue trauma, subsequent back pain with good needle technique.

Patient position-either prone or lateral.

- Injection tips-maintain plunger pressure, inject slowly, replace stylet before removing needle from disc.
- Deep injection of local anesthetic into para-spinous muscles is an option,

4. Post op Care

- Routine analgesics and or muscle relaxants, immediate ambulation, no bed rest, ice not heat for back pain. Leg pain usually gone or markedly reduced. Reassure patient if residual pain remains immediately post op. If back pain reported pre-op it may remain or in some cases increase post op. (Usually self limiting)

5. Follow Up

- Physical therapy, back stabilization, walking or swimming, or resume normal activities as symptoms permit.