Collagenase Injection for severe Dupuytren’s Contracture of the PIP joint: the role of orthotic intervention and therapy

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Dupuytren’s Disease

- Dupuytren’s disease is a progressive disorder characterized by fibroplasia of the palmar fascia
- Numerous surgical and non-surgical treatments have been described
- Almost universally, outcomes have been shown to be more successful for MCPJ contractures compared to PIPJ contractures

Collagenase Injection for Dupuytren’s Contracture

- Collagenase is injected into a palpable Dupuytren’s cord at the MCPJ or PIPJ level

Collagenase disrupts the collagen bonds of the Dupuytren’s tissue and weakens the cord

Patient returns 24 hours later for manipulation of the finger with rupture of the cord and reduction of the contracture

Results of collagenase injection for Dupuytren’s Contracture

- Hurst & Badalamente
  - CORD I - Collagenase Option to Reduce Dupuytren’s study
  - Multi-center study of over 400 patients with DC treated with collagenase

RESULTS OF COLLAGENASE INJECTION

- CORD 1 study
  - 30 days following collagenase injection
  - 77% of MCP joints and 40% of PIP joints met the primary end point of 0 to 5 degrees of full extension

Hurst LC, Badalamente MA et al.
CORD 1 Study

- PIP joints
  - 80.9% of PIPJ contractures of 40 degrees or less met the end point
  - 22.4% of PIPJ contractures over 40 degrees met the end point

Collagenase injection is significantly less effective for PIP joint contractures over 40 degrees.

CORD 1 Study

Therapy & orthotic intervention

- "Patients were given an extension orthosis to wear nightly for up to 4 months."
- "They did not undergo physical therapy."
- "Compliance with and effectiveness of the extension orthosis was not assessed."

Clinical Question

Can the results of collagenase injection for severe PIPJ contractures be improved when followed by a structured orthotic intervention and exercise program?

Contracture of the PIP Joint in Dupuytren’s Disease

- Dupuytren’s cord initiates the contracture
- Secondary changes
  - Contracture of the volar plate and collateral ligaments develops with severe longstanding contractures and persists after Dupuytren’s cord division. Andrew JG. J Hand Surgery 1991

- Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ. Smith P, Breed C. J Hand Surg 1994

Contracture of the PIP Joint in Dupuytren’s Disease

- Anatomic study of the PIPJ in 7 amputated fingers with severe Dupuytren’s contracture
  - Sequential sectioning of tissues in the amputated digits
  - Constant extension force applied and the amount of PIPJ extension measured as each structure was sectioned

Andrew JG. J Hand Surgery 1991

Contracture of the PIP Joint in Dupuytren’s Disease

- Skin and neurovascular bundles
- Dupuytren’s tissue
- Oblique retinacular ligament
- Flexor sheath
- Check-rein ligaments

Andrew JG. J Hand Surgery 1991
Contracture of the PIP Joint in Dupuytren’s Disease

- No improvement in the fixed flexion deformity after the first five structures were released

Results:
- Only when the volar plate was sectioned was full PIPJ extension permitted
- The extensor tendon was found to be “ballooned and stretched”

Implication:
- Collagenase treatment alone cannot be expected to correct the severe PIPJ contracture

Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ

- Longstanding PIPJ contractures of 60 degrees or more
- Identified at the time of surgical correction by a tenodesis test
- A cause of failure to correct the PIPJ flexion deformity

Tenodesis Test
- Fully flex the wrist and MCP joints
- Failure of the PIPJ to extend indicates central slip attenuation

Attenuation of extensor tendon apparent after fasciectomy to correct a severe PIPJ contracture
- Full passive PIP extension
- Active extension lag
Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ

- **Postoperative Treatment**
  - 3 weeks of a static PIPJ extension orthosis with DIPJ free for ROM exercises to mobilize lateral bands and the ORL

Smith P, Breed C. J Hand Surg 1994

Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ

- **Postoperative Treatment**
  - 3 weeks of a Capener orthosis to begin active mobilization of the PIPJ

Smith P, Breed C. J Hand Surg 1994

Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ

- **Postoperative Treatment**
  - 4-6 months active mobilization
  - Night extension orthosis

Smith P, Breed C. J Hand Surg 1994

Central Slip Attenuation in Dupuytren’s Contracture: a Cause of Persistent Flexion of the PIPJ

- **Results**
  - 70% improvement PIPJ flexion deformity

- **What does this study suggest?**
  - The contracture will re-occur if the attenuated extensor tendon is not addressed

Smith P, Breed C. J Hand Surg 1994

Clinical Research Study* at the Philadelphia Hand Center

**Purpose**
- To determine if the results of collagenase injection of severe PIPJ contractures can be improved with structured, supervised therapy and orthotic intervention
- The study protocol addresses the residual contracture and the attenuated central slip

*Supported by grant funding from Auxilium Pharmaceuticals

Clinical Research Study* at the Philadelphia Hand Center

**RESEARCH DESIGN**
- Prospective study
- IRB approved
- Inclusion criteria
  - PIPJ contracture of 40 degrees or greater (passive)
- Exclusion criteria
  - Patients with significant co-morbidities
- Data from CORD I & II subjects used for comparison

*Supported by grant funding from Auxilium Pharmaceuticals
PHC STUDY PROTOCOL

Measurements
- Pre-injection
- Post manipulation
- 1 week
- 4 weeks
- 6 months
- 1 year

Measurements recorded by 5 CHTs
- Following ASHT measurement guidelines

Central slip tenodesis test
- Fully flex the wrist and MCP joints
- Failure of the PIPJ to extend indicates central slip attenuation

RESEARCH STATISTICS

Paired Samples T-Test to compare contracture measurement before and after treatment

Repeated Measures ANOVA to compare Contracture at Baseline, Cord Rupture, 1 week and 4 weeks after treatment
- Bonferroni post-hoc analysis for ANOVA
- Statistical Significance set at p less than 0.05

Study Protocol

Phase 1 – Day of manipulation to 1-2 weeks
Phase 2 – 1-2 weeks to 6 weeks
Phase 3 – 6 weeks to 6 months/1 year

Phases organized according to observed stages of tissue response following injection

Post-injection - Phase 1
(day of manipulation to 1-2 weeks)

ORTHOTIC INTERVENTION

Custom fabricated extension orthosis
Phase 1 – Orthotic Intervention

Post-injection - Phase 1 Exercises
- MCPJ ROM
- ORL stretch
- Reverse blocking

Phase 2 (1-2 weeks) - Orthotic Intervention

Phase 2 (1-2 weeks) - Exercises
- Continue phase 1 exercises
- Add PIPJ flexion & light fisting if no significant extensor lag
- Limit PIPJ flexion & fisting when extension lag is apparent

Phase 3 - 6 weeks to 6 months or longer
- Orthotic Intervention
  - Wean from daytime finger based cylinder orthosis; used as needed to maintain extension
  - Hand based orthosis used at night as a retainer for 6 months or longer as needed
  - Monitoring for re-occurrence of contracture with adjustment of orthosis use as needed

Phase 3 - exercises
- Continue exercises
  - Ratio of exercises in favor of extension
  - Decrease frequency over time and based on maintenance of extension
- Avoid over-emphasis of fisting and grip strengthening
RESULTS - Study Population

- 27 Joints: 20 small finger; 5 ring; 1 long; 1 index
- 25 subjects enrolled
  - 22 male, 3 female
- 26 cases with 1 injection per contracture; 1 subject had 2 injections for 2 separate cords affecting 1 PIPJ
- All subjects with data at 30 days following the first injection

Complications

- Skin tears
- Swelling
- Bruising
- Itching

Comparing CORD I & CORD II results to PHC results

CORD I -

CORD II -

CORD I

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<th>Mean PIP Contracture at baseline</th>
<th>Mean PIP contracture 4 weeks after injection</th>
<th>% change in contracture 4 weeks after injection</th>
<th>Joints with contracture 40° or more reaching primary end point</th>
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OBSERVATIONS
Contracture improvement

- Continued reduction of the residual PIPJ contracture following cord rupture was striking at 1 and 4 weeks
- The continued reduction is attributed to continuous orthosis use and therapy during the first weeks after the injection/release
- What explains this response?

OBSERVATIONS
Contracture improvement

- It is unclear whether and to what extent the collagenase may diffuse to adjacent soft tissue after being injected into the cord
- It is possible, that collagenase weakens these structures, in addition to the pathological cord, thus rendering the residual deformity more receptive to therapy and orthotic intervention

OBSERVATIONS
Contracture improvement

- It is also unclear how long the enzymatic action persists
  - Study of the time to the finger extension procedure had no impact on success up to 72 hours
- Another factor: the contracted periarticular tissues are not directly injured or scarred (just adaptively shortened) which could explain how readily the residual contracture was reduced in the PHC study

Double correction can occur with just a single injection of one cord

- a single cord can cause contracture of 2 joints
- or because of connections between cords
  - MCPJ & PIPJ of same finger
  - Adjacent MCP joints

Dynamic Flexion Contracture (Raton)

- Cord crosses MCP and PIP joints
- Flexing one joint allows extension of the other
- Splint must incorporate both joints

Study weaknesses

- Short follow-up duration of 30 days
- Cost analysis
- Multiple therapists involved in measurements and treatment
Recurrence of DC after Collagenase treatment

- **CORDLESS study**
  - Collagenase Option for the Reduction of Dupuytren’s Disease Long Term Evaluation of Safety Study

- Recurrence - defined as a worsening of the contracture by 20° due to a palpable cord

42.1% contracture recurrence at 4 years

Recurrence rates higher for PIPJs

- MCPJs – 34.6% recurrence
- PIPJs – 61.6% recurrence

Clinical Question

Will recurrence rates of severe Dupuytren’s PIPJ contractures treated with Collagenase followed by a structured orthotic intervention and exercise protocol be reduced compared to the reported rate of 61.6% of the CORDLESS PIPJ subjects?

**CONCLUSION**

- Role of therapy and orthotic intervention following collagenase injection for Dupuytren’s contractures has not been well defined

- *Based on our clinical study: Severe PIPJ contractures treated with collagenase injection benefit from attention to the residual contracture and attenuation of the central slip through orthotic intervention and specific exercises*

- Long term follow-up needed to determine maintenance of contracture correction

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- Auxilium Pharmaceuticals

The effect of a therapy protocol for increasing the correction of a severely contracted PIPJ caused by Dupuytren’s Disease and treated with collagenase

*Skirven TM, Bachoura A, Jacoby SM, Culp RW, Osterman AL. JHandSurg 2013*