The Effect of a Therapy Protocol for Increasing Correction of Severely Contracted Proximal Interphalangeal Joints Caused by Dupuytren Disease and Treated With Collagenase Injection

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Purpose  To determine the effect of a specific orthotic intervention and therapy protocol on proximal interphalangeal (PIP) joint contractures of greater than 40° caused by Dupuytren disease and treated with collagenase injections.

Methods  All patients with PIP joints contracted at least 40° by Dupuytren disease were prospectively invited to participate in the study. Following standard collagenase injection and cord rupture by a hand surgeon, a certified hand therapist evaluated and treated each patient based on a defined treatment protocol that consisted of orthotic intervention to address residual PIP joint contracture. In addition, exercises were initiated emphasizing reverse blocking for PIP joint extension and distal interphalangeal joint flexion exercises with the PIP joint held in extension to lengthen a frequently shortened oblique retinacular ligament. Patients were assessed before injection, immediately after injection, and 1 and 4 weeks later. There were 22 fingers in 21 patients. The mean age at treatment was 63 years (range, 37–80 y).

Results  The mean baseline passive PIP joint contracture was 56° (range, 40° to 80°). At cord rupture, the mean PIP joint contracture became 22° (range, 0° to 55°). One week after cord rupture and therapy, the contracture decreased further to a mean of 12° (range, 0° to 36°). By 4 weeks, the mean contracture was 7° (range, 0° to 35°). The differences in PIP joint contracture were statistically significant at all time points except when comparing the means at 1 week and 4 weeks. The results represent an 88% improvement of the PIP joint contracture.

Conclusions  In the short term, it appears that severe PIP joint contractures benefit from specific, postinjection orthotic intervention and targeted exercises. (J Hand Surg 2013;38A:684–689. Copyright © 2013 by the American Society for Surgery of the Hand. All rights reserved.)

Type of study/level of evidence  Therapeutic IV.

Key words  Collagenase, Dupuytren disease, joint contracture, proximal interphalangeal joint, therapy.
ALTHOUGH THERE IS currently no cure for Dupuytren disease, numerous surgical and nonsurgical treatment options have been described. Almost universally, the results of these interventions show more successful outcomes for the treatment of metacarpophalangeal (MCP) joint contractures as compared to proximal interphalangeal (PIP) joint contractures.1–11 This phenomenon arises due to the secondary joint stiffness that develops within the ligamentous structures that comprise the PIP joint, including the collateral ligaments and volar plate.12 The ligamentous anatomy and articular morphology of the PIP joint is different from that of the MCP joint,13 and long-standing PIP joint flexion will lead to secondary tightening of the collateral ligaments and the volar plate, as well as the development of intra-articular adhesions. Furthermore, attenuation of the central slip has also been implicated as a cause of residual PIP joint extensor lag.12,14,15

The introduction of clostridium collagenase histolyticum (Xiaflex, Auxilium Pharmaceuticals, Malvern, PA) as a nonsurgical treatment option for Dupuytren disease provides another useful, minimally invasive treatment modality. Although early results appear to be encouraging, similar to other treatment options, severe PIP joint contractures have much less impressive outcomes in comparison to mild PIP joint and MCP joint contractures.4,7

The role of hand rehabilitation is an essential component in the treatment of fixed flexion PIP joint deformities.14 In both Collagenase Option for Reduction of Dupuytren’s (CORD) studies, patients were instructed to wear night orthoses for up to 4 months and perform at-home finger flexion and extension exercises. However, a standardized and monitored hand rehabilitation protocol was not applied.4,7 We hypothesized that relative to the literature, the results of collagenase injection for severe PIP joint contractures could be considerably improved with a specific orthotic and hand rehabilitation protocol.

METHODS

We defined a severe PIP joint flexion contracture as one measuring 40° or more. The decision to use this value as a cutoff number was based on the outcomes of the CORD I and CORD II clinical trials.4,7 Any patient with a passive contracture of less than 40° was excluded. Patients with previous surgeries or recurrence involving the involved PIP joint were included. In addition to reporting the overall results of treatment, we compared the results of the subgroups with primary disease and recurrent disease.

There were 22 fingers in 21 patients: 19 men and 2 women. The middle finger was involved in 1 case, the ring finger in 5 cases, and the small finger in 16 cases. Ten patients were treated for primary disease, and 12 patients were treated for a recurrence. The mean age at treatment was 63 years (range, 37–80 y).

This study was approved by our institutional review board and was conducted accordingly under its protocol and guidelines. All patients provided informed consent.

Collagenase injection

Collagenase was stored and prepared according to the manufacturer’s guidelines. A board-certified hand surgeon performed the injection between the palmar digital crease and no more than 4 mm distal to the palmar digital crease. At times, ultrasound guidance was used to ensure injection into the cord by ranging the digit and confirming the location of the diseased fascia. In particular, ultrasound was used when the surface anatomy overlying the metacarpophalangeal and PIP joints was distorted, primarily due to previous surgery. The next day, the patients returned to clinic for cord rupture. Digital block with 1% to 2% Xylocaine (lidocaine HCl) was used for pain relief, as this allowed patients to tolerate the procedure more effectively and could allow for more complete cord rupture. This was followed by digital manipulation to rupture the cord. The patients were referred to a certified hand therapist the same day or the next day. All patients received only 1 collagenase injection in the involved digit.

Therapy protocol

All patients were seen by a certified hand therapist before collagenase injection for active and passive goniometric measurements of the involved finger. Goniometer measurements were taken according to the accepted technique, and in every case, PIP joint extension was measured with the MCP joint flexed to ensure that the flexor tendon and Dupuytren cord were slack. Following manipulation performed 24 hours after injection, measurements were again recorded, and a custom-fabricated dorsal hand-based extension orthosis including only the injected finger was applied. The orthosis allowed for gradual and progressive extension of the PIP joint to correct residual flexion contracture (Fig. 1). Patients were instructed to wear the orthosis at all times except for exercises and hygiene. Exercises included blocking for PIP joint extension, MCP joint flexion and extension, and distal interphalangeal joint flexion with the PIP joint supported in maximum extension to lengthen the oblique retinacular ligament. Patients were instructed to perform these exercises...
hourly to every other hour with 10 repetitions every session. Full finger flexion to the distal palmar crease (fisting) was included, but the number of repetitions and frequency of this exercise were limited to avoid further attenuation of the central slip. The exact number of repetitions and the frequency were adjusted based on the degree of active extensor lag of the PIP joint. The frequency of this exercise ranged between 2 and 5 intervals of exercise a day with 3–5 repetitions for the fisting. The greater the active PIP joint extensor lag, the fewer the repetitions of fisting exercises with reduced frequency.

One week following manipulation, a custom-fabricated, finger-based cylinder PIP joint orthosis in maximum extension was made and provided for daytime use for 4 to 6 weeks (Fig. 2). This cylinder orthosis was used continuously during the day, removed only for exercises and hygiene, and was found to promote greater ease of hand use and patient compliance. The hand-based extension orthosis was continued at night for 6 months following the injection, although we report the results at 1 month following treatment. Exercises continued as described earlier. Patients were specifically instructed to avoid repetitious gripping exercises to avoid encouraging the return of the PIP joint flexion deformity. Over the 4-week treatment interval, the number of hand therapy visits ranged between 4 and 6. Measurements were recorded at 1 week and again at 4 weeks following cord rupture to monitor progress.

Statistics
An independent *t*-test was used to compare the contractures of the 2 subgroups. A one-way repeated measures analysis of variance was used to compare the means of the PIP joint contracture at each time point. Post hoc Bonferroni analysis was used. A *P* value less than .05 was considered statistically significant.

RESULTS
The mean baseline passive PIP joint contracture was 56° (range, 40° to 80°). At cord rupture, the mean PIP joint contracture was 22° (range, 0° to 55°). One week after cord rupture and therapy, the contracture decreased to a mean of 12° (range, 0° to 36°). At 4 weeks, the mean contracture was 7° (range, 0° to 35°). The differences in passive PIP joint contracture were statistically significant at all time points (*P* < .002) except when comparing the means at 1 and 4 weeks (*P* = .128). The results represent an 88% improvement of the PIP joint contracture.
The baseline contracture and response to treatment was similar, regardless of whether the patient was treated for primary or recurrent disease. The baseline contracture for the subgroup with primary disease was $53^\circ \pm 10^\circ$, and the baseline contracture for patients with recurrence was $58^\circ \pm 12^\circ (P = .389)$. The contractures at 4 weeks after treatment for the primary treatment and the recurrence subgroups were $8^\circ \pm 11^\circ$ and $6^\circ \pm 7^\circ$, respectively ($P = .575$).

In all cases, the complications were considered minor and included digital swelling and ecchymosis ($n = 18$; in 1 case, swelling involved the entire palm), skin tears ($n = 4$), skin blistering ($n = 2$), and localized pruritus ($n = 1$). Skin tears were treated with local wound care, and all healed uneventfully. There were no flexor tendon ruptures or annular pulley ruptures.

**DISCUSSION**

Draviraj and Chakrabarti studied the correlation between hand function and the change in PIP and MCP joint contractures and concluded that the PIP joint was functionally more important than the MCP joint. Hand therapy in conjunction with surgical treatment of PIP joint contractures has been advocated by a number of investigators. Rives et al conducted a prospective trial of surgical correction and dynamic extension orthoses for patients with PIP joint contractures greater than $45^\circ$ resulting from Dupuytren disease. The therapy protocol involved the first 6 postoperative months and consisted of close patient monitoring and gradual reduction in the use of the dynamic extension orthosis.

After a mean of 2 years, the overall correction for 23 digits was 44%. Patients who were compliant with the rehabilitation protocol were found to have a mean improvement of 59% compared to 25% for noncompliant patients, who voluntarily stated they had discontinued or reduced the use of the orthosis to less than half the recommended time. Misra et al also found that patients with Dupuytren disease who were compliant with hand therapy following fasciectomy had better outcomes than their noncompliant counterparts. Their therapy protocol consisted of active flexion under supervision starting on the third postoperative day, static night orthosis use in extension for up to 3 months, or a dynamic orthosis for patients with central slip attenuation or joint release. Similar to these studies, our report indicates a significant improvement in the PIP joint contracture following a monitored rehabilitation protocol. In addition to gradual stretching of the stiff volar plate and collateral ligaments, the central slip was specifically targeted. Long-standing PIP joint flexion deformities stretch the extensor tendon, including the central slip, and render it lax and incompetent when the flexion deformity is suddenly corrected. We attempted to gradually improve central slip function through specific blocking exercises for PIP joint extension, and we believe this step contributed to the results that we have observed.

Xiaflex (Auxilium Pharmaceuticals) is composed of 2 classes of collagenase enzyme that selectively degrade type I and type III collagen, which are major constituents of Dupuytren cords. Although the
acute-phase pharmacokinetics have been studied, many clinically relevant questions still surround the pharmacokinetics and pharmacodynamics of this drug. For example, it is unclear whether and to what extent the active enzyme diffuses to adjacent soft tissue after injection. It is also unclear how long the enzymatic action persists in vivo. These questions are relevant because the volar plate, the collateral ligaments, and the central slip all label for type I and type III collagens. It is possible that collagenase partially digests these structures in addition to the pathological cord, thus rendering the fixed flexion deformity more receptive to therapy. This concept is not unreasonable, given that complications of collagenase injection include flexor tendon rupture and pulley rupture. The CORD I and CORD II trials are the major studies that have comprehensively investigated the outcomes of collagenase treatment. In both studies, the results of PIP joint contractures were not as favorable as those for MCP joint contractures; however, a monitored and structured hand rehabilitation protocol was not instituted. One of the major differences between our study and the CORD trials was the number of injections that patients received. In our study, all patients received only 1 injection, whereas the number of injections in the CORD studies varied between 1 and 3. The primary end point in both CORD studies was defined as a reduction in contracture to 0° to 5° within 30 days of the last injection. Despite providing only 1 injection, we noted markedly improved results following rehabilitation. Only 22% to 25% of the PIP joints in the CORD trials reached the primary endpoint as compared to 55% of joints in our study, in which all patients were assessed 4 weeks after only 1 injection. Furthermore, 4 weeks after injection, we saw an improvement of 88% in the degree of contracture (Table 1).

Although local anesthesia is not recommended at the time of collagenase injection, it can be safely administered just before manipulation. We found lidocaine to be particularly effective during cord rupture because it allowed patients to tolerate manipulation more effectively. The CORD trials did not allow local anesthesia immediately before cord rupture, and this difference in technique may have been another reason that we observed superior results.

The limitations of this study include the short follow-up duration of 4 weeks. However, this time period enabled us to compare and place our results in the context of current literature. A longer follow-up duration will be necessary to determine the ultimate value of hand therapy following collagenase injection for severe PIP joint contractures. Furthermore, it is unclear how additional therapy will affect costs in comparison to the costs that may stem from additional surgical treatment or collagenase injection following unsatisfactory initial outcomes. A disproportionate involvement of the PIP joint of the small digit was observed, and future studies comparing collagenase injection for PIP joint contractures in different digits may be warranted in light of our skewed population.

Further investigation into the clearance mechanisms, diffusion, and duration of collagenase action may be warranted because this knowledge may provide insight into potentially new and useful applications for the treatment of other joint contractures.

**REFERENCES**


