INJECTABLE COLLAGENASE CLOSTRIDIUM HISTOLYTICUM FOR DUPUYTREN'S CONTRACTURE: RESULTS OF THE CORD I STUDY

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Hypothesis- Dupuytren's contracture limits hand function, diminishes quality of life, and may ultimately disable the hand. The purpose of this study was to conduct a Phase 3, FDA regulated, controlled, multicenter clinical trial to test the safety and efficacy of injectable collagenase clostridium histolyticum as a novel nonsurgical treatment for contractures caused by Dupuytren's contracture.

Methods- A total of 308 patients with joint contractures of $\geq$20° were randomized in this double blind, placebo-controlled, prospective study at 16 different sites in the U.S. There were 245 males and 63 females with a mean age 62.7$\pm$9.5 years. The patient's metacarpophalangeal or proximal interphalangeal joint contractures were randomized to receive, if needed, up to three collagenase (clostridium histolyticum) injections (0.58 mg per injection) or placebo into the affected cord at 30 day intervals. One day post injection, the treated joints were then manipulated up to three times with the use of a standardized procedure (finger extension) in an effort to rupture the cords. The primary endpoint was a reduction in primary joint contracture to 0° to 5° of full extension 30 days after the last injection. Primary efficacy analysis was done using the Cochran-Mantel-Haenszel test. Twenty-six secondary endpoints were evaluated, and adverse events were collected.

Results- Efficacy results on n=306 patients demonstrated that the proportion of joints that met the primary endpoint of 0° to 5° of full extension was significantly higher when injected with collagenase (clostridium histolyticum) as compared to placebo (64.0% vs. 6.8%, P<0.001) (Figure 1A and 1B). This was also true for all 26 secondary endpoints (P≤0.002). Overall, joint range of motion was significantly improved after collagenase treatment (43.9º to 80.7º) compared with placebo treatment (45.3º to 49.5º)(p<0.001). Most commonly reported adverse events were localized edema, pain, swelling, bruising, pruritus, and transient regional lymph node swelling and pain, which resolved without treatment in a median10 days. Three treatment-related serious adverse events were reported: two tendon ruptures and one complex regional pain syndrome. No significant changes in flexion or grip strength, no systemic allergic reactions, and no arterial or nerve injuries were observed.

Summary

- This study demonstrates the efficacy and safety of injectable collagenase as a novel non-surgical treatment in patients with Dupuytren's contracture.

- Injectable collagenase was significantly superior to placebo in reducing contractures and improving range of motion in affected joints.
- Collagenase injection(s) were generally well tolerated.

Figure 1A. Left hand of a 66 year old patient with a 75 degree contracture of the MP joint, little finger and 20 degree contracture of the MP joint, ring finger, pre injection.

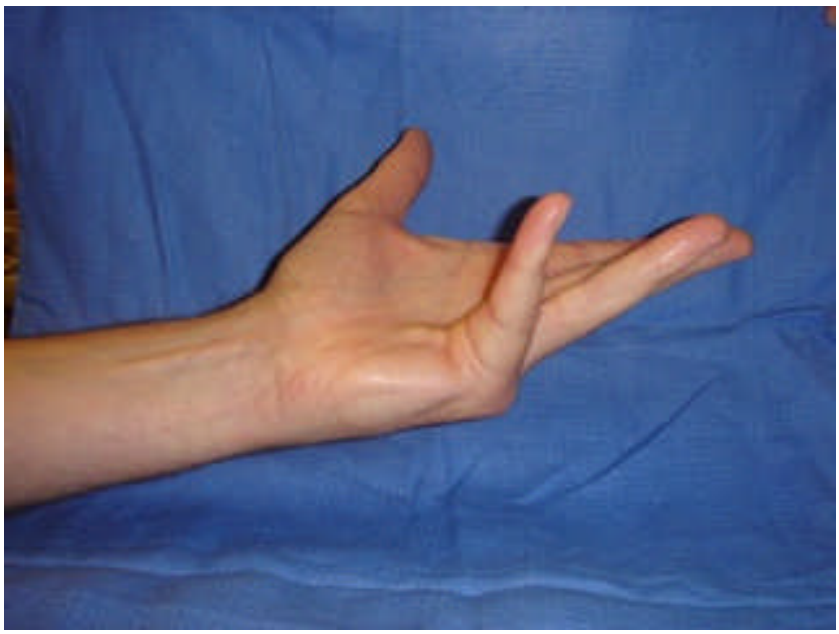

Figure 1B. Same patient as in Figure 1A, 30 days post one collagenase injection showing full correction of contractures.