SCIENTIFIC ARTICLE

The Use of Residual Collagenase for Single Digits With Multiple-Joint Dupuytren Contractures

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Purpose Standard 0.58 mg (0.25 mL) collagenase *Clostridium histolyticum* (CCH) preparations result in unused CCH that is often discarded. Our purpose was to assess the results on Dupuytren contractures affecting both the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints in the same digit utilizing an injection containing the maximum CCH volume that can be withdrawn from a single vial.

Methods A consecutive series of patients with MCP and PIP cords in the same digit received a single treatment with 2 injections totaling 0.30 mL distributed between the MCP and the PIP cords and underwent manipulation approximately 24 hours later. Reduction in contracture, clinical success, and complications were assessed 30 days after manipulation.

Results Thirty-one patients (34 digits) had a mean preinjection flexion contracture of 50° at the MCP joint and 53° at the PIP joint. Clinical success (reduction in joint contracture to 0°−5° of full extension 30-days postmanipulation) was noted in 65% of MCP cords and 38% of PIP joint cords. We had a 24% incidence of skin tears, which correlated with the degree of preinjection contracture.

Conclusions For Dupuytren contractures involving the MCP and PIP joints in the same digit, distributing the maximum amount of CCH that can be withdrawn from a single vial provides efficacy at both joints that is similar to that reported in previously published series, with a comparable complication rate. Utilizing excess CCH typically discarded may provide cost savings. *(J Hand Surg Am. 2017;■(■):1.e1-e6. Copyright © 2017 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, manipulation.

Online Exclusive

DUPUYTREN DISEASE IS A BENIGN fibroproliferative disorder involving the palmar fascia of the hand that can result in functionally limiting digital contractures. The prevalence of Dupuytren disease is greatest in older men of northern European descent.[1–3] Although the etiology is not completely understood, myofibroblast proliferation is involved in the joint contractures seen in Dupuytren disease.[4,5]

The U.S. Food and Drug Administration (FDA) approval of collagenase *Clostridium histolyticum* (CCH; Xiaflex; Auxilium Pharmaceuticals Inc., Chesterbrook, PA) in 2010 introduced a nonsurgical

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treatment option for patients with cords involving the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joint. The initial trials analyzed the safety and efficacy of up to 3 injection cycles for patients with single-joint contractures.[6] In the Collagenase Option for the Reduction of Dupuytren's (CORD) I trial, Hurst et al[6] noted that 38% of enrolled patients had more than one joint contracture at the time of treatment. More recent authors have demonstrated that concurrent CCH injections utilizing 2 CCH doses at 2 affected joints can result in high patient satisfaction and physician-rated improvement.[7] In addition, single CCH injections containing a dose higher than recommended by the FDA for 2 contractures have also been analyzed, with short-term results comparable with conventional CCH doses for single cords.[8,9]

The manufacturer- and FDA-recommended preparation of CCH results in unused CCH that is discarded. Some authors have advocated injecting this residual CCH into smaller secondary cords.[10] Although the unused CCH is below the conventional FDA-recommended dose for a single cord, this residual volume may be of benefit when treating a second contracture in the same digit. For patients with contractures affecting both the MCP and the PIP joints in the same digit, we hypothesized that distributing the maximum amount of CCH that can be withdrawn from a single vial to treat both cords results in a significant reduction in the contractures 30 days after manipulation.

MATERIALS AND METHODS

Institutional review board approval was obtained. We reviewed a consecutive series of patients from our database, which includes all patients treated with CCH at our institution. Patients 18 years and older with a diagnosis of Dupuytren disease and a cord involving both the MCP and the PIP joints in the same digit, treated between January 2014 and January 2016, were identified in the database and included in our analysis. Exclusion criteria included patients with thumb involvement, prior surgical treatment for Dupuytren contracture, contractures of either the PIP or the MCP joint less than 20°, or prior treatment with CCH. No patients met the exclusion criteria. All patients were treated by a single fellowship-trained hand surgeon (J.C.K.).

The FDA and manufacturer provide specific guidelines for the preparation and injection of CCH for a single Dupuytren-related joint contracture. Collagenase *Clostridium histolyticum* is supplied as a lyophilized powder and must be reconstituted with a diluent prior to injection. According to these guidelines, the dose of CCH is 0.58 mg per injection into a palpable cord with a contracture of the MCP or PIP joint. For MCP joints, 0.39 mL of the diluent is withdrawn and injected into the vial containing the lyophilized CCH to create the reconstituted solution. Per the manufacturer, 0.25 mL (containing 0.58 mg CCH) of this reconstituted solution is then withdrawn for injection into a cord affecting the MCP joints. The residual reconstituted solution is discarded. For PIP joints, 0.31 mL of the diluent is utilized and 0.20 mL of the reconstituted solution (still containing 0.58 mg CCH) is injected into the PIP cord.

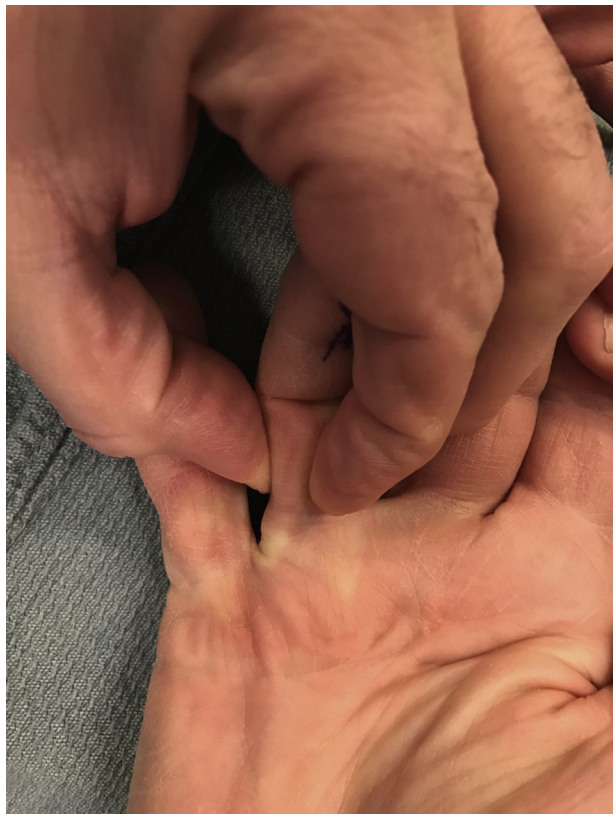

FIGURE 1: Clinical example of multiple cords resulting in MCP and PIP joint contractures.

We utilized an injection preparation process similar to Meals and Hentz.[10] An MCP joint mixture was used for all patients and, thus, 0.39 mL of the sterile diluent was added to the lyophilized vial containing 0.90 mg CCH. This creates 0.39 mL of the reconstituted solution. This reconstituted solution contains a concentration of 2.3 mg of CCH per mL. According to the manufacturer's internal user data, the maximum volume that can routinely be withdrawn for injection is between 0.30 and 0.35 mL with the remaining 0.04 to 0.09 mL adherent to the vial wall and unable to be withdrawn (Auxilium Pharmaceuticals Inc., personal communication, December 2016). In J.C.K.'s experience, the maximum volume