



Collagenase for Dupuytren's Contractures: A Prospective Case Series

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Abstract

Background: Dupuytren's disease (DD) is a fibroproliferative disorder with marked deposition of type I collagen in the palmar fascia of the hand. This causes flexure contractures of the fingers, which can be detrimental to a patient's hand function and quality of life. Collagenase injections derived from *Clostridium histolyticum* (CCH) have been growing in popularity for the treatment of DD, as such evidence has grown for short and long term outcomes, however there is limited evidence for long term complication rates.

Methods: Prospective cohort study measuring flexion of contracture's post collagenase injection with follow up at 5-12 weeks and 1-3 years.

Results: Four hundred and eighty seven fingers from 287 patients, 83% were either little or ring finger contracture's. There was an average of 37° of flexion in the cohort's metacarpophalangeal joint's (MCPJ). This was reduced to 18° post stretch, further reduced to 13° at early follow up and maintained at 18° at late follow up. The proximal interphalangeal joint (PIPJ) followed similar patterns reducing from 36° to 23° at early follow up. However did not maintain the improvement at late follow up, as is consistent with surgical outcomes. The complication rate was found to be 27%, with small skin tears reported in 16% of patients, this is again comparable to surgical treatment options.

Conclusions: The study shows collagenase injections are beneficial in the treatment of DD, with comparable results to surgical intervention literature. It remains a promising alternative to surgery due to the potential for high treatment rates, cost effectiveness and resource optimization.

Keywords: Dupuytren's Disease; *Clostridium histolyticum*; Collagenase; Joint Contracture; Complications

Abbreviations

DD: Dupuytren's Disease; MCPJ: Metacarpophalangeal Joint's; PIPJ: Proximal Interphalangeal Joint; CCH: *Clostridium Histolyticum*; PNF: Percutaneous Needle Fasciectomy; FDA: Food and Drug Administration; COD: Collagenase Option for the Reduction of Dupuyten

Introduction

Dupuytren's disease (DD) is a fibroproliferative disorder with marked deposition of type I collagen in the palmar fascia of the hand [23]. This causes contracture in flexion of the fingers, which can be detrimental to hand function and therefore quality of life

[28]. The current treatment options include open surgical fasciectomy, percutaneous needle fasciectomy (PNF), and enzymatic fasciectomy with collagenase. It remains a challenging disease to treat, with limited evidence to direct the management of patients with DD.

Since gaining FDA approval, collagenase injections have been growing in popularity for enzymatic treatment of DD [24]. This is due to reduced procedure time, noninvasive nature of the procedure and comparable outcomes to surgical intervention. Collagenase (*Xiaflex*) is derived from the bacteria *Clostridium histolyticum* it breaks down type I and type III collagen, when the joint undergoes passive joint extension cord rupture is induced [18]. This has

shown to increase range of movement in patients with contractures due to DD [22]. The current study aimed to gather long-term efficacy and complication data of collagenase injections for the treatment of DD in a Western Australian context.

Materials and Methods

The study is a prospective case series of patients that presented to a single centre from August 2015 to December 2020, that were injected with collagenase (*Xiaflex*). Written informed consent was gained by all participants prior to undergoing any treatment or procedure, with the ability to withdraw from the study at any time. The injections were performed as described in the Collagenase Option for the Reduction of Dupuyten (CORD) study, with simultaneous treatment of MCPJ and PIPJ as required [11]. The entire vial of collagenase was spread across the cord with three injections of approximately one third of the dose, starting proximally and working distal. Stretching was performed with the use of a digital nerve block using Xylocaine 1-2% within a median of 6 days, moderate pressure was applied for 10-20 seconds in order to induce cord rupture. Under the supervision of a hand therapist, patients were then splinted overnight for 12 weeks, and followed up at 6-12 weeks, and long term at 1-3 years. Measurements were taken pre intervention, post intervention and at the aforementioned follow up times. Ethics was approved by the Notre Dame University (Fremantle) Human Research Ethics Committee, approval number 2022-130F.

Results and Discussion

The study collected data from 287 patients, injecting 487 fingers. The average age was 65 years old with a 4:1 male to female ratio. Almost half of the patients had little finger contractures with 34% ring finger, 13% middle finger, 2% index finger and 1% thumb as seen in figure 1. The stretch procedure was performed with an average of 5 days, with 95% of patients stretched within 7 days of injection. Average short-term follow up was 7 weeks, and 25 months for long-term follow up. (Figure 1 to be inserted here).

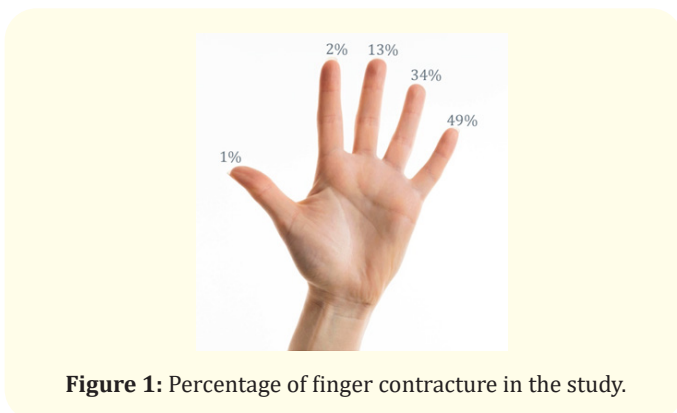


Figure 1: Percentage of finger contracture in the study.

The average contracture treated was 37° for the MCPJ joint, and 36° for the PIPJ. Immediately post stretch the MCPJ improved by 19° then a further 5° at early follow up. At late follow up the MCPJ contractures had regressed by 5° on average. The PIPJ joint followed a similar pattern with 13° of improvement post stretch and a further 4° at early follow up, with 6° of regression at late follow up as can be seen in table 1.

	Pre-Stretch° (n)	Post Stretch° (n)	Early Follow up° (n)	Late Follow up° (n)
MCPJ	37 (362)	18 (323)	13 (207)	18 (123)
PIPJ	36 (361)	23 (320)	19 (190)	26 (120)

Table 1: Average degree's of contracture improvement.

The incidence of skin tears was recorded. Over 70% percent of patients did not have a skin tear, 16% had a small tear, 2% had a moderate tear, 3% had a large tear, 6% had an unclassified tear or an alternate complication as seen in table 2. All skin tears completely healed after regular dressing changes in a dressing clinic. Fourteen cases still required surgical intervention due to recontracture. No sensory deficits were recorded. As per [20] the incidence of post injection swelling and bruising was considered a documented side effect but not a complication and was not recorded.

Tear classification	% (n)
No tear	73 (339)
Small	16 (76)
Moderate	2 (7)
Large	3 (16)
Unclassified/Other	6 (30)

Table 2: Percentage of Complications-Skin Tears.

Discussion

There are numerous advantages to CCH compared to other treatment methods. The technique is easier than PNF, and far easier to perform than surgical options [24]. It is also useful for thicker wider cords, with lower rates of injury to nerves compared to PNF [22,24]. Furthermore, patients are highly satisfied with comparable complication rates to PNF and surgery [6,7,24]. The benefits of CCH over surgery include; earlier recovery, shorter procedure time, not requiring theatre access and avoidance of general anesthetic [25]. Theatre time and resource allocation has become far more valuable since the COVID-19 pandemic, increasing the need for non-surgical interventions such as collagenase [25].

Due to licensing, the use of collagenase outside of the USA is no longer financially viable [25]. At the commencement of this study the cost of using collagenase was less expensive than an operation. Approximately 2,000 Australian dollars (AUD) verse 6,000 for an operation [5]. Due to the change of licensing outside of the USA the price of collagenase has effectively removed the opportunity for patients to have this treatment, in either the private or public sector [25].

The current study has one of the highest number of participants for studies identifying recontracture and complications, as can be seen in table 3 [18]. The range of improvement in contractures is varied in the literature, from MCPJ improvement of 60° to 29°, and 62° to 15° degrees for PIP joints [4,13,16]. In the current study there was an average improvement of 24° in the MCPJ and 17° in the PIPJ as seen in table 1 this is less than in other studies [2,4,8,9]. However, it has been shown that more severe contractures do not perform as well, with initial contractures >45° not responding as favorably [11,15]. The current study had 40% of both MCPJ and PIPJ >45° of contracture. Furthermore, 25% of patients had initial contractures greater than 60° in MCPJ (26%) and PIPJ (25%). This potentially accounts for results at the lower end of documented improvement compared to other studies. It is hypothesised that satisfied patients did not return for further assessment; where as less happy patients were more likely to return. This therefore may have influenced the results of the current study.

Authors	Year	Patients (n)	Follow up (months)
Badalamente., <i>et al.</i> [12]	2015	506	3
Glaston., <i>et al.</i> [13]	2015	715	2
Hanson., <i>et al.</i> [14]	2017	212	15
Hurst., <i>et al.</i> [6]	2009	203	13
Premier., <i>et al.</i> [15]	2015	644	60

Table 3: Comparative studies adapted from Sandler., *et al.* [4].

Long-term outcomes are focused on recontracture rates, and severity of recurrent contracture. Typically recontracture rates are lower for surgical fasciectomy, than both collagenase and PNF [17,27]. Compared to PNF the advantage of CCH is that it may be repeated far more easily and safely, without undergoing surgery. Moreover patients who have undergone PNF are more likely to undergo surgery for recontracture, rather than another PNF [1].

The average degree of recontracture documented in the literature is 24° and 45° for MCPJ and PIPJ respectively [18] The current study had an average recontracture of 5° and 7° at long term follow up for MCPJ and PIPJ respectively, this compares favorably

to other studies [2,9,27]. Recontracture can be related to severity of initial contracture, number of cords affected, age of the patients and other underlying comorbidities [3,11,21,29]. Average age was comparable to the literature, with an average age of 65 years old. Simon-Perez., *et al.*, found patients under 60 were more likely to have recontracture [21]. The current study only had 26% of patients under 60 and could explain the low degrees of recontracture. Thus the current study comparatively shows less regression of extension gains with long term follow up.

It is unlikely follow up timeframes have played a role in the reduced degree of recontracture in the current study. As based on a recent literature review by Sandler., *et al.*, 28% and 20% of PIPJ and MCPJ respectively will have recontracture within 12 months [18]. It is likely the reduced severity of recontracture in the current study is due to reduced initial contracture improvement compared to the literature.

Complications of collagenase injections are very common with studies suggesting over 90% complication rate [10]. However there is no standardized definition of a complication of CCH injections [12]. Many studies include minor complications such as edema, contusion, pain, ecchymosis and skin tears [2,7,9,12,18,19]. However major complications such as tendon pulley rupture and anaphylaxis are very rare [18]. As per Scherman., *et al.*, [20] we did not register side effects such as swelling, extremity pain and hemorrhage as complications. The current study focused solely on skin tears as this is the more common of significant complications. The current studies overall rate of skin tears was 27%, comparable to a recent systematic review by Sandler., *et al.*, who also found a 27% rate of skin tears [18]. Due to the use of local anesthetic prior to cord rupture, skin tears have been shown to increase, it is likely this occurred in the current study [14]. There was no instance of nerve injury, tendon injury or complex regional pain syndrome. It is important to note that complications of collagenase injections and subsequent cord rupture are comparable to that of surgical fasciectomy [26].

The study design of a prospective case series has inherent limitations without a control group or randomization. There were also challenges with patient follow up; the long-term follow up rate was 34%. Some potential causes for this may be patient demographics, with many people missing appointments due to travel. Fremantle Hospital was an early adopter of CCH treatments, being the first in the state. It was also the highest volume user. The study was performed as a statewide service in Western Australia, the largest state in Australia. Thus considerable distance and travel time may have limited patient follow up. There was also high potential for

patients who were sufficiently pleased with their results to not represent in 2 years time for late follow-up.

Conclusion

The current study adds to existing literature surrounding collagenase as a method for the treatment of DD. Collagenase injections are an excellent tool in the treatment of DD with reduced back to work timeframes, high levels of patient satisfaction and a faster procedure compared to other treatment modalities. Plus, the added ability to avoid a general anesthetic and use of theatre time which comes at a premium in a COVID world, with decreased theatre staff availability and resources [25]. The current study found complications are similar to that of the literature, while also being comparable to surgery. It also found reduced recontracture severity long term, that may be attributed to a reduction in initial contracture improvement compared to the literature.

Unfortunately, due to the increase in price of *Xiaflex* in Australia it is currently unviable to continue to treat patients with this method. The Authors hope this will change in the future so they can continue to provide a strong alternative treatment option for Australian patients suffering from DD. Especially when considering procedure time, theatre availability and recovery time [25].

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Conflict of Interest

The Authors declare that they have no conflict of interest.

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