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The Preeminence of Using Collagenase Clostridium Histolyticum Over Traditional Surgical Treatment Options for Maximal Resolution of Dupuytren's Contracture

Hamid A Khan[1]* and Sanjay Patari[2]

[1]*Research Associate, American Microsurgical Orthoplastic Society, USA*

[2]*Department of Orthopaedic Surgery, Center for Sports Orthopaedics, USA*

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***Corresponding author:** Hamid A Khan, Research Associate, American Microsurgical Orthoplastic Society, Chicago, USA, Tel: 773-655-3603; Email: khanha88@gmail.com

Abstract

Dupuytren's contracture is a disorder involving progressive fibrosis of the palmer fascia, eventually leading towards the inability of maintaining normal hand function. As the disorder continues to advance, those who are affected begin to lose satisfactory finger motion of the involved digit or digits and require appropriate medical action. Traditional treatment and management options for Dupuytren's contracture are based primarily on the severity and extent of the disorder and involve either surgical or non-surgical approaches. Historically, the main treatment modalities used involve either a fasciotomy, fasciectomy, limited-palmer fasciectomy or the less-invasive percutaneous needle aponeurotomy approach. Today, due to the many advancements made in medicine and the budding pharmaceutical market, the use of collagenase injections is attesting to provide numerous advantageous results when compared to the older and more traditional methods for the treatment of Dupuytren's contracture. This brief mini-review intends to provide insight behind our opinion on the superiority of using collagenase clostridium histolyticum over other treatment varieties based on relevant current literature and the outcomes observed in 25 of our patients, over a 3-year period.

Keywords: Dupuytren's disease; Finger contracture; Hand contracture; Collagenase; Fasciectomy; Fasciotomy; Needle Aponeurosis; Xiaflex

Abbreviations: CCH: Collagenase Clostridium Histolyticum; MCP: Metacarpophalangeal; PIP: Proximal interphalangeal; PNA: Percutaneous needle aponeurotomy; ROM: Range of Motion

Introduction

As healthcare providers, some of the most significant factors that aid in the decision-making process of choosing the best treatment for patients habitually revolves around what is the safest, most efficacious, and what provides the maximum benefit in improving a patient's overall quality of life. From an orthopedic perspective, the decision to treat patients with surgery should almost always deferred until other alternatives involving less-invasive measurements have been ruled out or unless the situation requires emergent surgical correction. Overtime, Dupuytren's contracture (Figure 1A & 1B) frequently poses the question of necessitating surgical attention as it progresses. Dupuytren's disease is a disorder involving the progressive development of fibroproliferation within the palmer fascia that overtime results in a variable loss of finger extension accompanied by imposed flexion at the MCP joint, PIP joint or both joints secondary to the contracture itself [1,2].

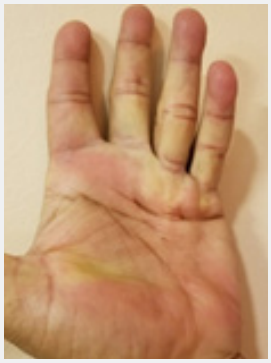

Figure 1A: Image of patient's left hand portraying the typical features associated with Dupuytren's Contracture: Note the nodular fibrosis on the ulnar aspect of the patient's left palm, the progressive fibrosis is causing both the fourth and fifth digits to lose complete extension abilities.

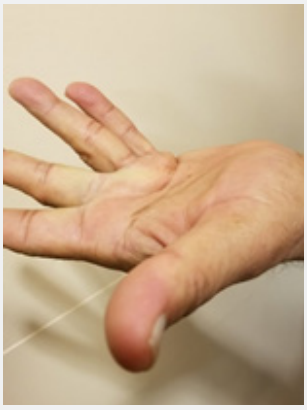

Figure 1B: Lateral view of the same hand depicted in image 1A: Here, it is easy to appreciate the obvious discrepancy between where the affected fourth and fifth digits rest as opposed to the other fingers while the hand is in a relaxed position. As these contractures progress it is very likely that a visible imposed flexion at the MCP joint, PIP joint or both joints will ensue warranting either surgical or non-surgical treatment.

With that said, when patients who are suffering from Dupuytren's contracture come into the clinic seeking treatment there is a clear sense of concern exhibited as this condition can lead to a disability of the involved area and therefore choosing the best treatment modality possible is of great importance. Although the exact source of Dupuytren's contracture has yet to be determined, there is strong evidence confirming that genetics, ethnicity, age and gender are all influential factors that play some role within the underlying disease [3,4]. Studies have shown that most individuals who develop Dupuytren's contracture are men of northern European lineage over the age of 50 [4].

From a pathophysiological and histological standpoint, the growth of the nodule or nodules develop due to unwarranted proliferation of fibroblasts in the superficial palmar fascia and histologically are composed of both fibroblasts and type III collagen [5]. Dolmans GH [6] published a study that described a more detailed explanation as to why this histological change might occur and the role of genetic susceptibility that is at play. The study proved that greater than 66% of genetic loci found within individuals of northern European descent contained genes that encoded proteins within the Wnt-signaling pathway and that it is the overstimulation of this signaling pathway that could be the source of the unwarranted fibroblast proliferation that occurs in patients affected by Dupuytren's contracture [6,7].

Treatment for Dupuytren's contracture involves either a surgical or non-surgical approach and although these options vary based on the severity and extent of the disease, all available treatment selections have the same goal in mind; to restore finger and hand motion of the affected area in order to improve the ability of carrying out normal daily functions. For this paper, the treatment Options that will be discussed are those which are warranted for advanced stages of Dupuytren's contracture and are further explained in Table 1.

Table 1: A general summary of the different treatment options approved for Dupuytren's contracture and outcomes that have been noted in clinic and throughout current literature.

Treatment	Description	Major Risks and Post-Treatment Findings
(Surgical)-Fasciotomy	Excisional surgery where the thickened cord or cords involved with the contracture are transected	-infection, scarring, skin necrosis, hematoma, nerve/vessel injury, inflammation -significant post-op pain -high rates of recurrence -splinting time= 6-8 weeks -lengthy duration of occupational therapy
(Surgical)-Fasciectomy/ Limited palmer-fasciectomy	Open surgical removal of the offending fascial bands involved with the contracture	-infection, scarring, skin necrosis, hematoma, nerve/vessel injury, inflammation -significant post-op pain -high rates of recurrence -splinting time= 6-8 weeks -lengthy duration of occupational therapy
(Non-surgical) Percutaneous Needle aponeurosis (PNA)	A routine performed with an 18-gauge needle being directly penetrated into the aberrant cord in order to weaken the contracture and attempt correction via mechanical force	-pseudoaneurysm development, Perceived nerve damage, flexor tendon injuries, inflammation, pain -high rates of recurrence -most patients regain immediate improvement of ROM. -high percentage of patient satisfaction following treatment. -splinting time= 3-4 weeks -minimal period of occupational therapy necessary as compared to surgical treatment.

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(Non-Surgical)-Collagenase clostridium histolyticum (CCH) enzyme injection	A dual-phase treatment approach requiring 2 back-to-back office visits that involves the administration of CCH into the Dupuytren's lesion on the first day, followed by manual contracture correction on the second day.	- Injection site pain, bruising, skin tears, inflammation, peripheral edema. -Very low rates of contracture recurrence - No current findings indicating associated nerve injuries -High percentage of patient satisfaction following treatment. -splinting time= 3-4 weeks -Minimal period of occupational therapy necessary as compared to surgical treatment.

In cases involving advanced stages of Dupuytren's contracture, surgical methods including either a fasciotomy, fasciectomy, or limited palmer fasciectomy have been the universal treatments of choice and studies have suggested that clear indications for surgery include any flexion deformities greater than 30 degrees at the MCP joint and or greater than 20 degrees at the PIP joint [8]. As with all surgical procedures, it is important to keep in mind that there will be both intra-operative and post-operative risks that need to be considered before making a final decision on your choice of treatment.

When a non-surgical treatment approach is being considered, one of the more commonly known procedures is that of a Percutaneous Needle Aponeurotomy (PNA). This needle aponeurotomy is a minimally-invasive technique performed under local anesthesia and involves the penetration of an 18-gauge needle passing through the skin and into the underlying affected cord, allowing for a release of the contracture and therefore enabling extension of the involved finger and palm [9]. Although PNA is less-invasive than surgery, one of the major concerns associated with the practice of this technique is that of perceived risk for nerve injury to occur [9,10]. This risk of nerve injury and the possibility of jeopardizing the integrity of the noble structures is so concerning that many physicians are completely against the idea of performing PNAs for digital cases and have concluded that these potential risks do not outweigh the benefits involved with the procedure [9]. Academically speaking, each method of treatment described above has proven to aid in some correction of Dupuytren's contracture despite the numerous risks involved, however there continues to be one major frustrating setback that physicians and patients continue to encounter after initial treatment and that is the incidence of recurrence. Recurrence rates of Dupuytren's contracture have been noted in all treatment options throughout literature and there is very little evidence that suggests surgical treatment outcomes being more advantages to those seen with PNA [9-11].

This brings us to the main topic of discussion, collagenase clostridium histolyticum. CCH is an enzymatic injection that is gaining popularity among orthopedic specialists and has proven to be an encouraged alternative to both surgical correction of Dupuytren's contracture and PNA, as current literature shows evidence of successful contracture resolution, less recurrence and presently no reports of associated nerve injury with its use have been documented [12-14]. Consequently, beginning in June of 2015, as further studies and evidence relating to CCH and its optimistic outcomes emerged, all patient encounters that required treatment for advanced staged Dupuytren's contracture in our office were given the enzymatic injection in hopes of complete contracture resolution and decreased recurrence rates. The overall results have been remarkable and will be explained in greater detail within the results and discussion portion of this paper but before going over those outcomes it is imperative to grasp a better understanding of the CCH injection procedure. The technique is carried out according to the company's standard protocol [17], which comprises of a two-step process that requires the patient coming in for treatment on two consecutive days and is briefly explained as follows:

The first step involves injecting CCH into the problematic cord that is responsible for causing the contracture and then wrapping that affected area with a bandage, it is also important to note that patients may experience ecchymoses and inflammation around the injection site as this is a common sign after receiving the CCH injection [15-17]. We encourage those patients who experience these adverse effects to simply apply ice over the involved area to help reduce symptoms. Patients should also be informed that from the point of the enzyme being injected until the next encounter on the following day, attempts to keep the injected hand elevated as much as possible, limit movement of the treated finger or fingers and avoiding self-correction to straighten their finger must be made [17].

The second step is achieved on the second day and encompasses a manual manipulation of the affected finger or fingers, requiring the physician to carefully apply passive extension at different locations of the involved digit to 'break' the cord and resolve the contracture. Small skin lacerations may be present at the time of manipulation and is common given the fact that the skin involved around the injected area becomes weakened and is put under manual stress of contracture correction. Following the manipulation procedure, patients are given a splint to wear as instructed by the physician and a follow up appointment should be scheduled at one-month and six-months post procedure to assess progress, function, patient satisfaction and to determine if further monitoring or management is necessary.

An imperative detail that must be mentioned is that although there is some debate as to whether administration of local

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anesthetic should be used with CCH treatment and current recommendation suggest that it should not [17], we strongly disagree. In our professional opinion and based on previous treatment outcomes, the administration of local anesthetic on both days and minutes prior to each procedure proves to be of great benefit as it aids in providing better tolerance to both the injection and manipulation process in comparison to patients who undergo treatment without it. This increase in patient tolerance not only decreases the concerns of having to undergo a procedure that may be painful, but it also significantly improved overall patient satisfaction. With that said, physicians must be conscious of their local anesthetic entry sites so that there is minimal risk of injury to the surrounding structures or interference between the enzyme injection area and the anesthetic itself. Therefore, we recommend that the anesthetic be administered just adjacent to the involved cord at both its medial and lateral borders as this has continuously provided aid in our practice.

Results and Discussion

Table 2: A break-down of patient demographics and results witnessed over a 3-year period (June 2015- June, 2018) who received CCH injections as treatment for Dupuytren's contracture as outpatients in the clinic. (CCH: Collagenase Clostridium Histolyticum).

Total number of patients treated with CCH	25 (20=male, 5=female)
Patients age range	50 years old to 85 years old
Number of patients that experienced complete or near complete resolution of their contracture(s) after initial CCH treatment	25 (20=male, 5=female)
Number of patients that developed recurrence and required a second treatment of CCH injection	3 (all male), these contractures recurred at different times between each patient and were noted at 5 months, 15 months and 17 months post initial CCH injection treatments
Number of patients that experienced treatment failure or contracture recurrence after receiving a second injection of CCH	0

From June of 2015 until June of 2018, a total of 25 patients (20 male, 5 female) with advanced stages of Dupuytren's contracture were encountered in clinic and treated with CCH as opposed to the other traditional treatment modalities mentioned above. Each patient was given local anesthesia on both days and the anesthetic was cautiously administered just adjacent to the involved cord at both its medial and lateral borders prior to patients receiving the CCH injection and before carrying out the manipulation phase of the treatment protocol. After receiving treatment, all patients were followed at regular one and six-month intervals for assessment and those who required additional follow ups were appropriately seen thereafter. The results encountered during this three-year period are tremendously satisfying when compared to those seen with previous surgical or PCA results of years prior. The results encountered between the 25 patients who received CCH treatment have been represented in Table 2.

Conclusion

As stated previously, surgical methods including either a fasciotomy, fasciectomy, or limited palmer fasciectomy for the management of advanced Dupuytren's contracture have traditionally been the universal treatments of choice. Although every surgical method mentioned has proven to be beneficial in numerous ways, due to the high rates of contracture recurrence demonstrated post-operatively, orthopedic surgeons have been forced to investigate other treatment alternatives. Thankfully, the approval of a CCH enzyme injection for the treatment of Dupuytren's was made and is beginning to brand a promising reputation for itself.

Based on the evidence found within current literature and the patient outcomes witnessed in clinic, it is our opinion that the administration of the CCH enzyme injection as a method for treating advanced stages of Dupuytren's contracture must not be overlooked by physicians. Our patients who initially received CCH injections as opposed to surgical treatment for their contractures all saw complete or near complete resolution, required less occupational therapy, less splinting time, established an immediate improvement with ROM and complained less about finger stiffness than those previous patients who had been surgically managed. Aside from these findings, the percent of contracture recurrence was significantly less than those seen in patients who received surgery as opposed to CCH injections. In closing, when it comes to the treatment of advanced staged Dupuytren's contracture and where surgery is warranted, we hope that physicians consider using CCH injections in place of surgical correction as there is a clear appreciation for the exceptional results, increase in patient satisfaction and overall influence its use has on improving a patient's quality of life.

Conflict of Interest

The authors have no conflict of interest to declare and did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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