Efficacy of Injectable Collagenase in the Treatment of Dupuytren's Contracture in Comparison to Partial Fasciectomy

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ABSTRACT

Background: Dupuytren’s disease as a benign fibroproliferative disease with an abnormal slowly progressive thickening and shorting of the palmar aponeurosis leads to severe functional limitations in the finger movements particularly of the Metacarpophalangeal (MCP) joints and/or the Proximal Interphalangeal (PIP) joints. The authors aimed to evaluate the role of injectable collagenase (CCH) in the treatment of Dupuytren’s contracture in comparison to surgical treatment.

Material and Methods: This study included 15 patients (33 rays), they were divided into two groups, Group A: 26 rays underwent open fasciectomy. (10 patients) and Group B: 7 rays were treated by collagenase injection. (5 patients). Exclusion criteria for group B were contraindications of injection of CCH. The primary efficacy variable was clinical success, contracture correction to within 5º of normal (normal = 0º) by using goniometry. Additional efficacy variables included the time and number of injections required to achieve success in the primary joint. Recurrence rate and adverse effects were recorded.

Results: Initial clinical experience was recorded of 5 patients (7 rays) (mean age 57 years) and compared to previously surgically managed 10 patients (26 rays) (mean age 59 years). Of all population, 51% for little, 47% for ring, 1% for middle and 1% for index fingers. The mean of the pre-intervention fixed flexion contracture in the MCP joint was 39º and improved to one-year postintervention 14º, and in the PIP joint 47º to 19º. In group B one ray with no improvement at all and recurrence in one ray. Partial stretching was achieved in one ray. No serious complications were observed after injections. In cases of group A (26 rays) that was treated by partial fasciectomy, recurrence occurred in 6 rays and nerve injuries as nerve division and neuropraxia occurred in 2 rays.

Conclusion: The treatment of Dupuytren’s disease with injectable collagenase is safe and effective. However, the financial aspects should be considered especially in developing countries.

Key Words: Dupuytren finger collagenase Fasciectomy.

INTRODUCTION

Dupuytren’s disease (MD) is a benign fibroproliferative disorder, named after Baron Guillaume Dupuytren’s (1777-1835) [1,2], with an abnormal slowly progressive thickening and shorting of the palmar aponeurosis. The etiology of this disease remains unclear, so far, no cure is possible. It particularly affects the Metacarpphalangeal (MCP) joints and/or the proximal interphalangeal (PIP) joints. It usually affects the ring and little fingers [2].

The management of the Dupuytren’s disease can be done with different modalities. The aim of all previously described therapeutic procedures is to restore normal hand function. Although surgical procedures (partial fasciectomy and fasciotomy) are still the standard, the collagenase Clostridium Histolyticum (CCH) has been approved as safe and effective treatment option for several years. This enzymatic substance can cleave peptide bonds and degrade collagens (all human collagen types). It has the advantages of the treatment of older patients with co-morbidities, an earlier return to work, eliminate the risks of surgery [3-11].

However, it should also be noted that the results of collagenase treatment of isolated MCP contractures are significantly better than isolated PIP contractures or combined MCP/PIP contractures. Also, repeated injections of collagenase appear to be safe and effective despite the patient’s antibody production because of repeated exposure. In a case report from a patient who received 15 injections over 4 years, it was found that the effect was still good in the MCP joint but slightly decreased in the PIP [12-15].

In Egypt, the commercially available collagenases (Xiapex®, 0.9mg vial, Swedish Orphan Biovitrum Ltd., Sweden or Xiaflex 0.9mg vial, Endo International plc) are a mixture, which is comprised mostly of interstitial collagen types I and III [16,17].
The most common complications of this non-surgical technique are swelling, effusion, hematoma or pain. Most of these adverse effects are mild or moderate and self-limiting within an average of 10 days. Regarding the financial aspects of collagenase treatment, another disadvantage of this procedure is the higher cost that could be 200 up to 400 USD per vial [18-20].

In a review by Chen et al., compared the recurrence rates of surgical versus Non-surgical procedures showed. It was significantly higher in needle aponeurotomy than in open partial fasciectomy, and in open partial fasciectomy also appeared to be significantly higher than in CCH injection [18].

In 2013, the safety and efficacy of CCH injections were explored again in two studies. A total of 879 joints in 587 patients at 34 institutions were treated in the study. The treatment at an early stage is more beneficial. In 57% of the patients treatment was successful (0-5º extension within 30 days), with more improvement in MCP than PIP joints (70 vs. 37%). [8]. The recurrence rate was comparable to standard surgical procedures [21].

For the treatment of Dupuytren’s related disease as Peyronie’s disease, the use of CCH is both effective and safe by injection of CCH directly into the tunica albuginea [22].

In this study, we aimed to evaluate the efficacy of injectable collagenase (Xiapex®, 0.9mg vial, Pfizer Limited, Kent, UK) in the treatment of Dupuytren's contracture in comparison to traditional partial fasciectomy.

**PATIENTS AND METHODS**

This study included 15 patients (33 rays), 4 patients with 1 ray, 6 patients with 2 rays 3 patients with 3 rays, 2 patients with 2 rays) with flexion deformities of the MCP and/or PIP joints of 20º or greater. Their age ranged from 40 to 65 years. They were divided into two groups:

- **Group A**: 26 rays underwent open fasciectomy. (10 patients).
- **Group B**: 7 rays were treated by collagenase injection. (5 patients).

Exclusion criteria for group B were contraindications of injection of CCH as pregnancy, hypersensitivity to collagenase or patients uses anticoagulant.

All the patients’ results were recorded at 3rd, 6th and 18th moths. The primary efficacy variable was clinical success, contracture correction to within 5º of normal (normal=0º) by using goniometry. Additional efficacy variables included the time and number of injections required to achieve success in the primary joint. Recurrence rate and adverse effects were recorded. Common side effects include local swelling, redness, or pain at the site of puncture was also recorded.

**Injection procedure:**

After injection of local anesthetic (Lidocaine 1:200000), 0.3mg per injection of Xiapex® (0.9mg vial, Pfizer Limited, Kent, UK) [23] was injected into the palpable cord. After 24-72 hours, we perform finger extension procedure to facilitate cord disruption for approximately 10-20 seconds. If the first attempt to extend the finger is unsuccessful, a second and a third attempt can be made at intervals of 5-10 minutes each without increasing the force. The patients were instructed to use splint for 10 days with active and passive extension exercises. Injection was repeated after four weeks, if the MCP or PIP contracture remains, up to a maximum of 3 injections in the same strand.

**RESULTS**

Initial clinical experience was recorded of 5 patients (7 rays) (4 males, 1 female, mean age 57 [range 40-61] years) Figs. (1,2) and compared to previously surgically managed 10 patients (26 rays) (7 males, 3 females mean age 59 [range 42-65] years) Figs. (3,4) (Table 1). Of all population, 51% were treated for little fingers, 47% for ring fingers, 1% for middle fingers and 1% for index fingers.

A successful strand solution was defined as achieving 0-5º extension of the affected joint. This was achieved in all group B cases except one ray with no improvement at all and recurrence in one ray. Partial stretching was achieved in one ray.

The mean of the pre-intervention fixed flexion contracture in the MCP joint was 39º and improved to one-year postintervention 14º, and in the PIP joint 47º to 19º Fig. (2).

No serious complications (tendon/ligament ruptures, nerve lesions or hypersensitivity reactions) were observed after injections. In cases of group A (26 rays) that was treated by partial fasciectomy, recurrence occurred in 6 rays and nerve injuries as nerve division and neuropraxia occurred in 2 rays (Table 2).
Fig. (1): Pre and 6 months after injection of right ring finger MCP joint (Group B).

Fig. (2): Lateral view show improvement of flexion deformity of left PIP joint of ring finger from 35º to 15º (Group B).

Fig. (3): Pre-operative and intraoperative of partial fasciectomy (Group A).

Fig. (4): Lateral view show improvement of flexion deformity of left MCP joint of little finger from 49º to 9º.

Table (1): Number of treated rays in each group.

<table>
<thead>
<tr>
<th>Group A: 26 rays underwent open fasciectomy (10 patients):</th>
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<tbody>
<tr>
<td>1 patient → 1 ray</td>
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<tr>
<td>4 patients → 2 rays</td>
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<tr>
<td>3 patients → 3 rays</td>
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<td>2 patients → 2 rays</td>
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<th>Group B: 7 rays were treated by collagenase injection:</th>
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<tr>
<td>3 patients → 1 ray</td>
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<td>2 patient → 2 rays</td>
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Table (2): Recorded complication in both groups.

<table>
<thead>
<tr>
<th>Open Fasciectomy (26 rays)</th>
<th>Collagenase injection (7 rays)</th>
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<tbody>
<tr>
<td>Recurrence 6/26</td>
<td>Recurrence 1/7</td>
</tr>
<tr>
<td>Nerve division 1/26</td>
<td>Failure of treatment 1/7</td>
</tr>
<tr>
<td>Neuropraxia 1/26</td>
<td>Partial stretch 1/7</td>
</tr>
<tr>
<td>Infection 0</td>
<td>Nerve injury 0</td>
</tr>
<tr>
<td>Skin sloughing 0</td>
<td>Hypersensitivity 0</td>
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DISCUSSION

Our experience has shown that the use of injectable collagenase is an effective and well-tolerated alternative to surgical treatment.

The patient must, however, be informed about the frequent occurrence of undesired side effects (especially cost and hypersensitivity) as well as recurrence rate and ineffectiveness of the treatment that may need surgical intervention.
As regard the undesirable side effects in group B, they were minimally and self-limiting like swelling, bleeding, pain, redness in the puncture site. No nerve lesions were detected.

In elderly patients with multiple co-morbidities, who should avoid anesthesia or postoperative wound healing problems, treatment with CCH is a very good alternative.

The effectiveness and patient satisfaction of collagenase treatment versus partial fasciectomy are comparable; in view of the earlier return to work and surgical complications, collagenase injection has the advantage.

However, the question of the significance in relation to partial fasciectomy cannot yet be answered conclusively. The published recurrence rate shows considerable differences. The method will have to be measured for the long-term recurrence rate and complications.

**Conclusion:**

The treatment of Dupuytren’s disease with injectable collagenase has been proven safe and effective, as confirmed by recent studies. However, the financial aspects should be considered especially in developing countries.

**Conflict of interest:**

There is no conflict of interest.

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