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Efficacy of Collagenase Injection in Dupuytren's Contracture

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Abstract

Introduction: Dupuytren's contracture is a debilitating hand condition characterized by progressive contracture of the palmar fascia. The use of collagenase clostridium histolyticum **i**njections has emerged as a minimally invasive alternative to surgical interventions, with varying degrees of efficacy and safety compared to traditional methods like limited fasciectomy and percutaneous needle fasciotomy.

Methods: A comprehensive literature review was conducted using PubMed to assess the efficacy and safety of collagenase injections for treating Dupuytren's contracture. The search focused on peer-reviewed randomized controlled trials, systematic reviews, and meta-analyses published in the last five years. Five relevant studies were selected based on the robustness of their data and relevance to the research question.

Results: The studies reviewed demonstrated that while collagenase clostridium histolyticum offers a less invasive treatment with quicker recovery times, they are associated with higher recurrence rates and more frequent minor complications compared to other options. Limited fasciectomy showed the greatest improvement in range of motion and the lowest recurrence rates but carried a higher risk of severe complications such as nerve injury. Percutaneous needle fasciotomy, although slightly less effective in range of motion improvement, had fewer complications, making it a safer option for patients with milder conditions.

Discussion: The choice of treatment for Dupuytren's contracture should be tailored to the patient's condition severity and personal priorities. Further research is needed to refine these recommendations and explore the long-term effects of these treatments on quality of life.

Efficacy of Dupuytren's contracture with collagenase injection

INTRODUCTION

Dupuytren's contracture is a condition characterized by the gradual thickening and tightening of tissue under the skin of the palm, leading to the formation of nodules and cords.[1] These changes often result in the fingers, especially the ring and little fingers, being drawn into a bent position at the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints.[1] This condition, first documented over 180 years ago, continues to be a prevalent cause of hand disability.[2] The incidence of Dupuytren's disease in Western populations ranges from 0.6% to 31.6%, with higher rates in older adults, particularly males over 50, and those of Northern European descent.[2] Risk factors include smoking, alcohol use, diabetes, dyslipidemia, epilepsy, use of anticonvulsants and antiretrovirals, and hand trauma.[3]

Dupuytren's contracture can significantly impair hand function, diminishing quality of life and interfering with daily activities. Addressing this condition is crucial due to its chronic and often debilitating nature. Traditional treatments have included surgical methods like percutaneous needle fasciotomy (PNF) and limited fasciectomy (LF).[3] However, these procedures carry risks such as infection, nerve damage, and extended recovery periods.[2] Consequently, there has been growing interest in less invasive treatments that offer effective results with fewer complications.

Recently, collagenase *clostridium histolyticum* (CCH) injections have emerged as a promising non-surgical option for treating Dupuytren's contracture.[2] CCH is an enzyme that breaks down the collagen cords causing the contractures which allows for manual extension of the affected fingers. This minimally invasive approach has shown potential for reducing contractures, improving hand function, and increasing patient satisfaction, all while presenting

lower morbidity compared to surgical alternatives.[3] Current medical research on CCH treatment highlights its balance between effectiveness, safety, and patient outcomes. Both clinical trials and real-world studies have demonstrated the benefits of collagenase injections in reducing contractures and enhancing hand functionality.[3] However, long-term data on complications and recurrence rates following CCH treatment remain limited.[3]

The goal of this review article is to provide a thorough analysis of the effectiveness of collagenase injections in treating Dupuytren's contracture. By examining the available evidence from clinical trials and observational studies, this review aims to assess the overall efficacy, safety, and patient outcomes associated with this treatment. Additionally, it seeks to identify existing gaps in knowledge and suggest directions for future research to improve the management of Dupuytren's contracture.

METHODS

To conduct a comprehensive literature review on the efficacy of collagenase injections in treating Dupuytren's contracture, the utilization of PubMed was used as the primary database. The search was conducted using a combination of Medical Subject Headings (MeSH) terms and free-text keywords tailored to capture relevant studies. The initial search terms included "Dupuytren's contracture," "collagenase injection," and "fasciectomy". For a more targeted search, the following search strategy: Dupuytren's AND fasciectomy AND collagen*. The asterisk (*) was used as a truncation operator to include all variations of the word "collagen." Filters were then applied to narrow down the search results to peer-reviewed articles published in the last 5 years, available in English, and categorized as randomized controlled trials (RCTs), systematic reviews, or meta-analyses. The initial targeted search on PubMed generated 9 articles.

The final selection of 5 articles was made based on their relevance to the research question and the quality of evidence they provided. Studies were prioritized if they included robust data on the efficacy of collagenase injections in reducing contractures, improving hand function, comparisons to other treatment methods and patient satisfaction.

RESULTS

Cooper et al. conducted a randomized controlled trial with 697 patients across multiple centers to compare the efficacy of LF and CCH injection in treating Dupuytren's contracture.[4] Patients were randomly assigned to either the LF group or the CCH injection group.[4] The primary endpoint was the degree of improvement in contracture at the MCP and PIP joints, measured six months after treatment.[4] The results showed that the LF group had a mean MCP joint contracture improvement of 45° (95% CI, 42°-48°) from a baseline of 55°, while the CCH group showed a mean reduction of 30° (95% CI, 28°-32°) from a baseline of 50° (p-value <0.001).[4] For PIP joint contracture, the LF group had a mean reduction of 20° (95% CI, 18°-22°) from a baseline of 40°, and the CCH group had a reduction of 15° (95% CI, 14°-16°) from a baseline of 35° (p-value 0.03).[4] Recurrence rates were 15% for the LF group and 25% for the CCH group at one year.[4] Major complications occurred in 2% of patients in the LF group, such as wound infections and nerve damage, whereas 20% of CCH patients experienced minor complications like localized pain and bruising.[4] The study concluded that LF resulted in significantly better contracture improvement, particularly at the MCP joint, with lower recurrence rates, although it had a slightly higher rate of major complications compared to CCH injections.[4]

Hirase et al. conducted a systematic review comparing PNF and CCH injection for treating Dupuytren's contracture.[5] The review included five studies with a total of 503 patients, analyzing 531 affected digits.[5] The primary focus was on contracture improvement, patient-reported outcomes, and complication rates.[5] Results showed that, for the MCP joint, PNF led to an average final contracture of 5° (95% CI, 3°-7°) from a baseline of 45°, while CCH showed a final contracture of 10° (95% CI, 8°-12°) from a baseline of 46° (p-value 0.01).[5] For PIP joints, PNF resulted in an average final contracture of 13° (95% CI, 11°-15°), compared to CCH's 19° (95% CI, 17°-21°) (p-value 0.04).[5] Patient-reported outcomes, measured by QuickDASH scores, indicated that PNF patients improved from a baseline score of 20 to a final score of 5, while CCH patients improved from 15 to 10 (p-value 0.03).[5] PNF had minor complications in 12% of patients, mostly temporary sensory disturbances, whereas CCH had complications in 25% of patients, including localized pain and swelling (p-value <0.001).[5] The review concluded that PNF generally led to better contracture improvement and fewer complications compared to CCH, suggesting that PNF might be a more effective and safer option for treating Dupuytren's contracture.[5]

Obed et al. performed a network meta-analysis of randomized controlled trials (RCTs) to evaluate the short-term efficacy and adverse effects of CCH injections, PNF, and LF in Dupuytren's contracture treatment. The analysis included nine RCTs with 903 patients.[1] The primary outcomes were contracture reduction to within 0-5° of full extension within 30 days, total passive extension deficit (TPED) reduction, and adverse event occurrence.[1] The results showed that both CCH and PNF significantly improved contracture compared to placebo, with no major differences between the two.[1] LF, however, was significantly superior to both CCH and PNF in reducing TPED (95% CI, 50.56-90.35).[1] The occurrence of adverse events was highest in

the CCH group, while PNF had fewer adverse events (i.e. pain, edema, bruising, rash, nerve injury, and tendon injury) when compared to placebo.[1] LF had fewer adverse events than CCH but was still associated with severe complications.[1] The study concluded that while LF provided the most effective short-term reduction in TPED, CCH and PNF were equally effective in contracture reduction, although CCH had a higher risk of adverse events.[1]

Alhebshi et al. conducted a systematic review and meta-analysis comparing complications and patient satisfaction following CCH injections versus LF in treating Dupuytren's disease.[2] Fourteen studies involving 967 patients and 1,344 joints were analyzed, with 498 joints treated with LF and 846 joints with CCH injections.[2] The review found that CCH injections led to 2.15 complications per patient on average, with common issues being contusion (22.54%) and edema (18.96%), although these were mild and typically resolved without long-term effects.[2] LF resulted in 0.25 complications per patient, including paresthesia (23.7%), scar sequelae (23.7%), and nerve injury (22.6%), which were less frequent but more severe.[2] Patient satisfaction improved faster with CCH injections, particularly during early follow-ups, as reflected in various satisfaction scales like QuickDASH. LF satisfaction increased over time, eventually matching that of CCH.[2] The study concluded that CCH injections may be more suitable for patients seeking quicker recovery, whereas LF may be better for more severe cases, despite its risk of significant complications.[2]

Wong et al. conducted a systematic review and meta-analysis to assess outcomes of surgical and non-surgical treatments for recurrent Dupuytren's contracture, focusing on range of motion (ROM) improvements and complication rates.[6] Twelve studies with 311 patients were analyzed, examining PNF, CCH, LF, and other surgical interventions.[6] LF showed the greatest MCP joint ROM improvement, with a mean increase of 26.5°, followed by CCH (23.0°) and

PNF (20.4°), with a significant difference between LF and PNF ($p<0.05$). For PIP joints, LF again provided the highest improvement (17.4°), followed by CCH (15.3°) and PNF (13.8°), though the differences between LF and CCH were not statistically significant.[6] LF had the fewest complications but with a higher risk of severe issues like nerve injury or infection, while CCH had more frequent minor complications.[6] Recurrence rates were lowest for LF (15%), followed by PNF (25%) and CCH (30%).[6] The study concluded that LF offered the greatest improvement in ROM and lowest recurrence rates but posed a higher risk of severe complications, while CCH had higher recurrence rates but fewer serious issues, making PNF a safer, though less effective, option.[6]

DISCUSSION

The studies reviewed show that each treatment for Dupuytren's contracture, like PNF, CCH injections, and LF, has its own strengths and weaknesses. LF generally offers the most significant improvement in finger movement and has the lowest recurrence rates, but it also carries a higher risk of serious complications like nerve injuries. CCH injections are less invasive and allow for quicker recovery, but they come with higher recurrence rates and more frequent minor issues, such as localized pain and swelling. PNF, while slightly less effective in improving finger movement, has fewer complications, making it a safer option for those with milder conditions or who prefer a quicker recovery with fewer risks.

Based on this information, the best treatment choice depends on the severity of the condition and the patient’s priorities. For severe cases, LF may be the best option because it most effectively improves movement and reduces recurrence, though it carries higher risks. CCH injections are suitable for those looking for a less invasive approach and quicker recovery, even

if it means a higher chance of recurrence and minor complications. PNF remains a good choice for those who prefer a safer, less invasive treatment with fewer complications, even if the improvement in movement is slightly less.

Future research should focus on high-quality studies that standardize how outcomes are measured and include longer follow-up periods to better assess long-term effectiveness and safety. It’s also important to explore how these treatments impact quality of life and to compare emerging therapies with current options. Overall, while LF seems to offer the best results in terms of movement improvement and reducing recurrence, the choice of treatment should be tailored to each patient’s needs, preferences, and risk tolerance. More research is needed to refine these recommendations and ensure the best possible care for those with Dupuytren's contracture.

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Final EBM Paper Rubric

Domain	Poor	Competent	Superior
Introduction	Introduction needs MAJOR improvements in it content	Intro attempts to be well crafted; attempt made at providing key information, the purpose of the paper, the importance of the topic, and a strong command of the current state of the literature; still needs some improvement	Intro is well crafted; provides excellent background information; answer key questions such as the purpose of the paper, the importance of the topic, and a strong command of the current state of the literature (max 10)
Methods	Unclear search methods; missing significant elements that would make replicating the actual search improbable	Mostly clear methods, search strategy is apparent and description of search is reasonable; missing some elements that would make replicating the actual search challenging	Clear methods, superior representation of search strategy, search results, and article selection process; any reader could copy/paste the search and find the same results (max 10)
Results	Missing or incomplete overview/description of any included studies; little or no evidence of article appraisal	Overview and description of results are reasonable; could use a few more details for one or more included studies that speaks to the power of the study or how it was appraised	Superior overview and description of included studies and their results; clear understanding of the important elements of statistical analysis for clinical review inclusion (max 10)
Discussion	Discussion is just an extension of the results; no clear summarization or final conclusion/ recommendation	Good discussion but displays some difficulty summarizing results or making a final conclusion/ recommendation	Superior discussion of results; able to draw correct conclusions and explain why; makes clear final recommendation and/or call for future direction; clear mastery of topic material (max 10)
Abstract	Sections omitted or missing significant key elements that summarize paper/topic	Sections are mostly short and summarize paper; section(s) could improve in brevity or word economy; or section(s) missing a key element	Sections are short but powerful, draws in a potential reader, avoid jargon; superior brief summary of paper (max 5)
AMA style and References	Writing is overall poor; several or major spelling or grammatical errors throughout; guidelines are not followed; major improvement needed; AMA ignored mostly	Writing attempts to be succinct and clear; some minor grammar or spelling errors; guidelines are mostly followed; some improvement needed; AMA attempted	Writing is succinct, clear, and free from grammatical/spelling errors; guidelines are followed; obvious writing excellence; AMA followed (max 5)
Overall Writing	Writing is overall poor; several or major spelling or grammatical errors throughout; guidelines are not followed; major improvement needed	Writing attempts to be succinct and clear; some minor grammar or spelling errors; guidelines are mostly followed; some improvement needed	Writing is succinct, clear, and free from grammatical/spelling errors; guidelines are followed; obvious writing excellence (max 10)
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