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Safety and Efficacy of Collagenase *Clostridium histolyticum* in the Treatment of Acute-Phase Peyronie's Disease

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ABSTRACT

Background: Peyronie's disease (PD), defined as the abnormal formation of fibrous plaque(s) in the tunica albuginea of the penis, is a chronic condition that afflicts 3% to 13% of the US male population; there is no current research on the efficacy and safety of collagenase *Clostridium histolyticum* (CCH) in the treatment of acute phase PD.

Aim: To examine the efficacy and safety of CCH in the treatment of acute-phase PD.

Methods: We retrospectively reviewed the records for all patients treated with CCH for PD from April 2014 through April 2017. Patients who reported penile pain and duration of PD no longer than 12 months at presentation qualified as being in the acute phase of PD. The primary outcomes of interest were final changes in curvature after CCH treatment regardless of the number of CCH cycles received and frequency of treatment-related adverse events.

Outcomes: Parameters of efficacy and safety were compared between acute- and stable-phase PD.

Results: A total of 162 patients were included in the study, of which 36 (22%) qualified as having acute-phase PD (group 1) and the remaining 126 (78%) qualified as having stable-phase PD (group 2). Median duration of PD was 8.5 months (range = 1−12) for group 1 and 18 months (range = 1−492) for group 2. There was no significant difference in final change in curvature between the acute and stable phases of PD (16.7° vs 15.6°; $P = .654$). There was no statistically significant difference in frequency of treatment-related adverse events between the acute phase (4 patients, 11%) and the stable phase (12 patients, 10%; $P = .778$).

Clinical Implications: CCH therapy is as safe and efficacious in acute-phase PD as it is in stable-phase PD.

Strengths and Limitations: This is the first report that assesses the safety and efficacy of CCH therapy focusing on acute-phase PD. This study was composed of a large cohort of patients receiving CCH therapy in acute- and stable-phase PD. Limitations include bias associated with retrospective studies, a small sample, and a single-center setting.

Conclusions: Although CCH is not clearly indicated for treatment during the acute phase of PD, these results suggest that CCH use during this phase can be effective and safe. There was no statistically significant difference in final change in curvature or treatment-related adverse events after CCH therapy delivered between the acute and stable phases of PD. **Nguyen HMT, Anaissie J, DeLay KJ, et al. Safety and Efficacy of Collagenase *Clostridium histolyticum* in the Treatment of Acute-Phase Peyronie's Disease. J Sex Med 2017;XX:XX−XXX.**

Key Words: Collagenase Clostridium histolyticum; Peyronie's Disease; Treatment Outcomes; Acute Phase; End Points

INTRODUCTION

Peyronie's disease (PD), defined as the abnormal formation of fibrous plaque(s) in the tunica albuginea of the penis, is a chronic condition that afflicts 3% to 13% of the US male population.[1−4] PD most commonly presents in men in their 50s with new-onset penile deformity, with pain in one third of cases. The symptoms can have a very negative emotional impact on men, often leading

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to depression and relationship difficulties.[5–8] Such a potent physical and emotional burden makes it essential to fully understand PD and how it is best treated.

After PD onset, the condition can be classified as acute or stable. In the acute phase of PD, penile pain is a common symptom, often accompanied by progression in curvature.[3,9] This phase can last up to 2 years, but most men (94%) report plaque stabilization and decreased pain within 5 to 7 months of onset.[3] If symptoms remain clinically unchanged for at least 3 months, then patients are considered to be in the stable phase of the disease.[9]

Collagenase *Clostridium histolyticum* (CCH; Xiaflex; Auxilium, Chesterbrook, PA, USA) is an injectable agent that enzymatically degrades the interstitial collagen present in PD plaques and has been documented to significantly decrease penile curvature.[10,11] Although effective in decreasing curvature, CCH therapy is not labeled for use by the Food and Drug Administration in certain scenarios. These include a penile curvature deformity less than 30°, ventral curvature deformity, isolated hourglass deformity, calcified plaque, and patients presenting in the acute phase of the disease. To date, there have not been any published studies analyzing the effect of CCH on patients in the acute phase of PD. The aims of this study were to examine the efficacy and safety of CCH in the treatment of acute-phase PD and to compare these outcomes with those in the stable phase of the disease.

METHODS

Patient Population

Retrospective data were collected for consecutive patients with PD who underwent treatment with CCH from April 2014 through April 2017 at one institution. A total of 162 patients were included in the study. Patients who reported penile pain and duration of PD no longer than 12 months at presentation qualified as being in the acute phase of PD (group 1). The remaining patients were considered to be in the stable phase of the disease (group 2). Patients with ventral curvature, hourglass deformity, initial curvature less than 30°, and calcified penile plaques were excluded. The medical records were reviewed and data were collected before and after treatment. Variables of interest included demographics, penile curvature measurements, penile vascular findings, sexual function measured with International Index of Erectile Function (IIEF) scores, stretched penile length, follow-up periods, and other treatment outcomes, including complications and the need for secondary procedures. This study was approved by our institutional review board.

Efficacy and Safety End Points

The primary outcome of interest was the final change in curvature after completing CCH therapy, regardless of the number of cycles received. Secondary efficacy outcomes of interest included overall change in IIEF score, change in curvature after the first cycle, and change in penile length. The primary end point used to evaluate safety was the frequency of a serious treatment-related adverse event (TRAE), defined as a complication that occurred during CCH treatment that the administering physician considered to be directly caused by CCH therapy. These included corporal rupture, penile hematoma, swelling, and hematuria after CCH injection.

Intralesional Injections of CCH

Patients qualified for CCH therapy if they had PD with a palpable, non-calcified penile plaque and a non-ventral curvature deformity of at least 30° at initial duplex measurement. At the first visit of each cycle, an erection was induced by an intracavernosal injection of alprostadil (6–20 μg). The area of maximal curvature was measured with a protractor and then marked for injection. The dose of CCH used was 10,000 biofactor units (ABU) per injection, which equates to 0.58 mg. Each treatment cycle consisted of two intralesional injections of CCH, separated by 24 to 72 hours, administered while the penis was stretched in the flaccid state. Treatment cycles were repeated every 6 weeks for up to four cycles for most patients. Four patients received more than four cycles because of residual curvature and approval by their insurance for additional CCH therapy. Penile modeling was initiated by the patient 24 to 72 hours after the second injection of each treatment cycle.

Statistical Analysis

Statistical analyses were performed using SAS 9.1 (SAS Institute, Cary, NC, USA). Continuous data are represented by mean and SD. Two-tailed Student t-test was used for intergroup (acute vs stable phase) comparisons for continuous variables and χ^2 tests were used for categorical variables. A P value less than .05 was considered statistically significant.

RESULTS

Pretreatment Characteristics

Of the 162 patients included in the study, 36 (22%) qualified as being in the acute phase of PD and the remaining 126 (78%) were in the stable phase. Median duration of PD was 8.5 months for group 1 and 18 months for group 2 ($P = .009$). There was no statistically significant difference in mean pretreatment curvature (60.6° vs 56.9°; $P = .230$) or pretreatment IIEF scores (18.4 vs 17.4, respectively; $P = .398$) between groups. The mean number of cycles for all patients was 3.2 (SD = 1.2), with 14% completing one cycle, 13% completing two cycles, 20% completing three cycles, 51% completing four cycles, and 3% completing more than four cycles, with no statistically significant difference observed between the two groups (3.2 vs 3.2 cycles; $P = .892$). Some patients in our cohort were still undergoing treatment at the time of data collection; however, reasons for treatment discontinuation before the completion of four cycles included lack of initial response, traveling a long distance,