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PEYRONIE'S DISEASE

Predictive Factors of Patients' and Their Partners' Sexual Function Improvement After Collagenase *Clostridium Histolyticum* Injection for Peyronie's Disease: Results From a Multi-Center Single-Arm Study

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ABSTRACT

Background: Collagenase *Clostridium histolyticum* (CCH; Xiapex) injections represent the only licensed medical treatment for Peyronie's disease (PD).

Aim: To evaluate the efficacy and safety of CCH injections in men with stable PD, using a modified treatment protocol and to assess partners' bother improvement in a large cohort of White-European sexually active heterosexual men treated in a single tertiary-referral center.

Methods: All the 135 patients enrolled underwent a thorough assessment, which included history taking, physical examination, and pharmacologically induced artificial erection test (intra-cavernous injection) to assess the degree of penile curvature (PC) at baseline and after the completion of the treatment. Patients with calcified plaque and/or ventral curvature were excluded. All patients underwent a modified treatment protocol, which consisted of 3 intra-lesional injections of 0.9 mg of CCH performed at 4-week intervals at the point of maximum curvature. After each injection, patients were instructed to follow a strict routine involving daily penile stretching in the intervals between injections.

Outcomes: International Index of Erectile Function (IIEF)−15, Global Assessment of PD, PD questionnaires (PDQ), and Female Sexual Function Index (FSFI) questionnaire were performed at baseline and at the end of treatment.

Results: Overall, 135 patients completed the study protocol. Before treatment, 18 (13.33%) partners showed a degree of sexual dysfunction. Baseline median IIEF−15, FSFI, and PDQ scores were, respectively, 59.0, 35.0, and 23.0. Overall, both IIEF−total and all domains significantly improved after treatment (all $P < .01$). A PC mean change of 19.07 ($P = .00$) was measured. At the univariate linear regression analysis, IIEF−15, IIEF−erectile function, IIEF−sexual desire, and IIEF−intercourse satisfaction were positively associated with FSFI (all $P \leq .03$); conversely, PDQ−penile pain, PDQ−symptom bother, and post-treament penile curvature ($P \leq .04$) were associated with a decreased FSFI score. Furthermore, median change of PC was significantly associated with median change of FSFI ($r = 0.25$; 95% CI 0.02−0.11; $P = .004$). Global satisfaction after treatment was 89.6% (121/135).

Clinical Translation: This modified CCH treatment protocol could improve both patients' and partner's sexual function.

Strength and limitations: This was an open-label, single-arm clinical study, without placebo. where only heterosexual couples in stable relationships were included. Furthermore, no real assessment of female sexual

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distress was carried out and long-term sexual function in both patients and female partners were not taken into account.

Conclusions: The modified treatment schedule with CCH injections for stable PD has a positive impact on both patients' and partners' sexual function in heterosexual couples with a stable sexual relationship. **Cocci A, Russo GI, Salonia A, et al. Predictive Factors of Patients' and Their Partners' Sexual Function Improvement After Collagenase *Clostridium Histolyticum* Injection for Peyronie's Disease: Results From a Multi-Center Single-Arm Study. J Sex Med 2018;15:716−721.**

Key Words: Peyronie Disease; Penile Curvature; Collagenase *Clostridium Histolyticum*; Efficacy; Sexual Partners; Female Sexual Function Index

INTRODUCTION

Peyronie's disease (PD) is a common condition, characterized by penile curvature, pain, palpable plaque, shortening of the penis, a degree of erectile dysfunction (ED), and difficulty in penetrative sexual intercourse. Epidemiological studies show that 3−9% of men experience PD.[1] 2 Pathophysiological mechanisms have been proposed for PD: (1) it may be the result of repeated minor penile injury during sexual activity[2]; or (2) it may be a connective tissue disorder, which may share similar pathways with the Dupuytren contracture and Ledderhose disease.[3−5]

The use of intra-lesional injections of collagenase *Clostridium histolyticum* (CCH; Xiapex, Swedish Orphan Biovitrum AB, Stockholm, Sweden) has been recently approved to address penile curvatures in men with stable PD.[6] Limited data are currently available about the impact that the use of intra-lesional injections of CCH in men with stable PD may have on their partners and on the quality of sexual relationship.

2 large phases III randomized, double-blind, placebo-controlled studies (IMPRESS I and II)[6] have tested the safety and efficacy of CCH for the treatment of PD patients with a curvature of 30−90 degrees in a dorsal or lateral direction, with absence of significant plaque calcification, and a disease duration of more than 1 year. The results of these clinical trials showed that CCH can reduce penile curvature up to 17 degrees or 34%, as well as improve the overall symptoms of PD. During the trials, each patient received a total of 8 injections divided into 4 cycles of 2 injections given 24−72 hours apart; cycles was repeated at 6-weekly intervals. Penile manual modeling after each cycle of injections was also part of the treatment protocol of the IMPRESS studies. Historically, traction therapy and penile modeling, typically performed with a stretcher or with the vacuum constriction device, have been used to help straighten penile curvatures.[7,8]

Symptoms associated with both acute and chronic phases of PD have been reported to potentially interfere with patients' sexual function, leading to serious psychological distress.[8] In this context, studies showed that up to 48% of men with PD may experience clinical depression.[6,9] Even though the negative impact of PD on patients has been studied in depth, the consequences on sexual partners has been scantly analyzed. Bothersome psychosocial effects have been observed among partners of men with ED and are likely to be observed also in the partners of men reporting PD.[10] Interestingly, clinical experience indicates that PD has detrimental effects on partners of affected men, and it is known that PD can adversely affect relationships.[11,12]

The current study was designed to: (1) evaluate the efficacy and safety of CCH in men with stable PD using a modified treatment protocol aimed to reduce both the number of injections and of patient visits, thus limiting the duration and the cost of the treatment; and (2) investigate partners' bother improvement in a large cohort of White-European sexually active heterosexual men treated at a single tertiary-referral center.

METHODS

Clinical data from 135 heterosexual sexually active patients assessed at 5 different centers and subsequently treated at a single tertiary-referral center from November 2016 to November 2017 were analyzed. Patients were prospectively enrolled after having been fully informed about the modified treatment protocol, accepted the trial voluntarily, and signed a written specific consent form. Entry criteria were: age $\geq$18 years, chronic PD phase with stable and distressing either dorsal or lateral penile curvature $\geq$30 degrees and $<$90 degrees, and no previous surgery for PD. According to European Association of Urology guidelines (2017),[13] chronic PD phase was defined as a disease stable for at least 3 months, without pain and deformity deterioration. Exclusion criteria were: PD in active phase, ventral penile curvature, and complete plaque calcification. In order to exclude all the confounding factors to measure the effectiveness of CCH therapy, patients with type 1 or 2 diabetes mellitus and/or a degree of ED were excluded from the study.

A comprehensive medical and sexual history was taken from each patient. All patients underwent a complete physical examination and dynamic penile duplex ultrasonography after the intra-cavernosal administration of prostaglandin E to assess the exact location, size, and severity of plaque calcification; the degree of the curvature; erect penile length; and penile hemodynamics. For the specific purposes of the current study, the severity of plaque calcification was classified into absence of calcifications, presence of few calcified spots, and perilesional