ORIGINAL RESEARCH—SURGERY

Surgical Correction of Persistent Peyronie's Disease Following Collagenase Clostridium Histolyticum Treatment

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ABSTRACT

Introduction. Collagenase clostridium histolyticum (CCH) is an Food and Drug Administration-approved intralesional injection for treatment of Peyronie's disease (PD) that has been shown to reduce penile curvature deformity and PD symptom bother in phase 2b and phase 3 placebo-controlled clinical trials. For some patients, nonsurgical treatment with CCH may not sufficiently improve penile curvature, and surgical correction may be pursued following CCH therapy.

Aim. This study aims to examine intraoperative and postsurgical outcomes of surgical correction of persistent penile curvature in patients with PD who had previously received CCH.

Methods. Retrospective chart review was used to identify patients with PD who had received CCH intralesional injection within either the phase 2b or phase 3 CCH clinical trials and then underwent surgical correction due to remaining penile curvature. Surgical techniques used were partial plaque excision and grafting (PEG) and/or tunica albuginea plication (TAP).

Main Outcome Measures. Primary assessments included pre- and postsurgery penile curvature, erectile rigidity, stretched penile length, intraoperative time, and occurrence of adverse events.

Results. Seven men were identified who underwent surgical straightening with TAP or PEG following CCH treatment. Mean number of days from the final CCH injection to surgery was 182 (standard deviation 118; median 127 days). Average penile curvature prior to surgical straightening was 58°. No anatomical difficulties or complications secondary to the effects of prior CCH treatment occurred during surgery. Intraoperative time was representative of standard TAP and PEG surgeries (range 88–146 minutes). All men reported penile curvature <20° postsurgery. One patient experienced a postsurgery subgraft hematoma that required aspiration. There were no postsurgery reports of decreased penile sexual sensation and no occurrence of vascular compromise or decreased penile rigidity.

Conclusion. This initial case series supports the hypothesis that prior CCH treatment is not a contraindication to PEG or TAP surgery in the treatment of penile curvature in patients with PD. **Levine LA and Larsen SM. Surgical correction of persistent Peyronie's disease following collagenase clostridium histolyticum treatment. J Sex Med 2015;12:259–264.**

Key Words. Peyronie's Disease; Penile Curvature; Treatment; Surgery; Collagenase Clostridium Histolyticum

Introduction

Peyronie's disease (PD) is characterized by formation of a collagen plaque(s) in the penile tunica albuginea that prevents normal expansion during erection and may alter penile shape, resulting in curvature deformity, shortening, and narrowing with an hourglass or hinge effect [1]. This disease has also been associated with devastating emotional, sexual, and relationship effects [2–4]. Most of the currently available nonsurgical treatments considered for patients during the disease course have shown inconsistent results in clinical trials, and placebo-controlled data are limited

[5–9]. One exception is intralesional injection therapy with collagenase clostridium histolyticum (CCH), approved by the U.S. Food and Drug Administration (U.S. FDA) in December 2013 for use in adult men with PD with a palpable plaque and a curvature deformity of ≥30° at the start of therapy. CCH has shown efficacy in treatment of PD by significantly reducing penile curvature deformity and PD symptom bother in phase 2b and phase 3 placebo-controlled clinical trials [10,11]. However, some patients may show unsatisfactory change in penile curvature in response to CCH treatment and decide to pursue surgical correction of remaining penile deformity. It is not known whether prior treatment with CCH negatively affects outcomes associated with surgical straightening procedures.

Surgical intervention for men with PD may be considered when the disease has stabilized, which typically occurs at least 1 year from disease onset with no change in penile deformity for at least 6 months [5,8]. Surgery is primarily indicated when penile curvature deformity or inadequate rigidity prevent successful sexual penetration. Other indications for surgery may include failure of nonsurgical treatment, extensive plaque calcification, and patients seeking the most rapid and reliable result [5,8,12]. Because of possible complications associated with surgical procedures and to ensure appropriate expectations for what surgery can accomplish, preoperative discussion with patients and patient consent to a particular surgical procedure are essential [8,12]. Critical topics of frank discussion include possible persistent or recurrent curvature, decreased rigidity, decreased sexual sensation, and change in erect penile length. Importantly, it is essential to determine whether there are predictable complications or poorer response to surgery when CCH treatment was previously administered.

Aim

The aim of this retrospective case series was to examine outcomes of surgical correction of persistent penile curvature in patients with PD who had previously received treatment with CCH.

Materials and Methods

Study Population

Men with PD who underwent surgical correction of penile curvature and who had previously completed intralesional injection treatment with CCH as participants in either the phase 2b or phase 3 CCH clinical trials were included in this study. These subjects all provided informed consent to participate. Eligibility criteria for participation in the phase 2b or phase 3 CCH double-blind, randomized, placebo-controlled clinical trials included age ≥18 years with symptoms of PD for ≥6 months (phase 2b) or ≥12 months (phase 3 studies) and penile curvature 30° to 90° in the dorsal, lateral, or dorsal/lateral plane. Men with ventral curvature or plaques with calcification that would interfere with the injections were excluded [10,11]. The treatment protocol for the phase 2b study included up to three cycles of CCH treatment, with up to six CCH (0.58 mg) injections [10]. Treatment cycles were separated by 6 weeks, and each treatment cycle included two injections of CCH 24–72 hours apart, with subjects additionally randomized to receive penile plaque modeling or no modeling. The CCH treatment protocol for the two identical phase 3 studies (the Investigation for Maximal Peyronie's Reduction Efficacy and Safety Studies [IMPRESS] I and II) included a maximum of four treatment cycles, with up to eight CCH (0.58 mg) injections [11]. Again, treatment cycles were separated by 6 weeks, and each treatment cycle included two injections of CCH 24–72 hours apart. All subjects in the phase 3 clinical trials received penile plaque modeling 24–72 hours following the second CCH injection in each treatment cycle. Following completion of their CCH study participation, the men presented for surgical correction of persistent penile curvature. All men were treated by a single surgeon (LAL) at the same medical center.

Study Design

This study used retrospective chart review to identify patients with PD who had received CCH intralesional injection within either the phase 2b or phase 3 CCH clinical trials and then underwent surgical correction, performed by the authors, due to persistent penile curvature. The surgical correction involved either partial plaque excision and grafting (PEG) and/or tunica albuginea plication (TAP). The determination of the appropriate surgical straightening procedure for each patient followed established surgical algorithm guidelines [8,13–15]. All of the subjects reported erectile rigidity adequate for coital activity, with or without phosphodiesterase type 5 inhibitors pharmacotherapy. Erectile rigidity was also assessed using penile duplex ultrasound with a pharmacologically