Commentary

Expanding the role of injectable collagenase clostridium histolyticum for the treatment of active phase Peyronie's disease

Louis A. Aliperti, Akanksha Mehta

Department of Urology, Emory University School of Medicine, Atlanta, GA, USA

Correspondence to: Akanksha Mehta, MD, MS. Department of Urology, Emory University School of Medicine, Atlanta, GA, USA. Email: ameht32@emory.edu.

Provenance: This is a Guest Commentary commissioned by Section Editor Yongde Xu, PhD (Department of Urology, First Hospital Affiliated to Chinese PLA General Hospital, Beijing, China).

Comment on: Yang KK, Bennett N. Peyronie's Disease and Injectable Collagenase Clostridium histolyticum: Safety, Efficacy, and Improvements in Subjective Symptoms. Urology 2016;94:143-7.

Submitted Nov 15, 2016. Accepted for publication Nov 21, 2016.

doi: 10.21037/tau.2016.12.09

View this article at: http://dx.doi.org/10.21037/tau.2016.12.09

Collagenase clostridium histolyticum (CCH) (Xiaflex™) has recently become the mainstay and gold standard of minimally invasive management of Peyronie's disease. Approved by the FDA in 2013 after phase III studies demonstrated efficacy and safety, collagenase is a popular and promising, albeit expensive treatment option. With the exception of phase II and phase III study data, there is a dearth of published outcomes and safety data. At present, Yang and Bennett's single-provider, prospectively collected series of 49 patients undergoing Xiaflex injections, is only the second published series cataloging efficacy and safety (1).

Yang and Bennett detail their experience with intralesional collagenase injections over a 17-month period. They demonstrate a mean curvature reduction of 15.4° or 32.4% after intralesional therapy. The authors performed a subset analysis on patients who received the full treatment course of four cycles of injection and found that these patients had a 17.7° or 45.7% improvement in curvature. These findings are in keeping with the IMPRESS I & II trials which reported a 34% improvement in penile curvature (2). They further note a 29.1% improvement in their patients' ability to engage in vaginal intercourse after treatment. This compares to Ziegelmann *et al.*, who report that 52% of their patients were able to achieve intromission after therapy (3).

The authors note a higher than expected rate of adverse events in 5 patients (10.2% of patients). They report four penile hematomas, all managed conservatively, and one corporal rupture, requiring operative intervention. The corporal rupture occurred 31 days after completion of the second injection cycle. Upon surgical exploration, the tunical defect was noted contralateral to injection location. This rate of adverse events is similar to that reported by Ziegelmann *et al.*, where 7/69 (10%) of patients experienced penile hematomas, and no patients experienced corporal ruptures (3). Phase III studies reported an incidence of corporal rupture of 0.3%, with only one patient reported to have suffered corporal rupture. In this cohort, two patients had penile hematomas requiring treatment, and 80% of patients reported penile ecchymosis (2).

The ideal time to initiating intralesional therapy is unknown. Based on the IMPRESS phase II and III clinical trial data, required 1 year of stable disease prior to initiation of intralesional collagenase injections, the AUA Guidelines for Peyronie's disease recommend that the clinician start therapy during the stable phase of disease, after pain has subsided, and when there is "non-progression of curvature" (4). Ziegelmann *et al.* discuss initiating therapy earlier in several patients, requiring only a 3-month period of disease stability (3). Yang and Bennett included 12 patients with active-phase disease in their study and demonstrated a mean curvature reduction of 20° compared to 13.9° among active phase patients compared to chronic phase patients. The authors propose that the increased efficacy noted in active phase patients may demonstrate a disease-modifying potential. Notably, their definition of 'active phase' consisted of onset of symptoms or subjective evolution of deformity within 1 year of the first injection cycle; they did not include pain or its resolution as a criterion for differentiating between

active and chronic phases of disease. Nonetheless, they challenge the conventional framework that only stable phase PD should be treated, and offer a nuanced and valid opinion that use of collagenase should be investigated in the active phase of disease.

Another interesting message from the clinical trial offered by both Yang and Bennett and Ziegelmann *et al.* is the instruction of penile modeling prior to injection and the recommendation that patients perform modeling at home. This obviates the need for a return to clinic for technique teaching after injection, minimizing cost, and streamlining post-procedural clinic care (3).

The clinical evaluation of Peyronie's patients includes a history and physical with a standardized physical exam and intracavernosal injection with or without penile duplex ultrasound. The purpose of the ultrasound is not only to document plaque location and consistency, which may have prognostic significance, but also to evaluate erectile function and vascular pathology, which may obviate the clinical significance of intralesional collagenase therapy. Yang and Bennett elected against duplex assessment, electing for intracavernosal injection and goniometry with documentation of curvature and plaque location at baseline and throughout treatment. In our clinical practice, we prefer to obtain penile duplex before proceeding with collagenase therapy. However, the investment in time, personnel and potential equipment expense may make this prohibitive for some practice settings.

The Peyronie's disease questionnaire (PDQ) was developed for use in the IMPRESS trials as a disease specific patient reported quality of life instrument. The instrument has been validated and demonstrated a high degree of internal validity and consistency (5). Yang and Bennett demonstrated a large improvement in PDQ bother score of 43.2% which in phase III studies was reported as −3.6 or about 22.5% improvement in score. As in the IMPRESS trial, there was no statistically significant change in pain domain scores (2).

By offering a clear view of their clinical outcomes, Yang and Bennett, as well as Ziegelmann *et al.*, have allowed other urologists the opportunity to interrogate their own outcomes in a more meaningful manner. Furthermore, by pushing the envelope, and treating men in active phase disease, these authors have opened the door to investigation of CCH as a potential disease modifying agent. Greater emphasis should be placed on following outcomes and honing technique after drugs and interventions come to market.

Cite this article as: Aliperti LA, Mehta A. Expanding the role of injectable collagenase clostridium histolyticum for the treatment of active phase Peyronie's disease. Transl Androl Urol 2017;6(1):114-115. doi: 10.21037/tau.2016.12.09

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Yang KK, Bennett N. Peyronie's Disease and Injectable Collagenase Clostridium histolyticum: Safety, Efficacy, and Improvements in Subjective Symptoms. Urology 2016;94:143-7.
2. Gelbard M, Goldstein I, Hellstrom WJ, et al. Clinical efficacy, safety and tolerability of collagenase clostridium histolyticum for the treatment of peyronie disease in 2 large double-blind, randomized, placebo controlled phase 3 studies. J Urol 2013;190:199-207.
3. Ziegelmann MJ, Viers BR, McAlvany KL, et al. Restoration of Penile Function and Patient Satisfaction with Intralesional Collagenase Clostridium Histolyticum Injection for Peyronie's Disease. J Urol 2016;195:1051-6.
4. Nehra A, Alterowitz R, Culkin DJ, et al. Peyronie's Disease: AUA Guideline. J Urol 2015;194:745-53.
5. Hellstrom WJ, Feldman R, Rosen RC, et al. Bother and distress associated with Peyronie's disease: validation of the Peyronie's disease questionnaire. J Urol 2013;190:627-34.

