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SEXUAL DYSFUNCTION

C. histolyticum collagenase effective against Peyronie

Data from a recent phase IIb, double-blind, randomized controlled trial has demonstrated the safety and efficacy of treating Peyronie disease with *Clostridium histolyticum* collagenase (CCh)—a purified mix of AUX-I and II enzymes that has shown promise in early clinical research.

> "Another proposed mechanism of action [of CCh plus modelling for Peyronie disease] is the induction of myofibroblast apoptosis"

In the study by Gelbard and colleagues, CCh or placebo was injected into the primary plaque at the point of maximal penile curvature and deposited along the needle track. After each treatment cycle (given at 6-week intervals), patients from each treatment group (CCh and placebo) were randomized to receive penile modelling—gentle stretching of the flaccid penis in the opposite direction of the curvature.

On average, patients who underwent modelling showed a 32.4% improvement in curvature (–17.5°) when treated with CCh, compared to a 2.5% worsening of curvature (+0.6°) for placebo. Patients in the modelling CCh-treated cohort also reported improved Peyronie disease symptom-bother scores.

In the absence of modelling, there were minimal differences between the active and placebo cohorts in terms of curvature (mean improvements of 27.1% [–15°] and 27.9% [–13°] for CCh and placebo, respectively) and symptom bother. However, the investigators noted that the data were significantly skewed by a subset (≈30%) of the patients in the nonmodelling placebo group, who demonstrated curvature improvements of more than 40%. Importantly, all five patients in this subgroup had a relatively recent history of Peyronie disease (≤15 months).

Supported by early data from this study, two phase III trials of CCh therapy for Peyronie disease (NCT01221623 and NCT01221597) were set up to provide additional safety and efficacy information. The release of final data from these trials is imminent.

"Although the phase IIb data were not statistically significant in supporting modelling, the non-modelling arm was eliminated from the phase III study," says Martin Gelbard, who has led both trials. "The use of physical force for tissue expansion has a long and successful track record in reconstructive surgery. Applying CCh for Dupuytren's contracture employs physical traction, and the results are excellent."

There are several theories to explain how CCh therapy could alleviate the symptoms of Peyronie disease. Collagenases could soften the plaque and reduce its resistance to tensile stress, restoring erectile symmetry by enabling the tunica albuginea to expand more normally. "Another proposed mechanism of action is the induction of myofibroblast apoptosis," explains Gelbard. "If the plaque were physically elongated by traction after enzymatic collagenolysis, then the stretched tissue would undergo less tensile stress in response to erections, removing the stimulus for ongoing myofibroblast activation and enabling apoptosis."

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Original article Gelbard, M. *et al.* Phase 2b study of the clinical efficacy and safety of collagenase *Clostridium histolyticum* in patients with Peyronie disease. *J. Urol.* doi:10.1016/j.juro.2012.01.032