

Keys from Kols: Some thoughts about the treatment of Peyronies disease with Intralesional collagenase clostridium histolyticum: Overview of data presented at the 2013 AUA meeting

by Martin Gelbard



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A prolonged and interesting conversation wound its way through the AUA in San Diego this May, examining the various outcomes of a large cohort of Peyronies patients who were treated with intralesional collagenase clostridium histolyticum (CCH). It began with a state-of-the-art lecture, and eventually included a point-counterpoint debate at the Endocrine Forum and six different poster presentations.

I don't know if the number of years I've worked with this agent gives me any special insight, but it certainly colors my own personal perspective on this body of data. I took great delight in Dr. Stanton Honig's state-of-the-art lecture "Intralesional collagenase in the treatment of Peyronies disease" not only because of its excellence and clarity, but because I had given a presentation to the Los Angeles Urological Society's chief resident dinner with exactly the same title in the spring of 1982. Time does not permit me to trace the long and winding road from that evening to this year's AUA, but I would like to offer my personal observations on this year's papers.

Dr. Honig presented data published in our Journal of Urology report of two large phase III placebo-controlled randomized clinical trials. Each study involved over 400 subjects, stratified by severity (30–60 or 31–90 degrees), then randomized to receive either CCH or placebo in a 2:1 ratio. Subjects were treated with up to 4 treatment cycles at 6 week intervals, each of which consisted of two intralesional injections 24–72 hours apart followed by stretching ("modeling") 24–72 hours after the second injections. The

2 primary endpoints consisted of goniometer measurement of pharmacologically – induced erectile curvature, and measurement of symptom bother by 4 questions from a fully validated questionnaire employing a 5 point Likert-type scale. CCH-treated subjects experienced a mean 34 % improvement in curvature compared to 18 % in the placebo group ($p < 0.0001$), and change in bother scores of 2.8 points compared to 1.8 in the placebo group ($p = 0.0037$). Three corporal tears occurred which were surgically repaired, and three hematomas occurred, one which was drained surgically, one that resolved with aspiration, and one spontaneously. Most patients had local, short-lived non serious adverse events such as penile bruising, swelling, or tenderness.

Among the poster presentations on these investigations, Dr. Larry Lipshultz looked at treatment efficacy in this cohort stratified by baseline severity. He found no material differences in the 2 co-primary endpoints among the 30 to 60 degree group compared to the 31 to 90 degree group, concluding that CCH treatment showed efficacy in both objective and patient-reported outcomes regardless of baseline severity.

Dr. Irwin Goldstein broke the subjects down by disease duration (1–2 years, 2–4 years, and >4 years), and calcification (no calcification, punctate non contiguous calcification, and contiguous calcification). He found similar end point responses regardless of disease duration and type of calcification. Interestingly, he also found no relationship between disease duration and type of calcification.

In another poster, Dr. Wayne Hellstrom showed how a combination of objective changes (>20 percent reduction in measured bend) and subjective effects (>1 point improvement in the 16 point bother scale or recovery of the ability to have intercourse) used to define "composite responders" resolved a very significant difference between drug and placebo cohorts ($p < 0.0001$). Dr. Cully Carson reviewed the safety profile on

954 subjects receiving a total of 6,701 injections in 4 phase II studies and 3 phase III studies. Nine subjects withdrew due to non serious adverse events. There were 8 treatment related serious adverse events: 4 penile hematomas and 4 corporal ruptures. No systemic hypersensitivity reactions were observed. Adverse events were largely nonserious (reported by 93% of subjects) and localized, consisting of ecchymosis, swelling, and tenderness.

In a poster tracking treatment changes over time, Dr. Chris McMahon found equivalent incremental curvature improvement at each of all 4 treatment cycles.

Dr. Jed Kaminetzky's poster failed to show any difference in curvature improvement with respect to age group or presence/absence of trauma or diabetes. Regarding subjective bother improvement, there was a tendency toward more improvement in the <45 year old group, but due to small numbers in some of the age subgroups, no definitive conclusions could be drawn about CCH efficacy on subjective bother by age group.

At the endocrine forum, Dr. Gerald Brock and I debated whether surgery was the best form of therapy for Peyronie's disease. He defended his position as a proponent of surgery by citing surgical outcomes, its ability to improve calcified or recalcitrant disease, and noting that the phase III CCH data did not demonstrate complete correction of angulation. I argued in favor of medical therapy based entirely on CCH data, emphasizing how our phase III study overcame most of the deficiencies that have plagued prior trials of conservative therapy – not the least of which has been lack of efficacy. I confessed that were it not for the results obtained with CCH, the entire body of work on "conventional" medical therapy to date would not have supported a viable argument against Dr. Brock's position. In my opinion, therapy with collagenase was rational: it was supported not only by high quality clinical data, but also by basic science. The effects of

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collagenase are accessible by standard laboratory methods, from measurement of tensile modulus on contracture explants to analysis of myofibroblast activation on stressed collagen gels. It certainly comports with what we know about wound healing and the pathophysiology of Peyronie's better than other medical therapies. Finally, I looked at insurance use data showing up to 120,000 new cases of Peyronie's disease diagnosed annually in the U.S., and about 1500 operations done. In other words, over 98% of patients were being treated nonsurgically. In

the end, Dr. Brock and I agreed that a safe and effective means of medical therapy would offer much needed improvement to the majority of men with this condition, while surgery would remain the best option in the presence of dense plaque calcification, disabling erectile dysfunction, or failure to improve with CCH.

In some ways, I think this sums up my perspective on the potential of the current CCH regimen – intralesional injection followed by stretching or “modeling”. If approved by the FDA, it will

not eliminate the need for surgery across the board, but for the majority of patients who have lost function and peace of mind due to Peyronie's disease it will offer what they have been seeking for a long time: Safe and effective office-based treatment.

A large watercolor illustration in shades of blue, yellow, red, and purple serves as a background for the lower half of the page. The text "ESSM Today" is overlaid on this background in a bold, white, sans-serif font. "ESSM" is in white and "Today" is in black.

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