INVESTIGATIVE UROLOGY

Liposomal recombinant human superoxide dismutase for the treatment of Peyronie's disease: a randomized placebo-controlled double-blind prospective clinical study

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Objective: To demonstrate the efficacy and safety of a topical gel containing liposomally encapsulated recombinant human Superoxide Dismutase (lrhSOD) in the treatment of painful Peyronie's Disease. The theoretical background is that lrhSOD, by scavenging of free oxygen radicals, might interrupt inflammatory cascades and thereby limit further disease progression.

Methods: In a placebo-controlled randomized clinical trial, 39 patients with Peyronie's Disease and significant pain symptoms were treated with lrhSOD or placebo for a 4 week period. At this time, statistical evaluation of pain resolution was performed as primary study endpoint. Patients then were continued in a cross-over study design to ensure a total of 8 weeks of lrhSOD therapy for all study participants. Pain, plaque and curvature assessment was performed at study entry and every 4 weeks until week 12.

Results: LrhSOD treatment resulted in a statistically significant reduction of pain (p=0.017) compared to placebo already after 4 weeks. At week 12 pain was significantly reduced in 89% of patients who all had received 8 weeks of lrhSOD therapy at that time. Response to other disease parameters was assessed at week 12: plaque size was reduced in 47% of patients, as was plaque consistence in 38%. Penile curvature was improved at 5-30 degrees in 23% of patients. The expected spontaneous disease progression rate of up to 40%, as reported by several investigators, was significantly reduced to <10% under lrhSOD therapy, and patients satisfaction was high, also consequent to the lack of therapy-related side effects observed in the present study.

Conclusion: LrhSOD is an easily administrable, safe and effective local therapeutic for the painful phase of Peyronie's Disease.

Editorial Comment

Around 4 years ago, the authors in an uncontrolled phase-2 study, treated 20 Peyronie's disease patients with a gel containing lrhSOD (1.5 mg/g). The study included patients with penile deviation greater than 45 degrees or plaque calcifications of greater than 5 mm. The authors found 100% pain relief and plaque size reduction in 56% of patients after a maximum of 6 weeks of lrhSOD therapy.

In the present placebo controlled study, the authors confirmed a statistical significant reduction of pain symptoms when compared to placebo, resulting in an overall efficacy of more than 80% after 8 weeks of therapy.

As the authors state, conservative therapies for Peyronie's disease are symptom-directed (analgesic and preventive against disease progression), while correction of deviation is surgical. The liposomally encapsulated recombinant human SOD is a good alternative because shows good efficacy when administered in patients with painful Peyronie's disease lesions. Also, the expected rate of spontaneous disease progression would be reduced, as well as morbidity and the need for future surgery. Probably, the association of clinical and minimally invasive therapy (such as ESWL) would be the future first line treatment for Peyronie's disease.

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The precise location and nature of the nerves to the male human urethra: histological and immunohistochemical studies with three-dimensional reconstruction

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Objectives: The precise location, origin and nature of nerve fibers innervating the male urethral sphincter have not been clearly established. Classical anatomical studies based on cadaver dissections have provided conflicting results concerning the location of somatic and autonomic nerve fibers. This study was designed to identify nerve fibers innervating the male urethral sphincter and to provide a three-dimensional representation of their tissue relations in the human male fetus.

Materials and Methods: Histology and immunohistochemistry (Hematein-Eosin-Safran, Luxol Fast Blue, Protein S 100 immunolabeling and smooth fibers actin immunolabeling) were performed in male external urethral sphincter of ten male fetuses (114-342 mm crown-rump length). Three-dimensional reconstruction of the urethral structure and innervation were obtained from serial sections using Surf Driver 3.5.3 software.

Results: The three-dimensional reconstruction of the same section levels with different strains allowed to identify the precise structure of the muscular layers and the nature of nervous elements (myelinated and unmyelinated), their distributions and their relations with the urethral wall, the prostate and the seminal vesicles.

Conclusion: Histological and immunohistochemical three-dimensional reconstruction of the nervous elements of the urethral sphincter gives a very didactical understanding of the three dimensional arrangement of the urethral nerves and their relationships with the urethral layers. It allows a better understanding of the origin, the course and the nature of the nervous elements participating in the urinary continence.

Editorial Comment

This is one more interesting applied anatomical study from Saint Peres, Paris, under the leadership of Vincent Delmas. The authors analyzed the innervation of the male urethral sphincter in 10 male fetuses of different CR lengths. After elegant and precise 3D reconstruction, the authors give an understanding of the origin and course of the nerves. They also confirmed the previous findings of Yucel and Baskin (1), that the majority of unmyelinated nerve fibers penetrates the male urethral smooth muscle layers at 5 o'clock and at 7 o'clock, where the majority of myelinated nerve fibers penetrates the striated muscles of the prostatic capsule and of the urethral sphincter at 9 o'clock and at 3 o'clock. This very intimate relations of somatic and autonomic nerve fibers place them at risk during any pelvic cancer surgery or urethral trauma. I strongly recommend all surgeons involved in pelvic surgery to read carefully this anatomical article.

Reference

1. Yucel S, Baskin LS: An anatomical description of the male and female urethral sphincter complex. J Urol. 2004; 171: 1890-7.

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