BASIC AND TRANSLATIONAL UROLOGY

Stereological and biochemical analysis of muscular and connective tissue components in the penile corpus cavernosum adjacent to the fibrous plaque of Peyronie's disease

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Objective: To investigate the structural organization of the connective tissue in the corpus cavernosum (CC) adjacent to the fibrous plaque in Peyronie's disease (PD) using stereological and biochemical techniques, as most studies on PD have focused on the analysis of the fibrous plaque that forms in the tunica albuginea (TA). Because this fibrotic reaction is mediated by various inflammatory soluble factors, adjacent connective tissues might also be affected and this secondary effect might explain, for example, the erectile dysfunction that occurs in PD.
Patients and Methods: During surgery biopsies were taken from the CC adjacent to the fibrous plaque and from the plaque itself in seven patients with PD (mean age 48.3 years). All the patients had normal erections. Control samples were similarly located samples from 'normal' penises obtained during autopsy of five men (mean age 52.3 years). Tissue samples were stained with Weigert's stain (elastic fibres), Van Gieson's stain (connective tissue), and Sirius red (collagen). Stereological analysis was done using a 42-point grid to determine volumetric densities (Vv). Total collagen content was estimated as micrograms of hydroxyproline per milligram dry CC.
Results: The Vv of elastic fibres was significantly reduced in PD by 17.3% compared with controls, at a mean (sd) of 19.49 (3.27)% vs 23.56 (1.87)% ($P < 0.05$). While in PD the Vv of smooth muscle at 34.46 (2.06)% and connective tissue at 35.39 (6.15)% were not significantly different from those of controls at 38.38 (3.17)% and 38.02 (5.03)%, respectively. The Vv of elastic fibres in the fibrous plaque was decreased by 38.3% compared with the normal TA, at 20.25 (5.49)% vs 32.81 (4.75)% ($P < 0.02$). The mean (sd) collagen concentration in the CC from controls was 77.94 (24.26) microg/mg and in the patients with PD was 66.57 (19.39) microg/mg, which did not differ significantly. Sirius red-stained sections under polarized light showed that, in the normal CC, collagen-associated colours were homogeneously distributed. However, in the PD samples, stained collagen had a disrupted orientation and had a more heterogeneous birefringence, implying looser collagen bundles.
Conclusions: The quantitative analyses indicated that collagen in the CC close to the fibrous plaque was not affected, although its organization was noticeably altered. The CC elastic fibres were reduced though, and there was a similar change in the fibrous plaque of the TA. These results suggest that, although occurring primarily in the TA, the PD fibrous plaque may induce changes in the adjacent CC.

Editorial Comment

The authors have carried out a study, which may provide new insights regarding the pathogenesis associated with Peyronie's disease (PD). It was studied men with preserved potency but with curvature changes of the penis for some select morphological endpoints. The main finding is that elastic fibers are decreased and collagen is disorganized but not decreased in cavernosal tissue adjacent to the plaque.

In the present study, the authors focused the analysis on smooth muscle cells and the extracellular matrix of the corpora cavernosa (CC), which are important components involved in normal erection and in erectile dysfunction. The results showed that these components are modified in the CC close to the fibrous plaque, which therefore supports an association between PD and erectile dysfunction.

In its earlier stages, PD does not affect sexual function, and the present findings were indeed obtained from PD patients that had normal erection. The results suggest, however, that these individuals may eventually develop erectile dysfunction as the CC already showed significant alterations. The results of the present research imply that PD is not restricted to the tunica albuginea, as it somehow affects the underlying erectile tissue. Our

results also indicate that, of the extracellular matrix components, elastic system fibers are one of the first to undergo modifications. Thus, it may be concluded that the high incidence of erectile dysfunction among PD patients is due to simultaneous and progressive alterations in the CC. Although our results refer only to the CC adjacent to the fibrous plaque, it is possible that the factors that induced this supposedly early alteration will eventually affect deeper regions of the tissue, thereby leading to erectile dysfunction.

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Nerve growth factor modulation of the cavernous nerve response to injury

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Introduction: Surgical therapies for prostate cancer and other pelvic malignancies often result in neuronal damage and debilitating loss of sexual function due to cavernous nerve (CN) trauma. Advances in the neurobiology of growth factors have heightened clinical interest in the development of protective and regenerative neuromodulatory strategies targeting CN recovery following injury.
Aim: The aim of this review was to offer an examination of current and future nerve growth factor (NGF) modulation of the CN response to injury with a focus on brain-derived nerve growth factor (BDNF), growth differentiation factor-5 (GDF-5), and neurturin (NTN).
Methods: Information for this presentation was derived from a current literature search using the National Library of Medicine PubMed Services producing publications relevant to this topic. Search terms included neuroprotection, nerve regeneration, NGFs, neurotrophic factors, BDNF, GDF-5, NTN, and CNs.
Main Outcome Measures: Basic science studies satisfying the search inclusion criteria were reviewed.
Results: In this session, BDNF, atypical growth factors GDF-5 and NTN, and their potential influence upon CN recovery after injury are reviewed, as are the molecular pathways by which their influence is exerted.
Conclusions: Compromised CN function is a significant cause of erectile dysfunction development following prostatectomy and serves as the primary target for potential neuroprotective or regenerative strategies utilizing NGFs such as BDNF, GDF-5, and NTN, and/or targeted novel therapeutics modulating signaling pathways.

Editorial Comment

Impairment of cavernous nerve function is a major cause of the development of erectile dysfunction after radical pelvic surgery. This is target for potential neuroprotective or regenerative strategies utilizing nerve growth factors such as BDNF, GDF-5, and NTN, and/or targeted novel therapeutics modulating downstream signaling pathways. I recommend this well written article for all those scientists involved with this subject.

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