Editorial Comment on: Suburothelial Myofibroblasts in the Human Overactive Bladder and the Effect of Botulinum Neurotoxin Type A Treatment

Christian Gratzke
Department of Urology, Ludwig-Maximilians-University, Campus Grosshadern, Marchioninistr. 15, 81377 Munich, Germany
Christian.Gratzke@med.uni-muenchen.de

Petter Hedlund
Department of Clinical Chemistry and Pharmacology, Lund University, Lund, Sweden

Recent studies indicate interactions between urothelial cells, suburothelial and mural myofibroblasts, afferent nerves, and smooth muscle in mechanosensory signals and in cellular communication in the lower urinary tract (LUT). Findings of altered myofibroblast-related activity in bladders from patients with detrusor overactivity (DO) suggest a role for these cells in the pathogenesis of the overactive bladder (OAB) [1]. Suburothelial myofibroblasts, or interstitial cells, belong to a group of cells with certain ultrastructural properties and exhibit elongated or stellate-shaped cell bodies that express connexin 43, vimentin, c-kit, cyclic guanosine monophosphate (cGMP), or transient receptor potential A1 (TRPA1) [1,2]. Connexin 43, a gap-junction protein, has been identified in the bladder and forms continuity between adjacent cells for numerous signaling molecules involved in cell hemostasis. In accordance with findings in neurogenic DO, Roosen et al show similar increases in connexin 43 in bladder biopsies of patients with neurogenic as well as idiopathic DO, underlining a role for altered intercellular coupling in OAB [3].

Treatment with intradetrusor injections of botulinum neurotoxin type A (BoNTA) is shown to provide significant benefit in DO. The action of BoNTA at the cholinergic neuromuscular junction is well characterized. Increasing evidence suggests a larger range of actions by BoNTA in the LUT that involves sensory as well as motor pathways [4]. It is not known whether BoNTA affects the expression or the function of myofibroblasts in OAB. Considering the putative role for myofibroblasts in sensory functions and in intercellular communication in bladder physiology and pathophysiology, Roosen et al analyze the expression of connexin 43, c-kit, and vimentin in cells of the detrusor from patients with neurogenic or idiopathic DO before and after intradetrusor injections of BoNTA [3]. Although signals for connexin 43 were increased suburothelially in nontreated DO compared with controls, no difference in the expression of c-kit were noted. Treatment with BoNTA did not change
the amounts of connexin 43 or c-kit. It is concluded that beneficial effects by BoNTA on DO do not involve effects on gap junctions on myofibroblasts; it may also be speculated whether permanent changes to cellular components of the bladder were established. Further research to evaluate the role of myofibroblasts in LUT physiology and pathophysiology is of importance to identify novel drug or cell-based therapies for OAB and may also disclose measures for prevention of disease. Recently, a subpopulation of cells that were isolated from urine were shown to have progenitor cell features with potential to differentiate into several bladder cells, including interstitial cells [5].

References


