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PRESENC OF SV2 AND SNAP-25 EXPRESSIONS IN BLADDER UROTHELIUM IN PATIENTS WITH OVERACTIVE BLADDER AND INTERSTITIAL CYSTITIS INDICATES THE POSSIBLE EFFECTIVE TREATMENT BY INTRAVESICAL INSTILLATION OF BOTULINUM TOXIN A

Hypothesis / aims of study

The neurotoxin, botulinum toxin type A (BoNT-A), was used in the treatement of lower urinary tract pathologies by its ability to block neurotransmitter exocytosis. Internalization of BoNT-A relies on the binding to the synaptic vesicle protein (SV2), and blocked neurotransmitter release by the cleavage of synaptosome-associated protein 25 (SNAP-25). SV2 and SNAP-25 have been found to distribute in the suburothelium and muscular layer but not urothelium in the normal human bladder. We investigated the distritution of SV2 and SNAP-25 in the bladder urothelium of patients of overactive bladder (OAB) and interstitial cystitis/ painful bladder syndrome (IC/PBS), which probably indicated the the possible effective treatment by intravesical instillation of BoNT-A in the future.

Study design, materials and methods

Bladder tissues from 2 patients of OAB, 3 patients of IC/PBS, and 1 control were analyzed in this study. In the patients of OAB, diaminobenzidine (DAB) and immunoflurorescence (IF) stains and Western blot analysis for SV2 and SNAP-25 were performed. In the patients of IC/PBS, Western blot analysis of SV2 and SNAP-25 were performed both before and after the treatment by intravesical BoNT-A injection.

Results

Both SV2 and SNAP-25 were detected either in the urothelium and suburothelium layers of patient of OAB after DAB staining or IF staining (Fig. 1). In Western blot analysis, both SV2 and SNAP-25 were present in the urothelium and suburothelium of both normal bladder and the bladder of patients of OAB (Fig. 2). In addition, the presence of SV2 and SNAP-25 in the urothelium and suburothelium of patients of OAB seemed to more significant than normal bladder. Either before or after the management of intravesical injection of BoNT-A, both SV2 and SNAP-25 were present in the bladder mucosa of patients of IC/PBS in Western blot analysis (Fig .3).

Interpretation of results

Previously, BoNT-A was thought to act on the nerve fibers in the suburothelium, and the application of BoNT-A to the bladder pathologies was through suburothelial injection. In our study, both SV2 and SNAP-25 distributed not only in the suburothelium but also in the urothelium of normal subject and patients of OAB and IC/PBS. It indicated the possibility of the application of BoNT-A to the bladder pathologies through the urothelium, for example, intravesical instillation. BoNT-A could act through SV2-mediated internalization on human urothelial cells thus blocking SNAP-25-relaed neurotransmitters' exocytosis. In addition, the diverse distribution of SV2 and SNAP-25 in the urothelium and suburothelium among subjects probably play a crucial role in the efficacy of BoNT-A treatment.

Concluding message

To the best of our knowledge, the present results show for the first time of the presence of SV2 and SNAP-25 in the human urothelium. The presence of SV2 and SNAP-25 expressions in the urothelium and suburothelium of human bladder indicated the possibility of the application of BoNT-A to the bladder pathologies, for example, intravesical instillation through appropriate vehicle such as liposome. In addition, the diverse presence of SV2 and SNAP-25 expressions in bladder urothelium and suburothelium of patients of OAB and IC/PBS was a probable indicator of efficacy of BoNT-A treatment in the future.

Fig. 1. DAB and immunofluroescence stains in the bladder mucosa of patients of OAB. (Arrows: significant staining)

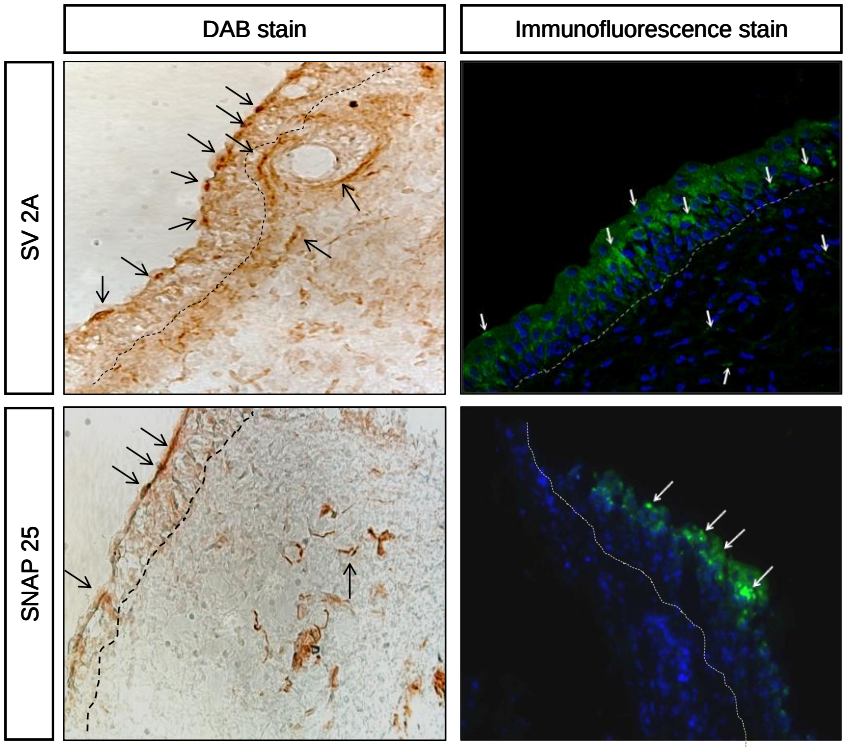


Fig. 2. Western blot analysis in the bladder mucosa of patients of OAB.

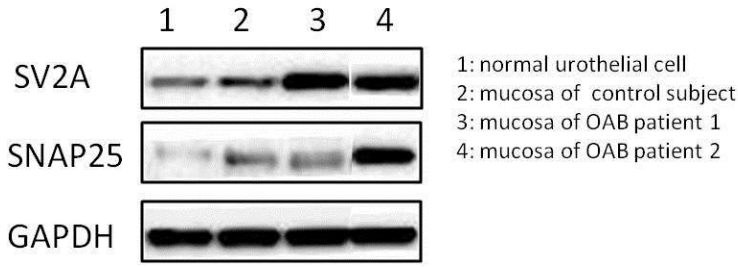
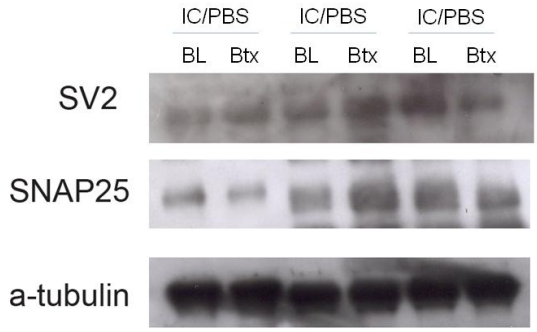


Fig. 3. Western blot analysis in the bladder mucosa of patients of IC/PBS before (BL, baseline) and after (Btx, Botulinum toxin) the management of intravesical injection of BoNT-A.



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