

CELLULAR CHARACTERIZATION OF CADHERIN WITHIN DETRUSOR SMOOTH MUSCLE CELLS AND SUBUROTHELIAL MYOFIBROBLASTS IN HUMAN BLADDER

Hypothesis / aims of study

It appears that attempts to explain the cause of OAB have been primarily focused on abnormal expression of the micturition reflex, the so-called "neurogenic hypothesis". However, a myogenic basis is gaining more and more support. Detrusor smooth muscle are electrically coupled via gap junctions, which play a crucial role in coordinated smooth muscle tone. In order to have good coordinated muscle contraction strong physical interaction between cells is critically necessary as well, which gap junctions cannot account for. This finding has prompted the search for adhesion molecules. Cadherins are adhesion molecules that mediate homophilic cell-cell interactions. It is now well established that loss and gain of cadherin function has profound cell biological consequences in way of cell shape, migration and differentiation. We therefore hypothesize that the critical adhesion and recognition signal between detrusor smooth muscle cells is mediated by a yet unknown member of the cadherin super family. The aim of this study was to prove our hypothesis.

Study design, materials and methods

Bladder biopsies (n=8) were taken from macroscopically non-pathological locations during transurethral resection of bladder tumors. Using haematoxylin-eosin staining techniques, tissue was analyzed for presence of intact urothelium and smooth muscle. Specimens were immunohistochemically treated with antibodies against adhesion complex molecules (E-Cadherin, OB-Cadherin, α -Catenin, β -Catenin, γ -Catenin) and differentiation markers for suburothelial myofibroblasts and smooth muscle cells (connexin-43, vimentin, smooth muscle actin, phalloidin, desmin and smoothelin). Immunolabelled sections were examined by digital binocular fluorescence and confocal microscopy. Cadherin and catenin expression profiles were related to tissue morphology and cytoskeletal markers.

Results

Specific positive membranous expression of all adhesion complex molecules was detected in all eight biopsies, albeit in different layers of detrusor tissue. All antibodies, except E-Cadherin, showed a similar punctate pattern of expression. Bundles of smooth muscle cells revealed intense expression of OB-cadherin and β -catenin at their membrane. Punctate staining was expressed line-wise, revealing the spindle-like shape of detrusor smooth muscle cells. α -Catenin expression was just above detection levels. Detrusor smooth muscle cells showed no γ -catenin expression. All smooth muscle cells showed positive staining for cytoplasmic desmin, smooth muscle actin and smoothelin. In addition, unexpected punctate membranous OB-cadherin staining was intensively expressed in a band of interstitial cells located in the suburothelial zone running parallel with and adjacent to the urothelium. Prominent punctate β -catenin expression was revealed within the same region as OB-cadherin. Punctate α -catenin was less intensively expressed, but much higher than found in detrusor smooth muscle bundles. The suburothelial cells showed positive cytoplasmic expression for membranous connexin-43, cytoplasmic vimentin, as well as smooth muscle actin, but revealed to be desmin and smoothelin negative.

Interpretation of results

In our study cadherin expression was revealed in the suburothelial compartment of the human bladder. Considering their cellular location we suppose they most probably play an important role in the intercellular physical coupling of detrusor smooth muscle cells and suburothelial myofibroblasts.

Concluding message

To our knowledge this is the first time evidence is provided for cadherin mediated smooth muscle cell-cell interaction in the human normal bladder. This in contrary to a previous report in which the authors concluded that cadherins are not part of the detrusor smooth muscle cell-cell adhesion complex¹. Further research will focus on the role of cadherins in the overactive bladder.

References

1. N. Wagener, A. Haferkamp: *Adherens junctions of the human detrusor*, *BJU Int.* 2005 Oct;96(6):843-7

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