

ESTIMATE OF EXPRESSION OF CALPAINS 1/2, CALPASTATIN, E-CADHERIN AND INTEGRIN IN PARAURETHRAL CONNECTIVE TISSUE IN WOMEN WITH URINARY INCONTINENCE AND PELVIC ORGAN PROLAPSE.

Hypothesis / aims of study

Aim of the study is comparing expression different proteases in paraurethral connective tissue in women with and without urinary incontinence and pelvic organ prolapse.

Study design, materials and methods

Urinary incontinence (UI) and pelvic organ prolapse /POP/ can be regarded as a social diseases because its incidence rate in the general population exceeds 5%. The incidence of stress urinary incontinence (SUI) and POP in women are dependent on age, type of work, coincident diseases, as well as obstetric and gynecological history. Elderly age plays an important role in the pathophysiology of SUI and POP because it is associated with hormonal deficiency, changes in connective tissue structure and long-term physical exertion. Findings from epidemiologic studies suggest that occurrence of SUI and POP can be attributed to genetic factors.

55 women were operated on because of stress urinary incontinence and pelvic organ prolapse.

26 women as control group without SUI and POP were operated per vagina due to other non-neoplastic gynecological diseases. From both groups we took paraurethral tissues for estimate of expression.

Calpains are intracellular Ca²⁺-dependent cysteine proteases which display limited proteolytic activity at neutral pH, proteolyzing substrates to transform and modulate their structures and activities, and are therefore called "modulator proteases". By making selective limited proteolytic cleavages, they modulate the activity of enzymes, including key signaling molecules, and induce specific cytoskeletal rearrangements, accounting for their roles in signal transduction and structural stabilization. Calpastatin is a widely distributed endogenous inhibitor protein specifically acting on calpains. Cell-cell and cell-substratum interactions are mediated through several different families of receptors. In addition to targeting cell adhesion to specific extracellular matrix proteins and ligands on adjacent cells, these receptors influence many diverse processes including cellular growth, differentiation, junction formation, and polarity. Adhesion receptors include, among other, integrins and cadherins.

Results

To investigate possible role of calpains, calpastatin and some adhesion proteins in the pathogenesis of urinary incontinence and pelvic organ prolapse we analyzed expression of genes coding above proteins at the mRNA levels by real-time PCR. Samples of 55 paraurethral connective tissues were obtained from patients undergoing surgery for urinary incontinence and pelvic organ prolapse. As control we examined 26 preparations derived from healthy women who were operated by other causes than UI/POP. Expression of calpains 1/2, integrin and e-cadherin mRNA was found to be significantly decreased compared with normal tissue (Mann-Whitney test; P<0.05 in all cases). In turn, calpastatin mRNA expression was slightly increased (Mann-Whitney test; P=0.054).

Interpretation of results

This study demonstrates aberrant expression of calpains 1/2, calpastatin and selected adhesion proteins at mRNA level in paraurethral connective tissues obtained from women with UI and POP.

Concluding message

We conclude that genes/protein studied by us are involved in the rearrangement/degradation of connective tissue in women with stress urinary incontinence and pelvic organ prolapse. Earlier education, providing women with information concerning genetic risk factor and possibility of developing this disorder, should result in higher proportion of women treated conservatively at the early stage of the disease.

Disclosures

Funding: none **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Local Ethics Committee Medical University of Lodz **Helsinki:** Yes **Informed Consent:** Yes