Urine biomarkers for monitoring the effectiveness of peptide complex treatment in recurrent urinary tract infections

Galkina N[1], Galkin A[2]

1. Penza State University, 2. Penza Regional Clinical Hospital

Hypothesis / aims of study

Urinary tract infections (UTIs) is the most common bacterial infection among women. It is generally accepted that the inflammatory process in the bladder wall persists even in the relapse-free period and is associated with increased apoptosis and urothelial dysfunction. We assumed that low molecular weight peptides of the bladder due to their known function regulation of apoptosis and inflammation will increase the duration of chronic cystitis remission. To assess the mechanism of action of peptides and their effectiveness, we decided to use the assessment of the level cytokine/chemokines in urine before, during and after treatment.

Study design, materials and methods

The study involved 40 women with recurrent UTIs in accordance with the inclusion criteria: disease duration of more than 1-year, persistent imperative urge to urinate and frequent urination in the interrelapse period, normal general urine analysis values for at least 2 weeks, receiving treatment according to current clinical guidelines. As a therapy during the remission period, they received a bovine bladder peptide complex (Vezusten) 5 mg. intramuscularly 3 times a week, 10 doses in total.

The levels of the following cytokines and chemokines were measured: tumor necrosis factor (TNF-α), monocyte chemoattractant protein-1 (MCP-1), IL-6, IL-8, macrophage migration inhibitory factor (MIF), regulated on activation, normal T-cell expressed and secreted (RANTES) using the enzyme-linked immunosorbent assay. Statistical analysis was performed using Statistica 6.0 software.

Results

Quantitative evaluation of urine cytokines and chemokines in the recurrent UTIs group in the remission period showed that the levels of cytokines IL-8, MCP-1, TNF-α, RANTES rose on the 10th day of bladder peptide complex treatment and fell 21 days after the end of treatment ($p < 0.05$). The biomarkers IL-8, MCP-1, TNF-α, RANTES decreased statistically significant both for the initial level and that on the 10th day of treatment. Changes in the levels of IL-6, MIF were not statistically reliable.

In addition, 21 days after the end of bladder peptide treatment the levels of RANTES and MCP-1 correlated with the duration of the relapse-free period, the lower the cytokine level, the longer the remission period (correlation coefficient = 0.51, $p = 0.014$)).

Interpretation of results

Our data indicate that bovine bladder peptides reduce the level of proinflammatory cytokines IL-8, MCP-1, TNF-α, RANTES in urine, probably due to the regenerative processes activation in the bladder wall in chronic cystitis. The levels of RANTES and MCP-1 biomarkers in urine can be considered as diagnostic and prognostic markers of therapy effectiveness and the duration of the relapse-free period. A decrease in biomarker levels after a course of treatment is a favorable prognostic factor.

Concluding message

The bladder peptide complex is effective in the treatment and prevention of exacerbations of infection. MSR and RANTES can be used as markers of treatment success and prognosis.