

URINE AND TISSUE GLYCOSAMINOGLYCANS AS BIOMARKERS FOR PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS – INSIGHT ON PATHOPHYSIOLOGY?

Hypothesis / aims of study

Abnormalities of the urothelial glycosaminoglycan (GAG) layer are thought to play a role in the etiology of painful bladder syndrome/interstitial cystitis (PBS/IC) (1). Attempts of correlating urine levels of GAG with PBS/IC have reached contradictory results (2,3). We investigated GAG in urine and bladder tissue of PBS/IC patients in an attempt to understand their relationship.

Study design, materials and methods

Urine was collected from 11 female patients with a clinical diagnosis of PBS/IC by bladder diary and a self-reported validated questionnaire, and cold-cup bladder biopsies were obtained before hydrodistension. Urine and bladder biopsies were also obtained from 11 female patients with pure SUI, as controls. Sulfated GAG (S-GAG) and hyaluronic acid (HA) were measured in the urine and tissue samples were used for proteoglycans, HA and extra-cellular matrix proteins immunostainings; and analyses of S-GAG levels and gene expression of HA synthases and hyaluronidase.

Results

Urine analysis of S-GAG in PBS/IC patients and controls exhibited a different pattern when compared to tissue evaluation. Urine S-GAG concentration was lower in PBS/IC patients ($0.45 \pm 0.11 \times 0.62 \pm 0.13$ µg/mg creatinine, $p=0.01$); while a similar concentration was found in the bladder tissue: $3.3 (0.58-7.08) \times 2.7 (0.15-5.3)$ µg/mg ($p=0.62$). Interestingly, their pattern of distribution remained the same, being chondroitin sulfate the predominant GAG. Decorin, a chondroitin and dermatan sulfate proteoglycan, was more intensely expressed in the urothelium of PBS/IC patients, while the expression of syndecan-4, a heparan sulfate proteoglycan, was scarcer in the urothelium of PBS/IC patients. Fibronectin was highly expressed in PBS/IC patients in the layers underneath the urothelium. These findings may represent local inflammation, superficial urothelial desquamation and extracellular matrix remodeling.

Urine HA levels was similar between the groups ($1.71 \pm 2.06 \times 2.46 \pm 2.07$ ng/mg creatinine; $p=0.48$). However, HA labeling in the urothelial and suburothelial layers was more intense without a corresponding increasing in the expression of its receptor CD 44. This may represent a shift in HA turnover with consequent deposition of HA in the interstitium, where interacting with other matrix components, it could participate in remodeling and recovery of the urothelium.

HA synthases 1, 2 and 3 and hyaluronidase gene expression was consistently lower in PBS/IC patients, which may also suggest changes in HA turnover.

Interpretation of results

Rather than possible biomarkers, analyses of GAG in patients with PBS/IC may be important in understanding the pathophysiology of the disease and the tissue changes occurring because of the dysfunctional urothelium. Since changes in HA synthases and hyaluronidase gene expression were consistent among PBS/IC patients, they could possibly be a marker of the disease.

Concluding message

PBS/IC pathophysiology is still not fully understood but the study of GAG behaviour and gene expression may help to improve that.

References

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Disclosures

Funding: none **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** CapPesq **Helsinki:** Yes **Informed Consent:** Yes