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Gousse A, Kester R, Schroeder G, Selzer M, Gibson X, Lokeshwar V
University of Miami School of Medicine

CORRELATION OF URINARY GLYCOSAMINOGLYCAN LEVELS, AND PROFILE WITH DISEASE SEVERITY IN INTERSTITIAL CYSTITIS PATIENTS

Aims of Study

Urothelial glycosaminoglycan (GAG) layer offers a protective coating to the bladder urothelium. An imbalance in this layer may either cause interstitial cystitis (IC) or be a result of it. We recently demonstrated increased urinary GAG levels in IC patients.[1] Other reports have documented elevated total GAG levels.[2] However, no study of urinary GAG levels in IC patients has correlated the clinical degree of IC symptoms, or pathological findings. Herein, we report on our study of the correlation of urinary GAG levels and GAG profile with disease severity, as judged by validated IC symptom questionnaires and pathological parameters.

Methods

Following approval by the human research committee of our institution's Interdepartmental Review Board, voided urine specimens were prospectively collected from 14 IC patients and 4 age-matched normals. Total urinary GAG and sulfated GAG concentrations were measured by Bitter and Muir and Farndale assays, respectively. The total and sulfated GAG levels were normalized to creatinine. Urinary GAG profiles were determined by G-50 gel-filtration chromatography. Results were correlated with a validated problem and symptom indices questionnaires,[3] and pathologic parameters (IC patients only: glomerulation, bloody efflux, cystometric and anesthetized bladder capacity, urine analysis).

Results

Total urinary GAG levels (269.8±37 μg/mg Cr) were 4 to 7-fold elevated in IC patients who have a problem index >50% (i.e., 8/16) and symptom index >50% (i.e., 10/20), when compared to the levels in IC patients with indices <50% (75±15.4 μg/mg Cr) and normals (39.5±11.2 μg/mg Cr) ($p<0.001$). Fisher's exact test showed a significant correlation between problem and symptom indices being >50% and GAG levels >100 μg/mg Cr (P=0.0128; two-sided; RR=7.9; OR=25). Sulfated GAG levels were not different among IC patients and normals. The analysis of GAG profiles showed that IC patients with >50% problem and symptom indices have 3 distinct urinary GAG peaks whereas, the GAG profiles of normals and IC patients with problem and symptom indices <50% have either one (peak III) or two (peaks I and III) peaks. Fisher's exact test showed a significant correlation between problem and symptom indices being >50% and the presence of 3 urinary GAG peaks (p=0.0076; two-sided; RR=8.3; OR=45). No significant correlation was observed between pathologic parameters and GAG levels/GAG profile (Fisher's exact test: P=0.6).

Conclusions

Urothelial glycosaminoglycan (GAG) layer offers a protective barrier in normal bladders. Measurable amounts of urinary GAG levels were detected by the methods used in the present report. We found significantly elevated levels of total urinary GAG in patients with IC symptom >50% of maximum scores. Of note, in patients with IC symptoms below 50% of maximum scores, total urinary GAG levels were not significantly different from controls. In neither IC patients nor controls were urinary sulfated GAG levels elevated. In addition, we found that pathological parameters did not correlate significantly with GAG levels or GAG profile. Based on the present findings, total urinary GAG levels may be useful as an objective measure to evaluate patients with severe symptoms of IC.

References:

1. The association of elevated urinary total to sulfated glycosaminoglycan ratio and high molecular mass hyaluronic acid with interstitial cystitis. J Urol 2000; 163(5): 1557-83.
2. Erickson DR, Sheykhnazari M, Ordille S, et al. Increased urinary hyaluronic acid and interstitial cystitis. J Urol 1998;160(4):1282-4.
3. O'Leary MP, Sant GR, Fowler FJ Jr, et al. The interstitial cystitis symptom index and problem index. Urology 1997;49(5A Suppl): 58-63.