

## ALTERED EXCRETION OF URINARY GLYCOSAMINOGLYCANS IN CHILDREN WITH NEUROGENIC BLADDER SECONDARY TO MYELOMENINGOCELE

### Hypothesis / aims of study

Proteoglycans are complex glycoconjugates of the extracellular matrix that contain glycosaminoglycan (GAG) side chains. Cleaved GAGs are produced as metabolites of normal proteoglycan turnover, but as their renal filtration is small, it is thought the most chains in the urine derive from the urinary tract. GAG urinary excretion can be affected by such factors as female steroids [1], and is altered in a number of urinary tract disorders. GAG excretion in children with neurogenic bladder secondary to myelomeningocele (MMC) may also be affected, but existing data [2] lack more detailed demographics, do not correlate excretion pattern with severity of bladder dysfunction, and only report data on total GAG. Here we analysed excretion of the different types of GAG in a well defined group of children with neurogenic bladder secondary to MMC. The aim was to determine whether the excretion pattern could be correlated with degree of bladder dysfunction as measured by cystometry.

### Study design, materials and methods

Urine specimens from 17 MMC patients (mean age  $\pm$  SD,  $4.6 \pm 2.9$  years) were obtained during cystometry. Control specimens were from 18 normal children ( $6.9 \pm 2.2$  years). All children were free from urinary infection, had normal renal function as determined by creatinine and urea serum levels, and were not under pharmacological treatment for at least six months prior to the present study. MMC patients were regularly doing clean intermittent catheterization and had been submitted to surgical repair for MMC shortly after birth. Total urinary GAG was assayed as  $\mu\text{g}$  hexuronic acid/mg urinary creatinine, and the different types of sulfated GAGs were assessed by agarose gel electrophoresis, as previously described [1]. Cystometry was done using a Dynapack MPX816 (Dynamed, São Paulo, Brazil), from which a cystometrogram score was calculated according to a published procedure [3]. Results are reported as mean  $\pm$  standard deviation. Comparisons between means of two groups were done using a two-tailed t-test. Correlation was determined by linear regression and by performing a t-test for the coefficient of correlation. Power analysis indicated that a sample size of 32 (controls and patients) would provide a power of 80% to detect a 1 standard deviation difference between groups with a type I error of 5%.

### Results

There were no significant differences in total GAG excretion between male and female individuals in the MMC ( $0.913 \pm 0.528$  vs  $0.867 \pm 0.434$ ,  $p > 0.05$ ) and control ( $0.546 \pm 0.240$  vs  $0.699 \pm 0.296$ ,  $p > 0.05$ ) groups. Also, urinary GAG did not correlate with age in the MMC ( $r = -0.28$ ,  $p > 0.05$ ) and control ( $r = -0.40$ ,  $p > 0.05$ ) groups. However, MMC patients excreted 52% more GAG than controls ( $0.894 \pm 0.477$  vs  $0.588 \pm 0.257$ ,  $p < 0.04$ ). In these patients, total GAG excretion was not associated with vesical compliance alone ( $r = -0.18$ ,  $p > 0.05$ ), but was significantly and negatively correlated ( $r = -0.56$ ,  $p < 0.05$ ) with the vesical score. On average, MMC patients with worst scores ( $< 9$ ) excreted 81% more GAG than those with better scores ( $> 9$ ) ( $1.157 \pm 0.467$  vs  $0.639 \pm 0.133$ ,  $p < 0.04$ ). Of the different types of GAG, chondroitin sulfate prevailed in both groups, but there were no significant differences between them.

### Interpretation of results

Evidence from animal models of MMC and overactive bladder suggests that neural overstimulation of cells markedly affects the turnover of collagen in the vesical wall. Additionally, fibroblast growth factor and collagen types are overexpressed in vesical smooth muscle cells from children with MMC. It is likely, therefore, that this neural disorder would also affect the metabolic pathways of other molecules of the vesical extracellular matrix, as for example, proteoglycans. This could be not only a direct result of neural stimuli, but also a consequence of higher levels of fibroblast growth factor in the tissue, which is known to enhance proteoglycan synthesis. Thus, these published data are consistent with our results showing higher GAG excretion in MMC patients.

### Concluding message

GAG excretion in MMC patients is significantly greater than in normal children, and higher values correlate with a more severely compromised bladder function. These results indicate that urinary GAG excretion might be used as an adjuvant analytical variable to characterize vesical dysfunction in patients with neurogenic bladder.

### References

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### Disclosures

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