223

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THE DETRUSOR GLYCOGEN CONTENT OF A DE-OBSTRUCTED BLADDER REFLECTS THE FUNCTIONAL HISTORY OF THAT BLADDER DURING PBOO

Hypothesis / aims of study

Children with functional or neurogenic partial bladder outlet obstruction (PBOO) are at risk for reflux related kidney damage. Guarding the bladder function is a pivotal element of their treatment. Urodynamic investigations are the prime tool to investigate changes in bladder function. However, in very young and non-toilet trained children standard (video) urodynamic observations are difficult to perform. Specifically in patients with urethral valves changes in bladder function will have occurred out of view in the prenatal period and the obstruction is removed before the first urodynamic investigations are performed. At that time it is difficult to establish exactly how far the bladder function actually had deteriorated before de-obstruction what the potential for recovery is.

Analysis of bladder structure may help. It will show adaptations to the historic dysfunction. Glycogen accumulation due to ischemia upon PBOO has already been described[1]. We have shown in a guinea pig model that during the period of surgically induced PBOO the intensity of glycogen deposition in the bladder correlates with the extent of bladder dysfunction.

Here we investigated bladder glycogen content after removal of a urethral obstruction to answer two questions:

Does bladder glycogen content after a period of recovery still reflect the situation of bladder dysfunction as it existed during the period of PBOO?

How do changes in bladder function after de-obstruction relate to the degree of glycogen deposition at the time of de-obstruction?

Study design, materials and methods

Bladder tissue was obtained from our guinea pig model for PUV. In short, bladder pressure was measured through a suprapubic bladder catheter and urine flow rate was measured by means of an ultrasound flow probe attached loosely around the penis. From these urodynamic data we assessed bladder overactivity (BO) as the number of instable contractions (NIC), bladder pressure at maximum flow rate (pQ_{max}), contractility (W_{max}) and compliance (ml H_2O/ cm H_2O). This model allowed for weekly urodynamic monitoring, both during PBOO as the recovery period after removal of obstruction. To achieve different levels of functional changes upon PBOO, different time-periods up to 10 weeks of obstruction were used. Follow-up after de-obstruction comprised from 2 to 8 weeks. In total 24 treated animals and 10 control / sham-operated animals were included.

After sacrifice, cross-sections of 4 μm covering all bladder wall layers were made for staining with the Periodic Acid Schiff's (PAS) protocol. This staining reveals granular glycogen deposits in the bladder detrusor of which the number was scored by three researchers in a blinded fashion. Scoring ranged from 0, no staining to 3, the most intense staining.

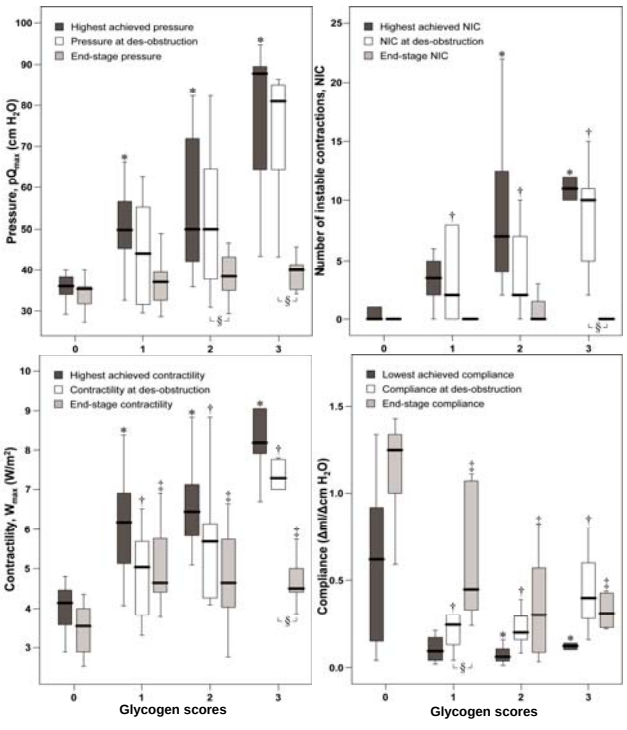
The glycogen scores were correlated to the urodynamic data and plotted in box-whisker plots that visualize the distribution within data, showing median values together with the 5%, 25%, 75% and 95% percentiles of each urodynamic parameter. The Mann Whitney U-test was used to determine the significance ($p<0.05$) of differences in urodynamic parameters between the group with glycogen score 0 and the groups with other glycogen scores. The Wilcoxon Signed Ranks test was used to determine the significance ($p<0.05$) of differences between urodynamic values measured at de-obstruction and end-stage urodynamics in each glycogen score group. All data analysis was performed in SPSS, release 12.0.1, Chicago, Illinois, US.

Results

In all samples the glycogen granules were found only in the bladder detrusor layer. With increasing score the location of glycogen deposition shifted. At a score of 1 a light glycogen granule staining was found only at the serosal side. A score of 2 represented more intense staining where glycogen granules were found deeper into the muscle layer. A score of 3 represented strong staining of glycogen granules that were present throughout the whole muscle layer.

Glycogen score	*0*	*1*	*2*	*3*
Control / sham	8	2	0	0
Treated animals	0	8	11	5
Total	8	10	11	5

In this table glycogen score results are shown for sham operated animals and treated animals. Glycogen scores were compared to all urodynamic parameters at end-stage, maximum achieved values and values at the moment of de-obstruction, shown in the figures aside. The controls and sham-operated tissues obviously did not undergo de-obstruction. * Denote $p < 0.05$ to highest



values at glycogen score 0, † and ‡ denote p< 0.05 to end-stage values at glycogen score 0 for values at de-obstruction end end-stage values respectively and § denote p < 0.05 between values at the time of de-obstruction and end-stage values.

Interpretation of results

The number and location glycogen deposits indicate that ischemic conditions begin at the serosal side and progress towards the urothelium as blood supply to the detrusor layer is more and more affected by increased bladder pressure due to PBOO. The number of glycogen deposits measured weeks after removal of the obstruction still reflects the degree of bladder dysfunction that occurred during the period of PBOO while the bladder function measured after de-obstruction does not.

A higher glycogen score at the end of the recovery period correlates with higher historic bladder pressure, more BO, lower compliance and higher contractility. In contrast the bladder pressure measured at the end of the recovery period is similar for the groups with glycogen scores of 1, 2 and 3 as compared to the glycogen score 0 group and BO has almost disappeared in all groups. The end-stage contractility values are similar for the glycogen scores 1, 2 and 3 and all high increased compared to controls. The end stage compliance improves more in the score 1 group but does not differ between groups 2 and 3.

Concluding message

When in the clinic the first urodynamic data is obtained from patients with PBOO after de-obstruction some of the apparently good-responders will show further loss of bladder function during follow-up. Our study subscribes that the bladder function measured some time after de-obstruction does not reveal the history of bladder dysfunction for the bladder in question. Bladder pressure normalizes and BO diminishes in all. Compliance may improve less with a history of severe bladder dysfunction but the wide value range precludes distinction of individual bad-responders. The contractility remains high in all animals. The bladder glycogen content, however, continues to reflect the history of bladder dysfunction also during the recovery period and may be of value for picking out potential bad-responders in the clinic.

References

1. Scand J Urol Nephrol Suppl (2004) 215; 84-92.

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