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POTENTIAL FOR RECOVERY IN BLADDER FUNCTION AFTER REMOVING A URETHRAL OBSTRUCTION.

Hypothesis / aims of study

Partial urethral obstruction caused by posterior urethral valves (PUV) evokes changes in bladder function and structure. At birth PUV patients express varying degrees of functional and structural bladder damage. Early recognition and removal of bladder obstruction followed by monitoring renal and bladder function and optional treatment with clean intermittent catheterisation have diminished the progression to a so-called valve bladder. Still, however, cases of continuing deterioration of bladder function and structure occur. In the clinic there is usually no urodynamic data obtained before valve ablation and scarce data obtained at the time of de-obstruction or shortly thereafter. Consequently it is still problematic to exactly determine how long and how far bladder dysfunction has proceeded up to the first time the patient is seen and to predict from that single time point data whether bladder function will improve, stabilise or deteriorate further.

We used an animal model for partial bladder outlet obstruction (PBOO) that provides us with detailed information on the longitudinal individual changes in bladder function during PBOO to examine the relation the bladder function at the time of de-obstruction and the potential for recovery of function after de-obstruction.

Study design, materials and methods

Guinea pigs received a partial urethral obstruction. Urodynamic studies were performed before obstruction (week 0) and weekly thereafter. Under anaesthesia bladder pressure (p_{det}, cm H_2O) and urine flow rate (Q, ml/s) were measured with continuous bladder filling until at least three voidings had been produced. From these data the maximum flow-rate (Q_{max}) and the accompanying detrusor pressure ($P_{det}Q_{max}$) were determined. Bladder overactivity (BO) was assessed as the number of contractions (NIC) with a Pdet>10 cm H_2O (1/3 mean voiding pressure at week 0) without urine flow. Compliance (ml/ cm H_2O) was calculated from the filling phase as infused volume/ increase in bladder pressure. Contractility (Wmax, w/m^2) was calculated from the pressure flow relation. The obstruction was left in place for 2-4 weeks (Short, n=12), 6-8 weeks (Medium, n=19) or 9-12 weeks (Long, n=10). Then the obstruction was removed and bladder function was followed for an extra 7 weeks. The groups were compared to historic groups receiving only obstruction (n=55) or a sham operation (n=11).

A paired Students t-test was used to determine the significance of the difference between the situation at the day of de-obstruction and that during the weeks thereafter. An unpaired Students t-test was used to determine the significance of the difference between the different groups (de-obstruction, obstruction and sham operated).

Results

During the obstructive period similar patterns of progressive loss in bladder function occurred in the three de-obstruction groups and the obstruction group. Compared to the sham group compliance had decreased significantly ($p<0.01$) at the time of de-obstruction while $P_{det}Q_{max}$, Wmax and BO had increased significantly ($p<0.01$). The flow rate did not change. After de-obstruction the response in the three de-obstruction groups varied, see the table.

In S bladder pressure decreased after 1 week and reached an average normal value after 7 weeks. Compliance increased immediately and was normal after 7 weeks. Wmax increased the first week then decreased towards high normal values after 7 weeks. BO remained high normal and flow rate increased.

In M bladder pressure and BO decreased the first week and reached above average normal respectively normal values after 7 weeks. Compliance improved the first weeks but remained below normal. Wmax slowly decreased to above the normal range. Flow-rate increased.

In L, bladder pressure and BO decreased the first week and reached high normal respectively normal values after 7 weeks. Compliance did not improve. Wmax decreased directly after de-obstruction and stabilised at an above normal level after 7 weeks. The flow-rate increased.

Bladder function parameters during recovery period

		$p_{det}Q_{max}$ cm H_2O		Q_{max} ml/s		Wmax w/m^2		compliance ml/ cm H_2O		BO NIC	
		mean	sem	mean	sem	mean	sem	mean	sem	mean	sem
mean normal		29		0.18		3.0		1.40		0.2	
95% normal		41		0.32		4.1		0.55		2	
group	time point										
S	d	37.5	2.6	0.22	0.02	4.3	0.3	0.24	0.08	2.9	0.8
	d +1	34.8*	1.4	0.37*	0.05	5.0*	0.3	0.60	0.22	1.3	0.5
	d+7	28.6*	2.8	0.44*	0.11	3.8	0.5	0.73*	0.02	4.8	2.0
M	d	52.1	3.8	0.27	0.03	5.5	1.6	0.31	0.05	6.2	1.8
	d+1	37.7#	1.9	0.57#	0.06	5.6	2.0	0.43	0.08	1.0#	0.5
	d+7	33.5#	1.8	0.50*	0.07	4.7	0.3	0.53	0.31	0#	0
L	d	61.3	16.2	0.26	0.03	6.3	1.4	0.32	0.09	5.0	1.6
	d+1	41.4#	11.5	0.48*	0.05	4.9*	1.3	0.32	0.08	0.3#	0.1
	d+7	37.8#	7.2	0.33	0.04	4.3#	0.9	0.23	0.14	0#	0

d= day of de-obstruction, d+1= 1 week recovery, d+7= 7 weeks recovery
*significance of difference versus d: * p<0.05, # p<0.01.*

Interpretation of results

When longitudinal individual data is available it is obvious that recovery in bladder function is inverse to the extent of obstruction. However, in the clinic longitudinal individual data from the obstructive period and immediately following de-obstruction will not be available. The decision if a bladder is recovering after de-obstruction must be based on urodynamic data obtained some time after de-obstruction. When our 7 week recovery point is taken to represent that time point the conclusion which bladder is recovering best is less obvious. Bladder pressure has entered the normal range for all and the subtle difference apparent in the longitudinal data is lost. Bladder overactivity recovers least in the bladders with the shortest duration of obstruction. Bladders with the longest periods of obstruction are characterized best by a lack of improvement in compliance. Interestingly the contractility remains abnormally high in all and even initially increases in the bladders that had experienced the shortest period of obstruction. The first finding indicates that a de-obstructed bladder remains capable of producing high pressures should any new event of outflow obstruction present itself. The last finding could be related to proposed mechanism of ischemic damage due to high pressure [1]. High bladder pressure may induce ischemia and anaerobic muscle action in the bladder wall. Because the bladder muscle works less efficient under anaerobic conditions its increase in mass in response to the increased demand needed to overcome the obstruction may be greater than would be required under aerobic conditions. When the obstruction is removed and the pressure needed for voiding decreases, aerobic conditions return and the increased muscle mass produces more force than needed untilit has adapted to the new situation. The muscle tissue in the bladders that experienced longer periods of obstruction may have started intrinsic changes that adapt the muscle cells to anaerobic conditions like the production of specific myosines [2]. Possibly this process is less reversible.

Concluding message

A detailed history of changes in bladder function during obstruction and follow-up can clearly identify the individuals that do and do not respond well to de-obstruction. Unfortunately obtaining such data is a practical impossibility in children with bladder obstruction. An option to still gain such insight into the history of bladder function could be to analyse its structure.

References

1 Scand J Urol Nephrol Suppl 2004; 215: 84-92.
2 J Urol 2001;165: 963-7.

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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by The protocol was approved by the institutional animal care and use committee of the Erasmus University and was in line with guidelines by the EU.