

LONGITUDINAL STUDY OF INFANTS WITH HIGH-GRADE VESICoureTERAL REFLUX

Akademisk avhandling
för avläggande av medicine doktorexamen vid Sahlgrenska Akademien,
Göteborgs Universitet

Avhandlingen kommer att offentligen försvaras i föreläsningssal 1,
Drottning Silvias barn- och ungdomsjukhus, Göteborg,
fredagen den 25 september 2009 kl 13.00

av

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Avhandlingen baseras på följande delarbeten:

- I. Sjöström S., Sillén U., Bachelard M., Hansson S. and Stokland E., *Spontaneous resolution of high grade infantile vesicoureteral reflux*. J Urol, 2004. **172**(2): p. 694-8; discussion 699.
- II. Sjöström S., Jodal U., Sixt R., Bachelard M. and Sillén U., *Longitudinal Development of Renal Damage and Renal Function in Infants With High Grade Vesicoureteral Reflux*. J Urol, 2009. **181**: p. 2277-2283.
- III. Sjöström S., Bachelard M., Sixt R. and Sillén U., *Changes in urodynamic patterns in infants with dilating reflux; three year follow up*. J Urol, **182(November)**. 2009, *in press*.
- IV. Sjöström S., Jodal U., Stokland E., Sixt R., Wahll L., and Sillén U., *Predictive factors for resolution of high-grade infantile vesicoureteral reflux - Results of uni and multivariate analyses*. Submitted.



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Background Infants with congenital high-grade vesicoureteral reflux (VUR) have been regarded as a special group amongst children with reflux, with their own characteristics concerning renal damage, gender, resolution rate and causative mechanism. A dysfunctional bladder has been suggested to be associated with the condition. In the past surgical intervention was considered necessary in infants with high-grade reflux to prevent further renal damage. In the last decades there has been a trend towards more conservative treatment and delayed surgical intervention influenced by reports of high rates of spontaneous resolution of VUR in this group of patients. Therefore increased knowledge of the natural course of high-grade VUR in infants and factors affecting the outcome is needed to meet the new trends for management.

Research questions The overall aim was to identify infants with high-grade VUR at risk of persistent reflux and deterioration in renal status and select those from patients with a better prognosis. Evaluation of bladder function and its significance for the VUR prognosis was included in this aim.

Material and Methods 134 infants with dilated VUR (grade III-V) were consecutively included in this prospective observational study. The patients were followed longitudinally according to a study protocol including repeated examinations for determination of grade of VUR, evaluation of bladder function (videocystometry) and evaluation of renal status (DMSA and MAG3 scintigraphy and Cr-EDTA clearance). The first investigations were made after diagnosis of VUR and then yearly during a 3-year study period. Surgical intervention was intentionally late and not performed until the end of the study.

Result A high frequency of renal abnormality was found at entry (85%), with characteristics of the congenital generalised damage in more than two thirds of the study patients. Despite the high frequency of renal damage, total renal function (GFR) was only subnormal in one third (30%). Deterioration in renal status during follow up was seen in 19 patients (18%), but only one had a significant decrease in total renal function. Predictive factors for deterioration were recurrent febrile urinary tract infection, bilateral abnormality and reduced total glomerular filtration rate. Breakthrough febrile urinary tract infections during follow up were seen in 47%, despite antibacterial prophylaxis, and were more frequent during the infant year, especially in boys. Bladder dysfunction was found in 42% and was mainly characterised by high bladder capacity and high postvoid residual, a dysfunction pattern described as dilated bladder dysfunction. This dysfunction could only be recognised at the second examination at 20 months, since the results from the first year of life showed an immature pattern with overactivity during filling, high voiding detrusor pressure and low bladder capacity; characteristics not possible to separate from normal function. A series of factors of importance for spontaneous resolution or downgrading of VUR were identified. Renal abnormality and subnormal renal function were negative predictors for spontaneous resolution and so was recurrent UTI. Bladder dysfunction significantly correlated to non-resolution, and so did both high bladder capacity and increased residual urine seen as separate variables. Reflux occurring passively during filling and higher grade of VUR at inclusion was also negative predictors for resolution. All these variables were included into a multivariate Cox proportional hazard model with stepwise selection. Three variables were identified as strong independent predictors for non-resolution of VUR in the multivariate analysis; renal abnormality, bladder dysfunction and breakthrough urinary tract infection.

Conclusion In this cohort of patients with congenital dilated VUR the overall spontaneous resolution rate to grade II or less was high (38%). Renal abnormality, bladder dysfunction and breakthrough urinary tract infection were found in many study patients and were also shown to be three strong independent negative predictors for reflux resolution in multivariate analyses.