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Incomplete bladder emptying is associated with febrile urinary tract infections in infants

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KEYWORDS
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Abstract *Objective:* To investigate lower urinary tract dysfunction in pre-toilet trained infants with and without history of febrile UTI (f-UTI).
Materials and Methods: Pre-toilet trained infants with f-UTI (Group 1) from pediatric nephrology and urology clinics, and those without f-UTI (Group 2) from infant-care centers were enrolled for the present study. Infants in Group 1 underwent four-hourly (4-H) observations for at least one month after treatment for UTI. Voided volume (VV) and post-void residual urine (PVR) were measured by weighting diaper and suprapubic ultrasound after finishing voiding, respectively. Average PVR was defined as the mean value of PVR during 4-H observation. Interrupted voiding was defined as two or three voidings within 10 min. Voiding efficiency was defined as VV/(VV + PVR).
Results: The mean ages of Group 1 ($n = 64$) and Group 2 infants ($n = 56$) were 10.6 ± 7.5 months vs 10.2 ± 5.1 months, respectively ($p = 0.70$). Group 1 infants had significantly higher voiding frequency (3.0times ± 1.2 vs 2.6times ± 0.9, $p = 0.04$), average PVR (14.5 ml ± 14.2 vs 8.9 ml ± 8.8, $p < 0.01$) and lower voiding efficiency (71.2% ± 20.5 vs 80.2% ± 18.5, $p = 0.01$) than Group 2. ROC curve analysis showed that the optimal cutoff values for PVR and voiding efficiency to differentiate Group 1 and Group 2 infants were 10 ml and 80%, respectively. Group 1 infants had significantly more repeat elevated PVR (≧ 10 ml) and repeat low voiding

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efficiency (≦ 80%) than Group 2 (44.8% vs 22.4%, $p = 0.03$; 62.0% vs 28.6%, $p < 0.01$, respectively).
Conclusion: Pre-toilet trained infants with f-UTI were associated with elevated PVR and lower voiding efficiency than normal controls.

Introduction

The prevalence of febrile UTI (f-UTI) is up to 5% in febrile young children aged between 2 and 24 months [1]. The incidence rates of f-UTI in both genders are highest in those younger than one year [2]. About 30–40% of children with acute pyelonephritis develop renal scarring, with a potential consequence of developing chronic kidney disease and hypertension in their adulthood [3]. Therefore, identifying children who are at risk of having f-UTI is an important issue. Lower urinary tract (LUT) dysfunction plays an important role in developing UTI [4] and its recurrence [5] in older children. However, for pre-toilet trained infants, the association of UTI and LUT dysfunction has not been adequately studied. Evaluating LUT dysfunction in pre-toilet trained children is difficult because during infancy bladder dysfunction cannot be recognized from symptoms. Performing standard urodynamic study in young infants is both invasive and difficult. There is also a lack of age-specific and gender-specific normal reference values for various urodynamic parameters. The 4-h voiding observation (4-H observation) was validated in the Swedish population to assess LUT function of non-toilet trained children during normal daily activities [6,7]. As such, an age-matched and gender-matched case control study was conducted using the 4H-observation to compare LUT function in pre-toilet trained infants with and without f-UTI.

Materials and Methods

This prospective study was reviewed and approved by the institutional review boards at the affiliated hospitals. From January 2012 to December 2012, pre-toilet trained infants aged 2–18 months of age with f-UTI were enrolled from pediatric nephrology and urology clinics for evaluation of LUT function (Group 1). Informed consent was obtained from parents after they were provided with detailed information about the nature of the study and its aims. The diagnostic criteria of f-UTI were in accordance with the guidelines detailed by the American Academy of Pediatrics [8]. Fever was defined as body temperature >38 °C. All urine cultures were obtained by suprapubic aspiration or bladder catheterization; positive results were defined as > 50,000 CFU/ml of one uropathogen. Babies with known neurologic disease, or genitourinary tract anomalies detected by prenatal ultrasound, were not included in the study. At least one month after adequate treatment of f-UTI, the infants were enrolled for 4-H observation.

Age-matched and gender-matched pre-toilet trained healthy infants from infant-care centers were invited as controls (Group 2). The inclusion criteria were infants without history of f-UTI and sterile urine on urinalysis at enrollment. Infants with congenital urological anomalies or neurological diseases were excluded for analysis.

Method of 4-h voiding observations

Each child was placed in a quiet place and was accompanied by a caregiver under the surveillance of a study nurse or urologist. The 4-H observation was performed on one child at a time in the daytime and the caregiver fed the child as usual. A dry diaper was weighed before the tests were conducted and the study nurse checked the wetness indicator on the diaper every 5 min to see if the child had voided. The wetness indicator turned from yellow to blue when urine was in the diaper. To avoid interfering with the child's voiding, PVR was checked 10 s after the color of wetness indicator on diaper turned from yellow to blue.

Voided volume and PVR were measured by weighing the diaper and performing a suprapubic ultrasound with a 4 MHz probe (Logiq Book1, GE Medical Systems, Milwaukee, WI). The PVR was determined with the formula: W (width)*H (height)*L (length) * 0.52 ml [9]. First PVR was defined as the PVR after the first voiding. Average PVR was defined as the mean value of all PVRs of each child during 4-H observation. Parameters including gender, fluid intake and voiding frequency were recorded. Expected bladder capacity was defined as (age in month * 2.5 + 30) ml [10]. Functional bladder capacity was defined as the highest value of bladder capacity (voided volume + residual urine) during the 4-H observation and expressed as percent of expected bladder capacity. Interrupted voiding was defined as two or more voidings within 10 min. Interrupted voiding was regarded as one voiding. The volume of urine remaining in the bladder after the final voiding was regarded as residual urine. In infants with f-UTI undergoing voiding cystourethrography, the grade of VUR was classified as the suggestion of the International Reflux Study in Infants [11] and determined by the grade of the worse side of VUR. Voiding efficiency was defined as voided volume/(voided volume + PVR) *100%.

Statistical analysis

Data were expressed as median and mean ± standard deviation values. Data were analyzed by MedCalc Statistical Software version 13.1.2 (MedCalc Software bvba, Ostend, Belgium). Demographic and voiding parameters were compared via an independent *t*-test (continuous demographic variables), Mann–Whitney *U*-test (ordinal data)