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Relationship of bladder dysfunction with upper urinary tract deterioration in cerebral palsy

Gökhan Gündoğdu^{a,*}, Mustafa Kömür^b, Dinçer Avlan^c,
Ferda Bacaksızlar Sarı^d, Ali Delibaş^e, Bahar Taşdelen^f,
Ali Naycı^c, Çetin Okuyaz^b

^a Pediatric Surgery, Bezmialem Vakıf University, Medical Faculty, Department of Pediatric Surgery, Division of Pediatric Urology, Istanbul 34093, Turkey

^b Pediatric Neurology, Mersin University Medical Faculty, Department of Pediatrics, Turkey

^c Pediatric Surgery, Mersin University Medical Faculty, Department of Pediatric Surgery, Turkey

^d Pediatric Radiology, Mersin University Medical Faculty, Department of Radiology, Turkey

^e Pediatric Nephrology, Mersin University Medical Faculty, Department of Pediatrics, Turkey

^f Biostatistics, Mersin University Medical Faculty, Department of Biostatistics, Turkey

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Abstract Although lower urinary tract dysfunction (LUTD) in patients with cerebral palsy (CP) has been previously documented by clinical observations and urodynamic tests, its correlation with upper urinary tract deterioration (UUTD) has not been demonstrated. This paper documents symptoms and urodynamic findings of LUTD and their relationship with UUTD in 33 children with CP. By sonography, 4 of these children were found to have UUTD. Age was found to correlate with UUTD, but gender difference and mental or motor functions did not. When comparing urinary symptoms with UUTD, incontinence ($n = 31$) did not correlate, but on the other hand symptoms of detrusor sphincter dyssynergia (interrupted voiding, urinary retention, hesitancy; $n = 5$) and culture proven febrile urinary tract infections ($n = 4$) did. Abnormal urodynamics findings were not diagnostic. We conclude that, apart from incontinence, dysfunctional voiding symptoms and febrile urinary tract infections are valuable indicators of UUTD. © 2012 Journal of Pediatric Urology Company. Published by Elsevier Ltd. All rights reserved.

* Corresponding author. Tel.: +90 533 565 7089; fax: +90 212 621 7580.
E-mail address: ggundogdu1@yahoo.com (G. Gündoğdu).

Introduction

Cerebral palsy (CP) is characterized by a non-progressive motor disorder caused by insult to the central nervous system in the early stages of brain development. Location and extent of the neurological damage determines motor and mental disabilities, and the severity of the disease. Dysfunctional bowel and urinary elimination problems commonly accompany CP, depending on motor, mental, cognitive, sensory, and other neurological disorders [1]. From information gathered during outpatient visits, most children with CP were found to suffer from complaints of lower urinary tract dysfunction (LUTD) such as incontinence, urgency, difficulty in urinating, urinary retention, and urinary tract infections [2,3]. LUTD in children with CP has also been demonstrated by urodynamic studies [3,4].

The association between LUTD and upper urinary tract deterioration (UUTD) in children has long been reported [5]; however, despite common dysfunctional voiding findings in CP, the relationship between LUTD and UUTD is not as clearly evident in CP as in healthy children. In addition, the literature is limited concerning this relationship in children with CP. This study focuses on urinary symptoms and urodynamic findings of LUTD in children with CP and investigates their relevance with regard to UUTD.

Patients and methods

Between 2009 and 2010, 33 children were included in the study from among the children with CP who were being followed up by the Mersin University Hospital pediatric neurology unit. A urinary system evaluation and urodynamic study were performed. Caregivers were informed about the urodynamics procedure and gave informed consent for the children to participate. The ethics committee approved the study and the procedures.

Age, gender, mental and motor capacity, LUTD symptoms and urodynamic findings were investigated in order to determine any correlations with UUTD. Children younger than five years of age were not included because of their lack of total voluntary day and night bladder control due to normal biological immaturity. Subclassification of CP and a mental and motor condition evaluation were made by the pediatric neurology unit [6]. To assess a child's capacity for self-urination, motor condition was classified as self-mobile or immobile. A standard questionnaire was completed for each child that was focused on daily urinary symptoms such as urgency, frequency, incontinence, and specific symptoms of detrusor sphincter dyssynergia (urinary retention, interrupted voiding, and hesitancy), and recurrent urinary tract infections. The latter was defined as at least two complicated culture proven febrile (temperature more than 38 °C) infections per year that were distinguished from asymptomatic bacteriuria, which could be detected incidentally in the outpatient control urine samples. Caregivers were questioned about their efforts in toilet training and about elimination problems of the children.

Lower urinary tract function was investigated with conventional urodynamic studies following the International Children's Continence Society rules and recommendations [7]. No sedation was applied; study position was

adjusted to each patient's anatomic condition. At least two optimal repeat fillings were performed in each urodynamic study. Estimated bladder capacity for age was calculated according to the Koff formula, i.e., $(\text{age} + 1) \times 30 \text{ ml}$ [8]. Bladder capacity was considered to be reduced when the actual cystometric capacity was below 80% of estimated bladder capacity [9]. Involuntary detrusor pressure increase over 15 cmH₂O was considered an overactive detrusor contraction [7]. Detrusor sphincter dyssynergia is defined as abnormal sphincter activity in voiding which results in a decrease or an interruption of urinary flow during cystometry.

By using sonography, positive sonographic findings of UUTD were sought by a single radiologist who was blinded to the urinary symptoms of any particular child. Findings included dilatation in renal collecting systems, renal parenchymal pathology, anatomic variations of the upper urinary system, and urinary tract stones.

Children with positive sonographic findings of either upper urinary tract pathology or history of complicated febrile urinary tract infections were investigated by voiding cystourethrography and nuclear scintigraphy. Intravenous urography was requested if an anatomic variation was suspected.

Statistical analysis

MedCalc Statistical analysis was performed by the v.11.5.1 package program and $p < 0.05$ was considered statistically significant. Independent *t*-test and Fisher's exact test were used to determine the factors that influence the sonographic pathology.

Results

Thirty-three children were included in the study. Diagnostic distribution of CP was listed as spastic quadriplegia, hemiplegic CP, dystonic CP, and diplegia ($n = 27, 3, 2,$ and 1 , respectively); however, statistical comparisons could not be made because of insufficient sample sizes in categories other than spastic quadriplegia (Table 1). Sonographic examination showed that four children (12.1%) had UUTD: three pelvicalyceal dilatations and one double collecting system with pelvicalyceal dilatation (Table 2). Gender difference has no statistical significance (21 boys and 12 girls; $p = 0.125$, Table 1). The mean age was 8.21 ± 2.35 years (range = 5–15 years). Mean age was found to be higher in the UUTD + group children (10.50 ± 1.915 vs. 7.90 ± 2.257 ; $p = 0.036$, Table 1). Three children (9.1%) were mentally normal and the remaining 30 (90.9%) had varying degrees of mental retardation (under 70 IQ, $p = 0.8003$; Table 1). Four children (12.1%) were self-mobile while the remaining 29 (87.8%) were immobile as to self-urination ability ($p = 0.9802$; Table 1).

Among the LUTD symptoms, most of the caregivers could not give adequate information about frequency and urgency symptoms in the questionnaires according to children's mental condition and thus a statistical comparison could not be made. Day and night urinary incontinence, the most common LUTD symptom, was present in 31 of the children (93.9%, $p = 0.5648$; Table 1). Five of the children

Table 1 Subtypes of CP, demographic findings, mobility, intellectual capacity, clinical findings, and urodynamic findings of children, and their relevance with UUTD.

Number of patients and percentages, <i>n</i> (%)	UUTD – (<i>n</i> = 29)%	UUTD + (<i>n</i> = 4)%	<i>p</i> value
Subtypes of CP			
• Spastic (quadriplegia, hemiplegia, diplegia; 27, 3, and 1 respectively), 31 (93.9)	27 (93.1)	4 (100)	∅
• Dyskinesia (dystonia), 2 (6)	2 (6.8)	0	
Demographic findings			
• Gender			
Male, 21 (63.6)	20 (68.9)	1 (25)	0.125
Female, 12 (36.3)	9 (31)	3 (75)	
• Age			
	7.90 ± 2.257	10.50 ± 1.915	0.036
Mobility			
• Self-mobile, 4 (12.1)	4 (13.7)	0	0.9802
• Immobile, 29 (87.8)	25 (86.2)	4 (100)	
Intellectual capacity			
• Normal, 3 (9)	3 (10.3)	0	0.8003
• Retarded, 30 (90.9)	26 (89.6)	4 (100)	
Clinical findings			
• Urgency	Not defined		
• Frequency	Not defined		
• Incontinence, 31 (93.9)	27 (93.1)	4 (100)	0.5648
• Detrusor sphincter dyssynergia, 5 (15.1) (urinary retention, interrupted voiding, hesitancy)	2 (6.8)	3 (75)	0.0048
• Recurrent urinary tract infection, 4 (12.1)	0	4 (100)	<0.0001
• Constipation 19 (57.5)	15 (51.7)	4 (100)	0.119
Urodynamic findings			
• Normal, 6 (18.1)	6 (20.6)	0	0.7533
• Abnormal, 27 (81.8)	23 (79.3)	4 (100)	
RCC, 14 (42.4)	14	0	
RCC, ODC, 9 (27.2)	8	1	
RCC, ODC, DSD, 4 (12.1)	1	3	
• Cystometric capacity	0.669 ± 0.149	0.545 ± 0.075	0.119

UUTD = upper urinary tract deterioration.

RCC = reduced cystometric capacity.

ODC = overactive detrusor contraction.

DSD = detrusor sphincter dyssynergia.

(15.1%) had two or more specific symptoms of detrusor sphincter dyssynergia, including interrupted voiding patterns, disturbance to starting voiding, and urinary retention ($p = 0.0048$; Table 1). Complicated febrile urinary tract infections more than two times per year were reported in 4 children (12.1%, $p < 0.0001$; Table 1). The questionnaire disclosed that none of the parents made additional effort or requested professional help to toilet train their children.

Urodynamic studies showed that 6 children (18.1%) had normal bladder functions; the other 27 (81.8%) had abnormal urodynamic findings ($p = 0.7533$; Table 1). The latter includes those with reduced cystometric capacity (in 14 children with below 80% of estimated bladder capacity), reduced cystometric capacity with overactive detrusor contractions (in 9 children), and reduced cystometric capacity, overactive detrusor contractions, and detrusor sphincter dyssynergia (in 4 children). Detrusor sphincter dyssynergia was detected in the urodynamic procedures of 3 children with UUTD; however, a statistical comparison was not possible due to insufficient sample size (Table 1).

Among the 4 children with positive sonographic findings, diagnostic studies showed that 2 of them had pelvicalyceal dilation without vesicoureteral reflux but without renal scarring on their DMSA nuclear scintigraphy, 1 child had pelvicalyceal dilation with reflux and renal scarring, and 1 child had a right double collecting system with reflux and renal scarring on DMSA (Table 2). Ureteroneocystostomy was performed in 2 children with reflux. Clean intermittent catheterization and anticholinergic medication were started in 3 children based on detrusor sphincter dyssynergia in urodynamic studies and bladder trabeculation appearance in their cystograms (Table 2). In addition, over half the children ($n = 19$, 57.5%) were found to have continuous constipation problems (fewer than 3 bowel movements in a week) for at least 6 months.

Discussion

Voluntary bladder control and symptoms of LUTD vary according to the neurologic limitations of children with CP.

Table 2 Diagnostic study results and management of four children with abnormal sonographic findings.

No. patients	Age	Gender	Diagnosis	Sonographic findings	Voiding cystourethrogram	DMSA	Urodynamic findings	Management
No. 1	10	Female	Spastic quadriplegia	Right dilated double collecting system	Right grade 3 refluxive double collecting system with normal bladder	Right renal parenchymal scarring	RCC (60% of EBC), ODC	Right ureteral reimplantation
No. 2	8	Female	Spastic quadriplegia	Bilateral mild pelvicalyceal dilatation	Bladder trabeculation without VUR	Normal	RCC (45% of EBC), ODC, DSD	CIC, antibiotic prophylaxis, anticholinergic medication
No. 3	12	Female	Spastic quadriplegia	Bilateral mild pelvicalyceal dilatation	Bladder trabeculation without VUR	Normal	RCC (52% of EBC), ODC, DSD	CIC, antibiotic prophylaxis, anticholinergic medication
No. 4	12	Male	Spastic hemiplegia	Moderate pelvicalyceal dilatation in right collecting system	Mild bladder trabeculation with right grade IV VUR	Right renal parenchymal scarring	RCC (61% of EBC), ODC, DSD	CIC, antibiotic prophylaxis, anticholinergic medication, Right ureteral reimplantation

EBC = estimated bladder capacity.

CIC = clean intermittent catheterization.

In the literature, no precise data exist regarding the rate and proportion of LUTD in subtypes of CP or its relevance with regard to UUTD. In our study also, we were unable to make a statistical comparison due to unequal distribution of CP subtypes; however, our clinical impression is that children with spastic CP, particularly quadriplegics, will have more LUTD symptoms than children with other types of CP. Out of 31 children with spastic type CP, sonograms showed that 4 (12.9%) had UUTD. Detrusor sphincter dyssynergia was also more frequently detected in urodynamic studies of children with spastic CP than for other subtypes. Both Roijen and Ozturk reported that gaining voluntary continence is delayed or unachievable in spastic quadriplegic children more than in other subtypes of CP, and that LUTD symptoms were found to be more frequent among them [10,11]. We believe that spastic quadriplegics are more prone to developing LUTD because of the frequency of their involuntary abdominal contractions and pelvic floor dysfunction. As a result of increased LUTD, UUTD may also occur more frequently in these children.

Anatomic differences between the male and female urethra were hypothesized to lead to LUTD symptoms, especially in the presence of pelvic floor dysfunction and overactive detrusor contractions. Incontinence was thought to be more common in girls because of their shorter urethra. Conversely, the longer urethra of males was assumed to cause both higher resistance to urinary flow and post-void residual urine [12]. Silva et al. found that in children with CP, LUTD symptoms are more common in girls than boys [13]. Female gender is known to be a risk factor for UUTD development in children with congenital neurogenic bladder, perhaps because of the prevalence of vesicoureteral reflux in girls [14]. In the current study, UUTD was observed primarily in the girls, but a statistical significance was not found.

The literature provides no evidence that children with CP will suffer from nephropathy in later life; however, in

our study we found a correlation between UUTD and age. One can reasonably conclude that detrusor sphincter dyssynergia and vesicoureteral reflux, if left untreated, will in time cause UUTD. In such a case, recognizing reliable detrusor sphincter dyssynergia findings, differentiating between presenting urinary symptoms, and determining the risk factors are crucial for predicting the children at risk for future UUTD.

Motor capacity of children with CP was shown to be involved with LUTD by Bross et al. [9]. They reported that urinary symptoms and pathological urodynamic findings increase with decreased motor functions; however, they also noticed that urodynamic findings could be pathological in either symptomatic or asymptomatic children. Van Laecke et al. investigated the effect of motor and mental capacity over bladder functions in a group of severely mental and motor disabled children [15]. They concluded that bladder functions were affected by the motor and mental capacity, but primarily determined by the severity of motor disability. Yang et al. studied the effect of mental capacity on bladder functions, specifically excluding children with CP in order to focus on the effect of mental capacity on voiding patterns. They noticed that higher incidence of voiding dysfunction correlated with the severity of mental cognitive functions [16]. As our group consisted mainly of children who were spastic quadriplegic and severely mentally retarded, the rate of incontinence might be related to the higher ratio of their mental and motor disabilities than comparable ratios in other studies. Despite a close relationship between motor and mental status with LUTD, in our study group we found no correlation between them and UUTD.

Frequency, urgency, and day and night incontinence are the most reported symptoms of LUTD in children with CP [2–4]. We were unable to document frequency and urgency symptoms in the questionnaires since most of the families

were far from able to define these symptoms because of the impaired communication skills of their children. Daytime urinary incontinence was the most common symptom of our study group, found in 93.9% of the children, a rate considerably higher than the 36%–73% reported in the literature. This discrepancy is most likely due to impaired communication and motor functions in our study group [13]. Besides mental and motor limitation, reduced cystometric capacity, overactive detrusor contractions, and detrusor sphincter dyssynergia may also be responsible for involuntary urine loss in these children. Many factors contribute to incontinence etiology in CP, but among the symptoms of LUTD incontinence itself is not a reliable clinical indicator of UUTD or an indication for a urinary system evaluation. Another point when considering incontinence etiology is that parents did not attempt to toilet train their children.

Excluding daytime incontinence, we noticed in our study that other findings of LUTD, particularly symptoms of detrusor sphincter dyssynergia (e.g., interrupted voiding, hesitancy, and urinary retention) were correlated with UUTD. Silva et al. investigated LUTD in children with CP in two consecutive studies [13,17]. They noticed pathological findings of LUTD present in almost one-third of the children and, excluding daytime incontinence, that dysfunctional voiding symptoms are more valuable for determining a true LUTD diagnosis. However, UUTD was detected in only a few children and they did not investigate the correlation with LUTD. In our study group, those children with interrupted voiding, hesitancy, and urinary retention also had detrusor sphincter dyssynergia findings in their urodynamic studies. We believe that symptoms of LUTD can be predictive of UUTD, but daytime incontinence should be distinguished from other findings of detrusor sphincter dyssynergia.

Urinary tract infections are observed in approximately one-fifth of children with CP [3]. Bladder dysfunction, elimination problems, constipation, and decreased hygiene conditions cause bacteriuria or cystitis in these children; however, these attacks seem not to cause pyelonephritis or renal scarring in the presence of an intact ureterovesical junction. Leonardo et al. investigated risk factors of renal scarring in children with LUTD [18]. They concluded that urinary tract infection does not lead to renal scarring unless accompanied by vesicoureteral reflux. The importance of asymptomatic bacteriuria in neurogenic bladders was investigated by Ottolini et al. [19]. They noticed that in the absence of reflux, asymptomatic bacteriuria is not a significant risk factor for scarring and does not require antibiotic therapy in congenital neurogenic bladders. In our study, four children with UUTD also had recurrent febrile urinary tract infections. We concluded that complicated urinary tract infections are related to UUTD and diagnostically valuable for urological evaluation of children with CP. In addition, we suggest distinguishing asymptomatic bacteriuria, which is frequently detected in routine urine analysis of these children.

Constipation was observed in over half of the participants. Mobilization skills and nutritional status may affect bowel movements of children with CP. In healthy children fecal load affects bladder functions, especially functional bladder capacity. Constipation may contribute to decreased bladder volumes in children with CP; however it was not correlated with UUTD in our study, probably because of its high frequency.

More than 80% of the children in our study displayed various pathologic urodynamic findings of LUTD, a rate similar to those of other published reports [20]. Reduced cystometric capacity and overactive detrusor contractions were frequently observed findings in the urodynamics of children with CP, but detrusor sphincter dyssynergia was less apparent. Urodynamic findings of LUTD have predictive value for UUTD in other conditions, such as congenital neurogenic bladder, but they have less diagnostic value in CP. Gross advocated that pathologic urodynamics findings could be a consequence of artificially provoked conditions during the investigation due to a child's specific condition [9]. The decreased communication capacity and irritability of these children may be related to the occurrence of reduced cystometric capacity, overactive detrusor contractions, and pelvic floor reaction to detrusor activity. Mayo advocated that classical detrusor sphincter dyssynergia with bladder wall changes rarely occurs in CP, and the cause of difficulty in urinating for these children seemed to be due to a lack of voluntary control over external urethral sphincter activity and the hypertonus of the pelvic floor [2]. We noticed, however, that three of the four children with UUTD had clinical and urodynamic findings of detrusor sphincter dyssynergia. Abnormal findings in urodynamics are common in children with CP, but they are unimportant if not accompanied by reliable signs of LUTD, particularly specific symptoms of detrusor sphincter dyssynergia. Urodynamic studies are warranted in the presence of upper urinary tract changes, recurrent urinary tract infections, or reliable signs of detrusor sphincter dyssynergia, such as interrupted voiding, urinary retention, and hesitancy; otherwise, routine urodynamic investigation seems to be unnecessary for urinary system evaluation in CP.

Management of LUTD in children with CP is a clinical dilemma in the literature. Brodak et al. gave a definitive comment for the urinary evaluation of CP [21]. In their study group, urinary tract abnormalities were detected in only 7 among their 90 patients ranging from 1 to 25 years old. They concluded that routine urinary tract screening in CP patients might not be required. Based on the urodynamic findings, Reid et al. advocated treating these children with antibiotic prophylaxis, anticholinergics, adrenergics, clean intermittent catheterization, and surgical procedures such as vesicostomy or bladder neck suspension [20]. Similar reports in the literature confirmed Reid's approach to management of bladder dysfunction based on the urodynamics results [3,4]. Febrile urinary tract infections, clinical signs of detrusor sphincter dyssynergia and radiologic findings of a urinary tract anomaly determined our treatment strategy. We believe that treatment modalities can be incorrect if they only depend on urodynamic studies and when other clinical findings are not considered.

Nonhomogeneous distribution of CP subtypes in our study group is a limitation of this study, but our CP population primarily consisted of spastic children who suffer from urinary complaints and are more at risk for urinary tract complications. In addition, these children are less able to communicate about their condition. Related studies should be focused on these severely mentally and motor impaired children in order to determine a relationship between LUTD and UUTD.

Conclusion

Regarding the frequency of bladder dysfunction in children with CP, preserving renal functions is a major concern for pediatricians. Excluding daytime incontinence, our study shows that other symptoms of bladder dysfunction (interrupted voiding, hesitancy and urinary retention) as well as culture-proven true febrile urinary tract infection attacks are valuable indicators of upper urinary tract anomalies in children with CP. Routine urological evaluation is not required in these children. Urodynamic studies should not be routine procedures, but may be warranted in the presence of these findings.

Conflict of interest

None.

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