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The Significance of Ultrasonography in Diagnosing and Follow-up of Cystic Cystitis in Children

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A B S T R A C T

Cystic cystitis is a separate form of urinary bladder inflammation, detected by cystoscopy in children with recurrent urinary infections. Cystoscopy is an invasive method, so the aim of this investigation was to determine the ultrasonographic characteristics of cystic cystitis and to assess the reliability of ultrasound in relation to cystoscopy in diagnosing cystic cystitis. The study included 115 girls with repeated urinary infections. Cystoscopy and ultrasonography was performed in all. According to the cystoscopic finding the subjects were divided into 4 groups. Lateral and posterior urinary bladder wall thickness was measured during ultrasonography. A statistically significant difference was found between all 4 groups, the method demonstrated a high degree of sensitivity (0.97) and specificity (0.91). Percentile calculations were determined for wall thickness. Ultrasonography can replace endoscopy in diagnosis and follow-up of cystic cystitis in children, with at least 50% fullness of the urinary bladder as a prerequisite.

***Key words**: cystic cystitis, children, cystoscopy, ultrasonography*

Introduction

Cystic cystitis is a disease whose pathogenesis isn't entirely clarified. It is believed to be a reflection of an immune response to chronic inflammation. Cysts are dispersed in smaller or greater numbers in the mucosa and the submucosa and they protrude into the lumen of the urinary bladder in the form of semispherical elevations of a pearl, brown, yellowish or pink color[1]. They are usually situated in the trigonum region, the bladder neck and around the ureterovesical junction, but they can be encountered in the ureter and in the renal pelvis[2]. Trabeculation of the bladder and mucosal edema are common. In children with recurrent urinary infections, the incidence of cystic cystitis ranges from 2.4 to 9%[4–6]. The disease is detected as early as infancy, but mostly between the 4. and 12. year[1], more commonly in girls. The symptoms include dysuria, frequency, macrohematuria, urgency incontinence, secondary daily or nocturnal enuresis and unpleasant urine odor. Infection is sometimes accompanied by fever. With the duration of the disease the general symptoms are less frequent and in the latter course only asymptomatic bacteriuria with or without voiding difficulties may persist. The cysts located at the ureterovesical junction contribute to reflux development, while those in the bladder neck can present a certain degree of obstruction to urine outflow[1]. The inflammatory response causes detrusor hyperactivity and decreased functional capacity of the bladder. Various urodynamic abnormalities have been found in these patients[6–11]. Treatment is prolonged. It consists of uroprophylaxis[12,13]. In children with urine control dysfunction and urodynamic abnormalities, anticholinergic medication and urination exercises are applied[14]. The average duration of disease is 14 months[1], and in a favorable course it resolves with the disappearance of cysts, bacteriuria and the complaints accompanying chronic cystitis[12]. The diagnosis of cystic cystitis is established by cystoscopy. As it is an invasive method, we have sought in this investigation the place of ultrasonography as a diagnostic tool in the detection and follow-up of this disease in children.

Patients and Methods

In this investigation 115 girls with recurring urinary infections have been included. In all cystoscopy was per-

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formed as a golden standard for diagnosis verification and was immediately followed by ultrasonic examination. At the time of the introduction of the cystoscope, the bladder was thoroughly emptied, and subsequently filled with a precisely known quantity of water which was noted for every patient. As it is known that the thickness of the bladder wall depends on the quantity of its liquid content, the percentage of fullness was calculated from the quantity of liquid that was introduced, taking into account the expected bladder capacity for the age group. On the basis of cystoscopic findings, the subjects were divided into four groups. Ultrasonographic examinations were performed with a convex probe 3.5 to 7 MHz, most often with 6 MHz frequency, in a transversal and sagittal position. Bladder wall thickness was measured in two sites. In the transversal view the lateral wall was measured, and in the sagittal one, measurements of the posterior wall in the thickest point were recorded. In this manner two values were obtained for each patient. All data was entered into forms that included: the age of the subject, lateral and posterior bladder wall thickness (mm), cystoscopic findings divided into 4 groups (0 = normal, 1 = <5 cysts, 2 = 5–10 cysts, 3 = >10 cysts), volume of the liquid introduced into the bladder during cystoscopy (ml) and the ratio of this volume to the expected bladder capacity according to the patient age group. In the statistical analysis of obtained results, parameters of descriptive statistics were used – median, range, minimal and maximal values, arithmetic mean, standard deviation and percentile distribution. In comparing of results analysis of variance, (ANOVA) was used in testing the null hypothesis that groups means are equal.

In the study children with major bladder anomalies (diverticula, fistulas with neighboring organs), ureterocele and acute urinary infection were excluded, as were children on chemotherapy, those with a neurogenic bladder or a posterior urethral valve as it is known that these conditions may also thicken the bladder wall.

Results

This study included 115 girls. The mean age of the subjects was 7.79±3.05 yrs. A normal cystoscopic result was found in 34 (29.6%), fewer than 5 cysts in 30 (26.1%),

TABLE 1
DESCRIPTIVE STATISTICAL DATA OF GROUPS DETERMINED BY CYSTOSCOPIC EXAMINATION

Groups		Lateral	Posterior	Fullness	(Lateral+Posterior)/2
0	X	2.409	2.868	0.551	2.638
	N	34	34	34	34
	SD	0.664	0.698	0.124	0.679
1	X	3.330	3.707	0.568	3.518
	N	30	30	30	30
	SD	0.547	0.510	0.157	0.522
2	X	4.204	4.641	0.544	4.422
	N	27	27	27	27
	SD	0.439	0.426	0.127	0.429
3	X	4.604	5.108	0.549	4.856
	N	24	24	24	24
	SD	0.608	0.618	0.122	0.610
Total	X	3.529	3.970	0.553	3.749
	N	115	115	115	115
	SD	1.029	1.042	0.126	1.033

Groups: 0 – normal, 1 – <5 cysts, 2 – 5–10 cysts, 3 – >10 cysts

TABLE 2
ANOVA TEST BETWEEN GROUPS BASED ON CYSTOSCOPIC FINDINGS

	Sum of squares	df	Mean square	F	Sig
Lateral	83.886	3	27.962	84.549	0.000
Posterior	86.643	3	28.881	86.278	0.000
Fullness	0.009	3	0.003	0.194	0.901
(Lateral+Posterior)/2	85.207	3	28.402	86.419	0.000

TABLE 3
PERCENTILE DISTRIBUTION OF URINARY BLADDER WALL THICKNESS IN 4 GROUPS

		Percentile						
Ultrasonic finding	Cystoscopic finding	5	10	25	50	75	90	95
Thickness of lateral wall	normal	1.50	1.75	2.00	2.50	2.50	3.50	4.12
	< 5 cysts	2.00	2.52	3.00	3.50	3.50	4.00	4.22
	5 – 10 cysts	3.50	3.50	4.00	4.20	4.50	4.76	5.00
	>10 cysts	3.12	3.75	4.12	4.75	5.00	5.25	5.50
Thickness of posterior wall	normal	2.00	2.15	2.30	2.85	3.00	4.00	4.63
	< 5 cysts	2.50	3.04	3.50	3.70	3.80	4.50	4.73
	5 – 10 cysts	3.88	4.00	4.50	4.70	5.00	5.10	5.50
	>10 cysts	3.62	4.25	4.57	5.50	5.50	5.75	6.00
Thickness of (lateral + posterior wall)/2	normal	1.75	1.95	2.15	2.67	2.75	3.75	4.38
	< 5 cysts	2.25	2.78	3.25	3.60	3.65	4.25	4.47
	5 – 10 cysts	3.69	3.75	4.25	4.45	4.75	4.93	5.25
	>10 cysts	3.37	4.00	4.35	5.125	5.25	5.50	5.75

5 to 10 cysts in 27 (23.5%), and more than 10 cysts in 24 (20.9%) patients. For each one the mean bladder wall thickness (lateral+posterior/2) and the percentage of bladder fullness in relation to age were calculated. In Table 1. the results of the examined parameters are presented, in relation to the cystoscopic findings groups (0 = normal, 1 = <5 cysts, 2 = 5–10 cysts, and 3 = >10 cysts). In the group with normal findings the mean value of bladder wall thickness and the median are 2.6 mm, in the group with less than 5 cysts it was 3.5 mm, in the 5–10 cysts group the mean value was 4.4 mm, and in the group with more than 10 cysts the mean value was 4.8 mm, median 5.1 mm. A statistically significant difference was found for all parameters except for the degree of bladder fullness, for which the mean value for all groups was about 55% (Table 1 and 2). There is a statistically significant difference even between the normal group and the one with minimal abnormalities (<5cysts). Thus the sum of squares for the mean bladder wall thickness (lateral +posterior/2), when comparing these two groups, amounts to 12.345, $F=33.108$, and $p<0.000$. These differences are most prominent when comparing the group with normal findings with that of profuse cystic cystitis (>10 cysts); the square sum is 69.214, $F=163.048$ and $p<0.000$.

If a bladder wall thickness of 3.0 mm is presumed a borderline measure, from the results obtained from measurements under ultrasonographic control sensitivity and specificity of the ultrasonic method was established. The sensitivity for all groups is 0.97 and specificity 0.91. In the group with fewer than 5 cysts the sensitivity of the method is lower (0.83), and in groups with more cysts sensitivity is better (0.94). The probability that a positive test confirms the disease (likelihood positive ratio=LPR) is 10.95, and the ability for a negative test to confirm health (likelihood negative ratio=LNR) is 36, calculated for all groups. In the group of patients with less than 5 cysts LPR was 17.35 and LNR 5.7. According to the results obtained, a percentile value for wall thickness was calculated for each group (Table 3).

Discussion

Judging from the relatively small number of studies in recent literature dealing with the problem of cystic cystitis in children, it seams to be in a way a forgotten or more precisely a neglected disease. This is probably due to several factors. Some are associated to cystoscopy, the golden standard for the diagnosis of the disease. It is an invasive procedure performed in most countries by surgeons, urologists, and less frequently by pediatrician nephrologists. Due to fewer endoscopic examinations, patients with cystic cystitis are all the more rarely detected. This is not favorable as it is an exceptional disease[1,12], that is, a disease group per se that can be correctly defined, treated and controlled only with a clearly established diagnosis. On the other hand, as far as is known at present, ultrasonography is harmless and painless, widespread and accessible in health facilities. It is an ideal method especially for the pediatric population; it is possible to perform at the bedside and to repeat in short intervals. Ultrasonography has already demonstrated its possibilities for analyzing the urinary bladder, for the assessment of its volume[16], variations of shape and wall thickness in healthy children[17]. The goals of this study are therefore: to determine the ultrasonographic characteristics of cystic cystitis in children and to establish the reliability of ultrasonography in the diagnosis of cystic cystitis, compared to cystoscopy.

As the indications for cystoscopy vary in children with recurrent urinary infections, the data varies regarding the incidence of disease – from 2.4%[15] to 8.6[1] and more[3,4].

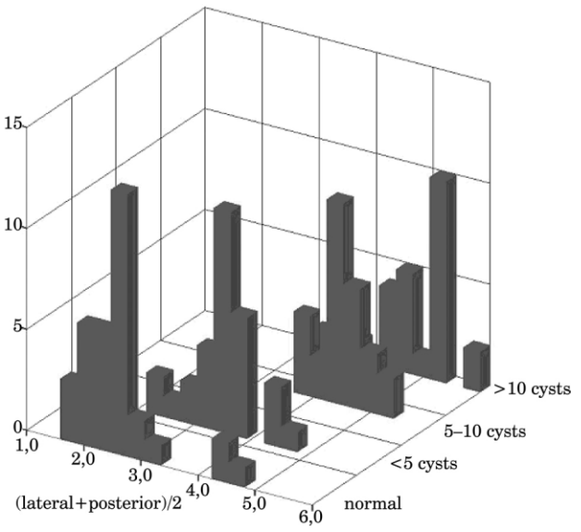

Fig. 1. Distribution of relative wall-thickness (posterior+lateral) /2 (mm), in groups of patient according to cystoscopic finding.

The majority of patients are girls; from 94%[5] to 97%[1]. In this study only girls with repeated urinary infections were included. The youngest was 1.75 and the oldest 16.57 years old. The mean age was 7.79±3.05 years, a finding similar to that of other authors[4].

Jequier and Rousseau have measured the urinary bladder wall thickness by means of ultrasonography in 410 healthy children aged 1 day to 19 years and have reported 2.76 mm as the mean value for a normal bladder in a nearly empty state, and 1.55 mm when it is distended[17]. They didn't observe a statistically significant difference in wall thickness in relation to the age and sex of the subjects, but they did find a difference depending on the degree of fullness. In this study the volume was determined according to a known quantity of liquid introduced during cystoscopy, and subsequently the percentage of fullness was determined in relation to age[18]. The mean value for bladder fullness was over 50% in all groups. Statistical analysis has demonstrated a significant difference in the lateral wall thickness as well as in the posterior wall, and their mean value (lateral and posterior/2) between all 4 groups of subjects (Figure 1). It is notable that there is a statistically significant difference between the group with normal and that with minimal cystoscopic changes (<5 cysts). That group (<5 cysts) also differs from the group with 5–10 cysts, and from the one with more than 10 cysts. We consider even this minimal finding as pathological, and that it can be found either at the beginning of the evolution of the disease, or at the end when the number of cysts diminishes and the disease moves from a higher into a lower group. If 3.0 mm is designated as the border measure between a normal and pathological finding at bladder fullness over 50% corresponding to age, 2 girls were considered false negative; one aged 3 years and the other 10, with bladder fullness 70.46% and 59.20% of capacity for age, both from the group with less than 5 cysts. False positive results were found in 3 girls; one aged 9 years with very low bladder fullness (26.08%), and two aged 8 and 10 years with bladder fullness 62.08% and 60.35%, but who had detrusor thickening (3.3 mm in the younger and 3.0 mm in the older girl), while their urodynamic findings corresponded to bladder instability. These data uphold the presumption that greater caution is necessary in diagnosing children with minimal cystoscopic changes (the sensitivity for this group is 0.83), at low bladder fullness, and in children with urodynamic disorders and with detrusor thickening, which affects the overall wall thickness.

Ultrasonographic examination of the urinary bladder enables the precise measurement of its wall thickness, the calculation of volume and the assessment of bladder fullness in relation to the expected capacity according to age. The values for wall thickness with at least 50% fullness can be used in disease staging. In the study percentiles were calculated for the wall thickness values obtained, and can act as guidelines for the diagnosis and follow-up of children with cystic cystitis. In view of the high sensitivity (0.975) and specificity (0.911) of the method, it is possible to differentiate healthy from ill children. In children with recurrent urinary infections and a borderline ultrasonographic finding, we recommend more frequent clinical, laboratory and ultrasonographic checkups. In uncertain cases cystoscopy remains the method of choice. In the event of known disease course, ultrasonography should be repeated annually. Taking into account invasiveness, possible complications, the cost of examination and the number of personnel involved, ultrasonography also has a favorable effect on cost-benefit.

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VAŽNOST ULTRAZVUKA U DIJAGNOZI I PRAĆENJU CISTIČNOG CISTITISA KOD DJECE

S A Ž E T A K

Cistični cistitis je poseban oblik upale mokraćnog mjehura koji se otkriva cistoskopijom u djece s opetovanim uroinfekcijama. Budući da je cistoskopija invazivna metoda, cilj ovog istraživanja bio je odrediti ultrazvučne karakteristike cističnog cistitisa te odrediti pouzdanost ultrazvuka pri dijagnosticiranju cističnog cistitisa u usporedbi s cistoskopijom. U studiju je uključeno 115 djevojčica s opetovanim uroinfekcijama. U svih je učinjena cistoskopija i ultrazvučni pregled. Prema cistoskopskom nalazu ispitanice su podijeljene u 4 grupe. Prilkom ultrazvučnog pregleda izmjerena je debljina postranične i stražnje stjenke mokraćnog mjehura. Nađena je statistički značajna razlika između sve 4 grupe ispitanica, visoka senzitivnost (0.97) i specifičnost (0.91) metode, a određene su i percentile debljine stjenke. Uz preduvijet ispunjenosti mjehura od barem 50%, ultrazvučna pretraga može zamijeniti endoskopsku u dijagnosticiranju i praćenju cističnog cititisa u djece.