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Ultrasound Distinction between Simple Recurrent Urinary Tract Infections and a Specific Bladder Wall Inflammatory Entity called Cystitis Cystica

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A B S T R A C T

A specific representative of recurrent urinary tract infections (UTI) called cystitis cystica (CC) was assessed by ultrasound. The aim of the study was to delineate, by means of ultrasound measurement (US) of bladder wall thickness (BWT), the children with mere repeated UTI from those prone to frequent UTI due to CC. Two groups were compared, the control group of 30 with recurrent UTI without US CC BWT changes, and the group of 30 children with characteristic CC bladder wall thickening in whom cystoscopy was performed for verification the diagnosis of CC. BWT of >3 mm (>2.8 mm and >3.3 mm) was found as cut-of value for distinction of CC versus simple recurrent UTI. US BWT measurement is useful in diagnosing CC and therefore valuable in decision about need of UTI prophylaxis.

***Key words**: Cystitis cystica, recurrent UTI, ultrasound, bladder wall thickness measurement, children*

Introduction

Cystitis cystica (CC) is a specific long-term inflammation of the urinary bladder characterized by nodular changes of bladder mucosa[1]. The etiology of CC is still debated, but its significance arising from its connection with recurrent urinary tract infections (UTI) is quite plausible[2]. It is believed that CC represents local immunologic response to a chronic inflammatory stimulus[3–6]. A self perpetual inflammatory/immunologic circuit establishes which enhance and maintain CC in turn with recurrent UTI[4,5]. The recommended treatment of CC consists of prolonged antimicrobial prophylaxis[1–5]. The diagnosis of CC is established primarily by cystoscopy. Recently, we established a non-invasive ultrasound (US) technique to assess CC by bladder wall thickness (BWT) measurement[6].

The aim of the study was to delineate, by means of US BWT measurement, the children with mere repeated UTI with no need for prolonged antibacterial prophylaxis from those prone to frequent UTI due to CC and therefore in a need for the same.

Patients and Methods

The main criterion for inclusion of children in this study was their clinical presentation with recurrent UTI of at least 3 episodes in one year period or 2 episodes within a period of less than 6 months. Presuming that acute UTI cause thickening of bladder mucosa *per se*, we decided not to perform the US examination in patients during or immediately after the acute UTI, but to validate BWT with a 3 months delay, presuming that the aforesaid period guarantees sufficient time duration for inflammatory changes resolution. Children with bladder diverticula, ureterocoele, children on chemotherapy, those with neurogenic bladder or posterior urethral valves were excluded, as these conditions may also thicken the

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bladder wall. As CC is extremely rare in boys, we conducted the study with pre-pubertal girls alone as they are particularly prone to CC development. Two groups were formed, the group with recurrent UTI without US CC BWT changes, and the group with characteristic CC bladder wall thickening in whom cystoscopy was performed for verification the diagnosis, thus ruled out US BWT by mere bladder overactivity. Both were equal in size, consisting of 30 children, age, gender and frequency of UTI-matched.

Children were instructed to come on US examination with a full bladder. The examinations were performed with a convex probe 3.5 to 7 MHz, most often with 6 MHz frequency, in a transversal and sagittal position[6]. The bladder length, width and height were measured and volume was calculated using the formula (prolate ellipsoid method): bladder volume = L (length) x W (width) x H (height) x 0.523[7–9]. Bladder fullness was expressed as percentage of maximum bladder capacity for age[6,10]. BWT 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. The mean bladder wall thickness (lateral + posterior / 2) was calculated. An informed consent was obtained from patient's parents prior to cystoscopy. The study was approved by the local Ethics Committee.

Statistics

Data on patients' age, bladder fullness (%) and BWT measurement (mm) are presented as arithmetic mean and standard deviation. In comparison of the groups t-test was used[11]. ROC statistical analysis of US BWT data was performed[12]. Sensitivity, specificity, positive likelihood ratio and negative likelihood ratio were calculated.

Results

Descriptive statistics for the children with recurrent UTIs and children with CC is shown in Table 1. There was statistically significant difference in BWT measured by US between the children with recurrent UTI and children with CC.

Table 2 shows values of sensitivity and specificity, positive likelihood and negative likelihood ratio of BWT measurement for range of diagnostic criterion values between 1.8 and 4. The best distinction between children with mere recurrent UTI and children with CC using sensitivity, specificity, positive and negative likelihood ratios was found for BWT measurement >3 mm. Using the same statistical criteria, fair chance for distinction was found for BWT measurements of >2.8 mm and >3.3 mm respectively.

TABLE 1
DESCRIPTIVE STATISTICS FOR AGE, BLADDER FULLNESS AND BLADDER WALL THICKNESS FOR BOTH GROUPS OF CHILDREN

	Children with recurrent UTI (N=30)	Children with CC (N=30)	p value
Age (years, mean±SD)	6.6±3.03	6.4±2.91	>0.05
Bladder fullness (% mean±SD	70.31±9.41	68±8.89	>0.05
Bladder wall thickness (mm, mean±SD)	2.7±0.49	3.8±0.84	<0.001

Data are presented as mean±SD.

TABLE 2
VALUES OF SENSITIVITY AND SPECIFICITY USED TO CALCULATE ROC CURVE. CUT-OFF VALUE OF 3 MM WAS DETERMINED AS THE OPTIMAL CRITERION FOR DISCRIMINATION BETWEEN CHILDREN WITH SIMPLE RECURRENT UTI AND CHILDREN WITH CC

Criterion (mm)	Sensitivity (95% C.I.)	Specificity (95% C.I.)	Positive Likelihood Ratio	Negative Likelihood Ratio
≥ 1.8	100.0 (95.5–100.0)	0.0 (0.0–10.4)	1.00	
> 1.8	100.0 (95.5–100.0)	8.8 (2.0–23.7)	1.10	0.00
> 2.2	100.0 (95.5–100.0)	26.5 (12.9–44.4)	1.36	0.00
> 2.3	97.5 (91.3–99.6)	44.1 (27.2–62.1)	1.75	0.06
> 2.6	97.5 (91.3–99.6)	50.0 (32.4–67.6)	1.95	0.05
> 2.8	96.3 (89.5–99.2)	82.4 (65.5–93.2)	5.46	0.04
> 3.0*	93.8 (86.2–97.9)	88.2 (72.5–96.6)	7.98	0.07
> 3.3	87.7 (78.5–93.9)	91.2 (76.3–98.0)	9.93	0.14
> 3.6	74.1 (63.1–83.2)	91.2 (76.3–98.0)	8.40	0.28
> 3.7	67.9 (56.6–77.8)	91.2 (76.3–98.0)	7.70	0.35
> 3.8	60.5 (49.0–71.2)	91.2 (76.3–98.0)	6.86	0.43
> 4.0	59.3 (47.8–70.0)	91.2 (76.3–98.0)	6.72	0.45

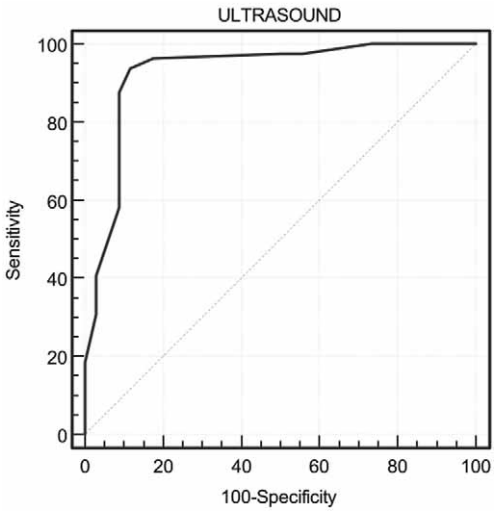

Fig. 1. Area under the ROC curve for BWT measured by US for discrimination between children with simple recurrent UTI and children with CC.

Figure 1 presents ROC curve based on data from Table 2. Area under the ROC curve (95% confidence interval 82–97%) correctly identifies patients with CC with 90% accuracy.

Discussion and Conclusion

The debate of the need for antibacterial prophylaxis in children with recurrent UTI is ongoing with pro- and contra among pediatricians for quite some time. We are aware of the controversies of the decision for introducing the prophylaxis with its potential harmful effects, contrary to the decision to treat UTI recurrences only sporadically when they appear. Both decisions could lead to a wide contact with bacterial flora and possible increase of bacterial resistance, of which chemoprophylaxis bears frequent accusation[13–15]. If it will be possible to delineate the children in real need of prophylaxis, we believe that their absolute number could be significantly reduced, consequently minimizing effect on microbial resistance[16,17].

With our research we tried to contribute to the debate by bringing into focus a neglected and nearly forgotten specific bladder condition called CC. As was shown before, children with CC are highly prone to UTI recurrences. The long-lasting antimicrobial prophylaxis is presumed in these children, and actually cures the condition with disappearance of recurrent UTI[5]. In this study we showed that US BWT measurement can replace cystoscopy in diagnosing CC, at least in pre-pubertal girls. The cut-off BWT of >3 mm for the decision of CC presence (fair range >2.8 mm – >3.3 mm) was found adequate for the purpose[6]. The children with BWT ≥3 mm (with absolute certainty ≥2.8 mm) should be considered CC free. Antibacterial prophylaxis was therefore not appointed to these children. BWT>3.3 mm is almost certainly CC related, and such children should be treated with the prophylaxis. If our work contributes to discussion about more clear criteria for UTI prophylaxis we will be fairly satisfied.

REFERENCES

1. VLATKOVIC G, BRADIC I, GABRIC V, BATINIC D, Br J Urol, 49 (1977) 57. DOI: 10.1111/j.1464-410X.1977.tb04523.x. — 2.AABECH HS, LIEN EN, Acta Paediatr Scand, 71 (1982) 247. DOI: 10.1111/j.1651-2227.1982.tb09409.x. — 3. BELMAN AB, J Urol, 119 (1978) 661. — 4. HANSSON S, HANSON E, HJALMAS K, HULTENGREN M, JODAL U, OLLING S, et al, J Urol, 143 (1990) 330. — 5. MILOSEVIC D, BATINIC D, TESOVIC G, KONJEVODA P, KNIEWALD H, SUBAT-DEZULOVIC M, et al., Coll Antropol, 34 (2010) 893. — 6. VRLJICAK K, MILOSEVIC D, BATINIC D, KNIEWALD H, NIZIC L, Coll Antropol, 30 (2006) 355. — 7. HVARNESS H, SKJOLDBYE B, JAKOBSEN H, Scand J Urol Nephrol, 36 (2002) 177. DOI: 10.1080/003655902320131839. — 8. DICUIO M, POMARA G, FABRIS FM, ALEIS V, DAHLSTRAND C, MORELLI G, Arch Ital Urol Androl, 77 (2005) 60. — 9. LIU JX, LEUNG YF, CHIU-WING, CHU W, SREEDHAR B, METREVELI C, YEUNG CK, Pediatr Radiol, 38 (2008) 1084. DOI: 10.1007/s00247-008-0958-y — 10. KOFF SA, Urology, 21 (1983) 248. DOI: 10.1016/0090-4295(83)90079-1 — 11. DE VEAUX R VP, BOCK D, Intro Stats. 3rd ed. (Addison Wesley, 2008). — 12. KUMAR V R, ANTONY GM, Drug Information Journal, 44 (2010) 659. DOI: 10.1177/009286151004400602. — 13. CHENG CH, TSAI MH, HUANG YC, SU LH, TSAU YK, LIN CJ, et al., Pediatrics, 122 (2008) 1212. DOI: 10.1542/peds.2007-2926. — 14. DAI B, LIU Y, JIA J, MEI C, Arch Dis Child, 95 (2010) 499. DOI: 10.1136/adc.2009.173112. — 15. NARCHI H, AL HAMDANI M, Microb Drug Resist, 16 (2010) 151. DOI: 10.1089/mdr.2009.0115. — 16. CRAIG JC, SIMPSON JM, WILLIAMS GJ, LOWE A, REYNOLDS GJ, MC TAGGART SJ, et al., N Engl J Med, 361 (2009) 1748. DOI: 10.1056/NEJMoa0902295. — 17. KARPMAN E, KURZROCK EA, J Urol, 172 (2004) 448. DOI: 0.1097/01.ju.0000130653.74548.d6.

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ULTRAZVUČNO RAZLIKOVANJE JEDNOSTAVNIH INFEKCIJA MOKRAĆNOG MJEHURA I CISTIČNOG CISTITISA KAO SPECIFIČNOG UPALNOG ODGOVORA SLUZNICE MOKRAĆNOG MJEHURA

S A Ž E T A K

Ultrazvučnom metodom procjenjena je mogućnost postavljanja dijagnoze cističnog cystitisa, specifičnog uzročnika ponavljanih infekcija urinarnog trakta. Svrha studije je preko ultrazvučnog mjerenja debljine stijenke sluznice mokraćnog mjehura razlučiti djecu s jednostavnim ponavljanim infekcijama od djece s opetovanim uroinfekcijama uzrokovanim cističnim cistitisom. Uspoređivane su dvije skupine djece, kontrolna skupina od 30 djece s ponavljanim uroinfekcijama bez promjene debljine sluznice mokraćnog mjehura i grupa od 30 djece s zadebljanjem mukoze mokraćnog mjehura u koje je cistoskopskim pregledom dokazan cistični cystitis. Debljina sluznice mokraćnog mjehura >3 mm (>2.8 mm do >3.3 mm) je nađena karakterističnom za razlikovanje cističnog cistitisa od jednostavnih opetovanih uroinfekcija. Ultrazvučnim mjerenjem debljine mukoze moguće je postaviti dijagnozu cističnog cistitisa i prema tome procijeniti potrebu za profilaksom uroinfekcija.