The role of tissue harmonic imaging ultrasound combined with power Doppler ultrasound in the diagnosis of childhood febrile urinary tract infections

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Abstract

Aim: This study assessed the ability of tissue harmonic imaging ultrasound combined with power Doppler ultrasound in the detection of childhood febrile urinary tract infections in comparison with the gold standard reference method: Tc-99m dimercaptosuccinic acid renal cortical scintigraphy.

Material and Methods: This prospective study included 60 patients who were hospitalized with a first episode of febrile urinary tract infections. All children were examined with dimercaptosuccinic acid scan and tissue harmonic imaging ultrasound combined with power Doppler ultrasound within the first 3 days of admission.

Results: Signs indicative of acute infection were observed in 29 patients according to the results of tissue harmonic imaging ultrasound combined with power Doppler ultrasound while dimercaptosuccinic acid scan revealed abnormal findings in 33 patients. The sensitivity, specificity, positive predictive value and negative predictive value of tissue harmonic imaging combined with power Doppler ultrasound using dimercaptosuccinic acid scintigraphy as the reference method in patients diagnosed with first episode febrile urinary tract infections were calculated as 57.58% (95% confidence interval: 40.81%-72.76%); 62.96% (95% confidence interval: 44.23%-78.47%); 65.52% (95% confidence interval: 52.04%-77%); 54.84% (95% confidence interval: 41.54%-67.52%); respectively.

Conclusions: Although current results exhibit inadequate success of power Doppler ultrasound, this practical and radiation-free method may soon be comprise a part of the routine ultrasonographic evaluation of febrile urinary tract infections of childhood if patients are evaluated early and under appropriate sedation. (Türk Pediatri Ars 2015; 50: 90-5)

Keywords: Acute pyelonephritis, childhood, urinary tract infection, power Doppler ultrasound

Introduction

Urinary tract infection (UTI) is an important clinical problem which is observed commonly in childhood. In large-scale prospective studies related with this issue and in a meta-analysis, the prevalence of UTI in febrile infants and young children was found to be

approximately 7%, though it varied depending on the age, gender, status of circumcision and ethnic origin (1). Especially upper UTI (acute pyelonephritis) which recurs in the accompaniment of structural urinary system abnormalities may lead to long-term complications including renal scarring and resulting hypertension, renal failure and problems which may arise

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in pregnancy (2-5). Therefore, the diagnosis of acute pyelonephritis (APN) should be made timely, accurate treatment should be administered, risk factors should be determined and the patient should be referred accordingly. However, it is mostly difficult to definitely differentiate APN from lower UTI by clinical findings and acute phase reactants which have low sensitivity and specificity especially in children below the age of 2 years (2, 4, 6). Currently, Tc-99m dimercaptosuccinic acid (DMSA) is considered the gold standard imaging method in detecting renal parenchymal involvement in patients diagnosed with APN (7-9). This investigation method has negative aspects including exposure to radiation, need for intravenous access and high cost (10). Conventional urinary system ultrasonography (USG) is still accepted as the first-line imaging method in all children below the age of 2 years who have first febrile UTI and all children with recurrent febrile UTI (11). Its most important advantages include easy applicability, absence of involvement of ionizing radiation, absence of need for intravenous access and low cost. The main objective of USG is to detect anatomical abnormalities which require further evaluation. In addition, it also enables assessment of the renal parenchyma, size and form (11). Its success in demonstrating renal parenchymal involvement in the acute phase, in the diagnosis of vesicoureteral reflux (VUR) and in demonstrating scarring in the advanced phase is insufficient (12).

Power Doppler ultrasonography (PDUS) is a relatively newer method which demonstrates regional decreased blood supply in the kidney in the acute phase. In this study, the contribution of tissue harmonic imaging ultrasound (THI-USG) PDUS to increase the success of conventional USG was investigated in comparison with DMSA renal scintigraphy.

Material and Methods

Primarily, approval was obtained from the ethics committee of Ankara University Medical Faculty to conduct this study (Number: 25-2002/562; date: 12.30.2002). Sixty patients who were hospitalized in Ankara University Medical Faculty, Division of Pediatric Nephrology with a diagnosis of first febrile UTI were included in the study. The ages of the patients ranged between 3 months and 9.5 years (median value: 15 months, mean value: 27 months). Written informed consent was obtained from the parents of all patients. The patients whose parent did not give consent, who had recurrent UTI and who were found to have obstructive uropathy

and 4-5th degree VUR in further examinations were not included in the study. All patients had fever. The diagnosis of urinary tract infection was made by evaluating midstream urine samples obtained following appropriate cleaning in children who had received toilet training and by evaluating urine samples obtained by bag or catheter in young children and infants and, $\geq 10^5$ colonies/mL in midstream or bag urine and $\geq 10^4$ colonies/mL in urine obtained by catheter was considered significant culture growth.

In all patients, scintigraphic examination was performed in accordance with a basic protocol in the first three days after presentation in Ankara University Medical Faculty, Department of Nuclear Medicine. The radioactive substance named "technetium 99m-DMSA" (1.5-2 MBq/kg, minimum dose 15 MBq) was administered by the intravenous route. Planar anterior, posterior, left and right oblique images were obtained with the assistance of SPECT gamma camera 2-4 hours after administration of radioactive substance. All scintigraphic tests were evaluated by the same nuclear medicine specialist who did not know the patient's clinical properties and USG results. The results were interpreted in accordance with the International Radionuclide Nephrology Group (IRN) consensus criteria (13). Accordingly, single or multiple, cortical or diffuse areas of decreased activity in at least two different angles in the renal parenchyma was accepted as indication of acute infection (Figure 1). Disruption in the renal borders or cortical thinning were accepted as scar findings and the patients with these findings were not included in the study.

THI-USG and PDUS were performed in all patients in the first three days after presentation by the same pediatric radiologist who was working in Ankara University Medical Faculty, Department of Radiology. No information was given to the radiologist about the clinical findings and renal scintigraphy result of the patient. Chloral hydrate (50 mg/kg) or hydroxyzine (1 mg/kg) was given by the oral route to the infants who had difficulty in cooperation 30 minutes before the examination to prevent impact on the quality of the imaging technique. On ultrasonographic examination, axial, sagittal and coronal plane images were obtained in the supine position with the most appropriate TGC adjustments for each modality using central frequency 3.5 MHz convex and 7.5 Mhz linear probes with SSA-770A (Aplio XG, Toshiba, Japan) for PDUS together with THI USG which provides better image quality com-

Figure 1. Decreased activity uptake in the left kidney indicating parenchymal inflammation in dimercaptosuccinic acid renal scintigraphy

pared to grey scale and conventional ultrasonography. On tissue harmonic imaging ultrasonography, increase in renal dimensions, echogenicity changes related with renal parenchyma and sinus (Figure 2), loss of corticomedullary distinguishability, enlargement and wall thickening in the collective system which indicated infection were noted (Figure 3). On Power Doppler ultrasonography, vascular map of all areas of both kidneys was obtained. Decreased parenchymal blood supply and areas of perfusion defect were reported as findings of infection (Figure 4).

THI-USG strengthened with PDUS was compared with DMSA which is considered the gold standard imaging method in the diagnosis of childhood febrile UTI.

Statistical analysis

Statistical analysis of all data were performed in the Ankara University Medical Faculty, Department of Biostatistics using SPSS 11.5 package program. Frequency (percentage) was expressed as the descriptive measure for variables obtained by counting. In assessment of diagnostic performance, the sensitivity, specificity, positive predictive value and negative predictive value were calculated together with confidence intervals in comparison of tissue harmonic imaging USG-PDUS with DMSA renal scintigraphy. A p value of <0.05 was considered statistically significant.

Figure 2. Parenchymal hyperechogenicity in the upper pole of the left kidney on tissue harmonic imaging ultrasonography

Figure 3. Wall thickening and mild enlargement in the left renal pelvis on tissue harmonic imaging ultrasonography

Figure 4. Regional reduction in blood flow of the left kidney on power Doppler ultrasonography

Results

Acute infection was found in 29 of the patients who were evaluated with THI USG-PDUS (n=60), where-

Table 1. Comparison of the results of Tc-99m dimercaptosuccinic acid renal scintigraphy and tissue harmonic imaging ultrasonography-power Doppler ultrasonography in the diagnosis of childhood febrile urinary tract infection

	Tissue harmonic imaging ultrasonography-Power doppler ultrasonography		
Dimercaptosuccinic acid scintigraphy	Abnormal (n)	Normal (n)	Total (n)
Abnormal (n)	19	14	33
Normal (n)	10	17	27
Total (n)	29	31	60

Table 2. The results of tissue harmonic imaging ultrasonography-power Doppler ultrasonography of the patients

Tissue harmonic imaging ultrasonography-power Doppler ultrasonography	n	%
Normal	31	51.6
Reduced blood flow	1	1.7
Enlargement in the collective system	18	30
Enlargement in the collective system and reduced blood flow	3	5
Change in the parenchymal echogenicity	7	11.7
Total	60	100

as abnormality was found in 33 of the patients (n=60) with DMSA renal scintigraphy (Table 1). The THI USG-PDUS results of the patients are shown in table 2 and Tc-99m DMSA renal scintigraphy results are shown in Table 3. In the light of these findings, the success of THI USG-PDUS in demonstrating renal involvement in the acute phase in patients diagnosed with febrile UTI was calculated in comparison with Tc99m DMSA renal scintigraphy which is accepted as the gold standard method. The sensitivity of the method was found to be 57.58% (95% confidence interval: 40.81%-72.76%) and the specificity was found to be 62.96% (95% confidence interval: 44.23%-78.47%). Tissue harmonic imaging USG-PDUS showed normal findings (false negative) in 14 of the patients who had abnormal findings on DMSA renal scintigraphy, while it indicated abnormal findings (false positive) in 10 of the patients who had normal DMSA renal scintigraphy findings. The positive predictive value was found to be 65.52% (95% confidence interval: 52.05%-77%), the negative predictive value was found to be 54.84% (95% confidence interval: 41.54%-67.52%).

Table 3. The results of Tc-99m dimercaptosuccinic acid renal scintigraphy of the patients

Dimercaptosuccinic acid renal scintigraphy	n	%
Normal	27	45
Reduction in the cortical activity uptake	33	55
TOTAL	60	100

Discussion

Urinary tract infection is one of the common infections in children and is observed in 1-3% of girls and in 1% of boys (14). It is known that the rate of renal scarring due to recurrent acute pyelonephritis ranges between 25%-40% and recurrent UTI with or without VUR is the cause in 10-25% of the children who develop end stage renal disease (2, 14). Early diagnosis and treatment is very important to prevent irreversible complications.

Tc-99m renal scintigraphy which is accepted as the gold standard method in demonstrating renal parenchymal inflammation in the diagnosis of febrile UTI was used by Davies et al. (8) for the first time in 1972. Its sensitivity and specificity were reported to be %86 and %91, respectively (15). The sensitivity and specificity of contrast enhanced computerized tomography (CT) are also high similar to DMSA renal scintigraphy (16). However, the mutual disadvantages of both methods include exposure to radiation, need for intravenous access and high cost. In fact, DMSA renal scintigraphy is not recommended in the acute phase in patients with first febrile UTI according to the final guidelines published by the American Academy of Pediatrics (AAP) and National Institute of Health and care Excellence (NICE) (11, 17).

Currently, an easily applicable method which does not involve radiation is needed to increase the low success of urinary system USG which is recommended as the first-line method in children with a diagnosis of febrile UTI in defining inflammation of the renal parenchyma. In this context, PDUS is a technique reflecting the integrated strength in the renal parenchyma which promises hope. This imaging method is based on visualization of decreased arteriolar and capillary blood supply in the parenchyma in the form of a triangle due to edema and intravascular neutrophil accumulation together with peripheral arteriolar vascular contraction in the infected area of the kidney in the early phase of APN (4). Egli et al. (18) were the first investigators who showed that the sensitivity of USG in detecting inflammation in renal parenchyma increased from 38% to 63% with

addition of PDUS method in the study they conducted in 1992. Majd et al. (16) investigated the success of imaging methods by accepting histopathologically proven APN model in pig models as the gold standard in the diagnosis of APN. As a result, they found the sensitivity and specificity values to be 92.1% and 93.8% for DMSA, 86.8% and 87.5% for CT, 89.50% and 87.5% for magnetic resonance imaging (MRI) and 74.3% and 56.7% for PDUS. After this study, more satisfactory results were published both for adult and pediatric patient groups (4, 5, 7, 10). In fact, a marked advancement occurred in the USG technology after the first studies which evaluated the success of this method and the sensitivity has been reported to be 74-89% in recent studies (19, 20).

The sensitivity value (57.58%) in our study was lower compared to recent studies. We associated this finding with some reasons. Although all investigators have concluded that PDUS should be performed in the first 48 hours after fever starts, the mean presentation time of the patients included in our study was 84 hours after the beginning of fever (16-20). In contrast, partial venous obstruction due to edema in the beginning phase of infection may be interpreted as increase in blood volume in this area on Doppler examination. Thus, decreased blood supply which is considered as a finding of infection may be missed (16). We thought that these factors were among the reasons of the low sensitivity of THI USG-PDUS method found in our study in the patients who were evaluated very early or relatively lately.

In many studies measuring the efficiency of PDUS in the diagnosis of APN in children, the age of the patients were older and uncooperative children were excluded. In our study, infants constituted the majority of the patients and patients who were uncooperative despite sedation were also included. We think that the sensitivity of the method might have reduced as a result of movement artefact. In addition, SPECT method in scintigraphic examination increases the sensitivity of DMSA method in the diagnosis of APN, but decreases the specificity. This is related with the fact that normal heterogeneous distribution of Tc-99m DMSA substance in the renal cortex in the SPECT technique may be perceived as decreased activity uptake in the kidney (21). The SPECT technique was used also in our study. Another observation of us was that most of the false negative results of our patients were related with the left kidney. As emphasized in other studies, this can be explained with affection of the image quality

of the blood flow in the upper pole of the left kidney because of lack of hepatic acoustic window of the left kidney (10, 16, 19).

In our study, the specificity of THI USG-PDUS was also found to be low. However, it is known that the sensitivity of DMSA renal scintigraphy is not 100%, though it is accepted as gold standard in the diagnosis of APN (16). It is known that the finding of "pyelitis" which is known as enlargement and thickening in the collective system can not be defined sufficiently with DMSA renal scintigraphy. In fact, enlargement of the collective system is not a specific finding for APN and can be observed in VUR, conditions leading to obstruction in the urinary tract and acute tubular necrosis. However, when further examination was performed 6 months after infection in 16 of 21 patients who were found to have pelvicalyceal enlargement on USG, it was observed that this finding was improved in 14 patients (87.5%). This suggested that the finding demonstrated on the first examination was in favour of pyelitis. However, scintigraphic examination was found to be normal in 14 of 21 patients who were found to have enlargement in the collective system on USG. Therefore, we think that the specificity of THI USG-PDUS might have been underestimated.

In patients with a diagnosis of acute pyelonephritis, higher success rates have been obtained in studies related with intravenous contrast enhanced (levovist) PDUS in the diagnosis of renal parenchymal involvement (22). However, this substance is not available in our country at present. Therefore, our study was conducted without administering levovist.

Conclusively, the most successful imaging method in demonstrating renal parenchymal inflammation in febrile urinary tract infection in children is still DMSA renal scintigraphy. Currently, it is not recommended in the early phase because of need for intravenous access and exposure to radiation and because of the fact that no alteration in the follow-up of patients according to the results would take place. based on the results. We think that the success of USG which is the first-line imaging method in demonstrating parenchymal inflammation will increase if performed in association with PDUS especially with evaluations performed in the 48-72 hours after the onset of complaints using appropriate sedation and with future technical advancements in devices, PDUS would become a part of routine imaging.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was obtained from the families of patients who participated in this study.

Peer-review: Externally peer-reviewed.

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References

1. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta-analysis. *Pediatr Infect Dis J* 2008; 27: 302-8. [\[CrossRef\]](#)
2. Hansson S, Jodal U. Urinary tract infection. In: Avner E D, Harmon WE, Niaudet P, (eds). *Pediatric Nephrology*. 5th ed. Lipincott Williams and Wilkins, Philadelphia 2004; 1007-25.
3. Ghasemi K, Montazeri S, Pashazadeh AM, Javadi H, Assadi M. Correlation of 99mTc-DMSA scan with radiological and laboratory examinations in childhood acute pyelonephritis: a time-series study. *Int Urol Nephrol* 2013; 45: 925-32. [\[CrossRef\]](#)
4. Bykov S, Chervinsky L, Smolkin V, Halevi R, Garty I. Power Doppler sonography versus Tc-99m DMSA scintigraphy for diagnosing acute pyelonephritis in children: are these two methods comparable? *Clin Nucl Med* 2003; 28: 198-203. [\[CrossRef\]](#)
5. Salo J, Ikäheimo R, Tapiainen T, Uhari M. Childhood urinary tract infections as a cause of chronic kidney disease. *Pediatrics* 2011; 128: 840-7. [\[CrossRef\]](#)
6. Zorc JJ, Kiddoo DA, Shaw KN. Diagnosis and management of pediatric urinary tract infections. *Clin Microbiol Rev* 2005; 18: 417-22. [\[CrossRef\]](#)
7. El Hajjar M, Launay S, Hossein-Foucher C, Foulard M, Robert Y. Power Doppler sonography and acute pyelonephritis in children: comparison with Tc-DMSA scintigraphy. *Arch Pediatr* 2002; 9: 21-5. [\[CrossRef\]](#)
8. Davies ER, Roberts M, Roylance J, Penry JB, Stadden G. The renal scintigram in pyelonephritis. *Clin Radiol* 1972; 23: 370-6. [\[CrossRef\]](#)
9. Lee J, Kwon DG, Park SJ, Pai KS. Discordant findings of dimercaptosuccinic acid scintigraphy in children with multi-detector row computed tomography-proven acute pyelonephritis. *Korean J Pediatr* 2011; 54: 212-18. [\[CrossRef\]](#)
10. Halevy R, Smolkin V, Bykov S, Chervinsky L, Sakran W, Koren A. Power Doppler ultrasonography in the diagnosis of acute childhood pyelonephritis. *Pediatr Nephrol* 2004; 19: 987-91. [\[CrossRef\]](#)
11. Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. *Pediatrics* 2011; 128: 595-610. [\[CrossRef\]](#)
12. Nelson CP, Johnson EK, Logvinenko T, Chow JS. Ultrasound as a screening test for genitourinary anomalies in children with UTI. *Pediatrics* 2014; 133: 394-403. [\[CrossRef\]](#)
13. Piepsz A, Blaufox MD, Gordon I, et al. Consensus on renal cortical scintigraphy in children with urinary tract infection. Scientific Committee of Radionuclides in Nephrourology. *Semin Nucl Med* 1999; 29: 160-74. [\[CrossRef\]](#)
14. Elder JS. Urinary tract infections. In: Kliegman RM, Stanton BF, Schor NF, St. Geme JW III, Behrman RE, (eds). *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia: Elsevier, 2011; 1829-34. [\[CrossRef\]](#)
15. Craig JC, Wheeler DM, Irwig L, Howman-Giles RB. How accurate is dimercaptosuccinic acid scintigraphy for the diagnosis of acute pyelonephritis? A meta-analysis of experimental studies. *J Nucl Med* 2000; 41: 986-93.
16. Majd M, Nussbaum Blask AR, Markle BM, et al. Acute pyelonephritis: comparison of diagnosis with 99mTc-DMSA, SPECT, spiral CT, MR imaging, and power Doppler US in an experimental pig model. *Radiology* 2001; 218: 101-8. [\[CrossRef\]](#)
17. La Scola C, De Mutiis C, Hewitt IK, et al. Different guidelines for imaging after first UTI in febrile infants: yield, cost, and radiation. *Pediatrics* 2013; 131: 665-71. [\[CrossRef\]](#)
18. Egli KD, Egli D. Color Doppler sonography in pyelonephritis. *Pediatr Radiol* 1992; 22: 422-5. [\[CrossRef\]](#)
19. Basiratnia M, Noohi AH, Lotfi M, Alavi MS. Power Doppler sonographic evaluation of acute childhood pyelonephritis. *Pediatr Nephrol* 2006; 21: 1854-7. [\[CrossRef\]](#)
20. Stogianni A, Nikolopoulos P, Oikonomou I, et al. Childhood acute pyelonephritis: comparison of power Doppler sonography and Tc-DMSA scintigraphy. *Pediatr Radiol* 2007; 37: 685-90. [\[CrossRef\]](#)
21. Hoberman A, Charron M, Hickey RW, Baskin M, Kearney DH, Wald ER. Imaging studies after a first febrile urinary tract infection in young children. *N Engl J Med* 2003; 348: 195-202. [\[CrossRef\]](#)
22. Erbaş G, Özdemir H, Yücel C, et al. Diagnostic value of intravenous contrast enhanced power doppler ultrasound in children with acute pyelonephritis. *Gazi Tıp Dergisi* 2007; 18: 81-5.