Serum Procalcitonin Level for Prediction of High-grade Vesicoureteral Reflux in Urinary Tract Infection

Nahid Rahimzadeh, Hasan Otukesh, Rozita Hoseini, Shiva Shadani, Nakysa Hooman

Pediatric Transplantation and Dialysis Research Center, Tehran University of Medical Sciences, Tehran, Iran

Keywords. procalcitonin, vesicoureteral reflux, urinary tract infections

Introduction. Procalcitonin is a reliable and specific marker of bacterial infections such as urinary tract infection. Some authors suggest measurement of serum procalcitonin as a predictor of vesicoureteral reflux (VUR). We investigated this association in children admitted because of acute pyelonephritis.

Materials and Methods. Forty-eight children with the first febrile urinary tract infection were included. Twelve patients had low-grade VUR, 9 patients had high-grade VUR, and 27 patients did not have any VUR in their imaging assessment.

Results. There was a significant association between high-grade VUR and higher levels of procalcitonin (P = .04). The sensitivity of a procalcitonin level of 0.31 ng/mL or greater was 90% and the specificity was 32% for diagnosis of high-grade VUR.

Conclusions. We concluded that serum procalcitonin concentration is a sensitive and promising predictor of high-grade VUR.

IJKD 2014;8:105-8
www.ijkd.org

Original Paper

INTRODUCTION

Vesicoureteal reflux (VUR) predisposes acute pyelonephritis, renal damage, and scarring. Renal insufficiency, hypertension, electrolyte and acid base disturbances, somatic growth impairment, and morbidity during pregnancy are reported in severe forms of reflux nephropathy. Diagnosis of VUR usually requires bladder catheterization and these techniques are expensive and irradiating. On this basis, many centers changed their guidelines regarding the utilization of imaging studies in patients with urinary tract infection (UTI). In these guidelines, it is important to find high-risk children with UTI. Thus, it is suggested to perform technetium Tc 99m dimercaptosuccinic acid (99mTc-DMSA) scan and ultrasonography at the first step. Voiding cystourethrography (VCUG) and radionuclide cystography (RNC) are recommended in patients with abnormal DMSA or ultrasonography.[1]

There are also some serum and urinary biomarkers that help for recognizing high-risk patients. These markers may be useful in early diagnosis of renal scarring and VUR, especially high-grade VUR. As low-grade VUR is not recommended for antibiotic prophylaxis in recent studies[2] and resolves spontaneously in most patients without renal damage, the use of some techniques is suggested to early diagnose patients with high-grade VUR and to select them for VCUG or RNC. Procalcitonin is one of these markers that is suggested to rise remarkably in high-grade VUR and is useful for this aim,[3-6] but this supposition needs more studies for confirmation. The purpose of this study was to determine whether we can use serum procalcitonin concentration as a marker of VUR presence or VUR degree in children with UTI.

MATERIALS AND METHODS

Patients

Patients with the first febrile UTI who admitted in Rasool Akram Hospital were included in this

prospective study. Urinary tract infection was diagnosed by clinical symptoms and positive urine culture obtained by midstream in children and suprapubic or catheter in infants. All patients had undergone VCUG or RNC. Voiding cystourethrography was performed in infants. Patients with neurogenic bladder were excluded from this study. Infants with signs or symptoms or VCUG findings of neurogenic bladder were excluded, too. The first VUR grading on VCUG was performed based on the international system of radiologic grading of VUR. Patients were divided into those without VUR, with low-grade VUR (grades 1 and 2), and patients with high-grade VUR (grade 3 and higher). On admission, the serum procalcitonin was measured in all patients.

Statistical Analysis

Data were analyzed using the the SPSS software (Statistical Package for the Social Sciences, version 18.0, SPSS Inc, Chicago, Ill, USA). Descriptive results were expressed as mean ± standard deviation. All of the quantitative variables were compared using the analysis of variance test. The receiver operating characteristic curve analysis was performed to assess the predictability of serum procalcitonin for the presence and severity of VUR. A receiver operating characteristic curve is obtained by plotting sensitivity against the false positive rate (1 - specificity) for all possible cutoff points of the serum procalcitonin level. A *P* value less than .05 was considered significant.

RESULTS

A total of 48 children with their first febrile UTI were assessed. The mean age was 2.0 ± 0.8 years. Eight patients (16.7%) were boys. Twenty-one patients (43.8%) had VUR. Low-grade VUR was diagnosed in 12 patients and high-grade VUR was detected in 9 patients. Bilateral VUR was seen in 8 patients (16.7%). The mean procalcitonin level was 0.14 ± 0.10 ng/mL in patients without VUR, whereas it was 0.23 ± 0.03 ng/mL in patients with VUR. This difference was not significant (*P* = .26). The mean value of procalcitonin concentration was 0.13 ± 0.10 ng/mL in patients with low-grade VUR, and it was not different from that in patients without VUR. The mean of serum procalcitonin level was 0.40 ± 0.40 ng/mL in those with high-grade VUR and it was significantly higher in comparison with patients with low-grade VUR or patients without VUR (*P* = .04; Figure 1).

The receiver operating characteristic curve analysis demonstrated that the serum procalcitonin could be considered as potentially useful marker to predict high-grade VUR (area under the curve, 0.65; Figure 2). The cutpoint of 0.31 ng/mL for serum procalcitonin level could potentially separate the patients with high-grade VUR from those with low-grade VUR or patients without VUR. The diagnostic values of this cutpoint for the serum procalcitonin were calculated at sensitivity and specificity of 90% and 32%, respectively.

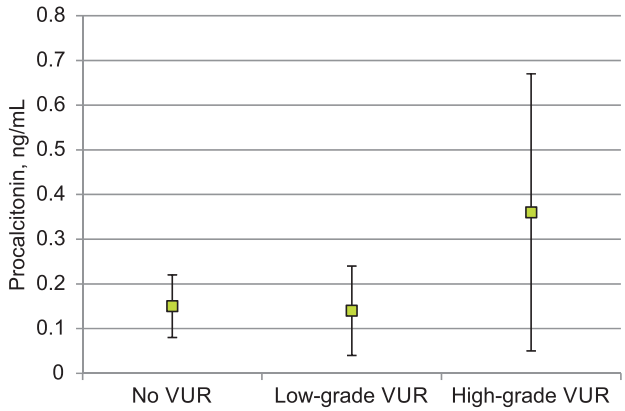

Figure 1. The mean serum procalcitonin concentration in patients without vesicoureteral reflux (VUR) and those with low-grade or high-grade VUR.

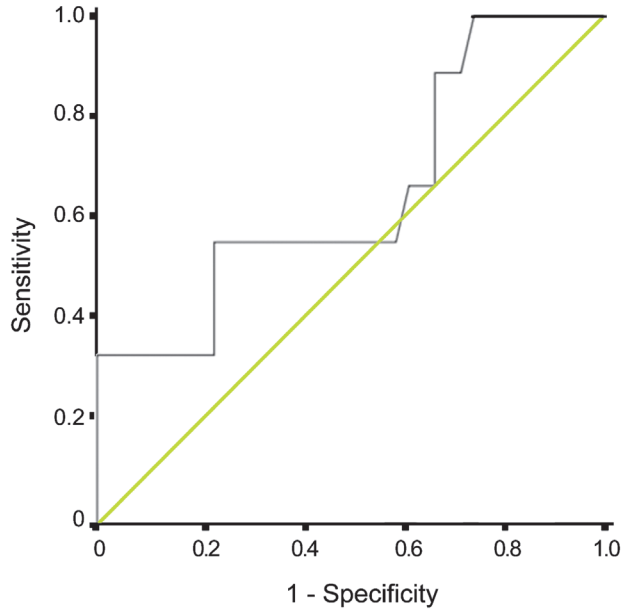

Figure 2. Receiver operating characteristic curve for serum procalcitonin level in detection of high-grade vesicoureteral reflux (area under the curve, 0.65).

DISCUSSION

Procalcitonin is a peptide precursor of calcitonin without hormonal activity. It is produced by parafollicular cells of the thyroid gland. Infective stimuli, especially bacterial infections, raise the blood procalcitonin levels, thus it is a reliable marker for bacterial infection in children. Procalcitonin is undetectable in normal conditions or viral infections. Its concentration also determines the severity of bacterial infection. Procalcitonin has been shown to differentiate between upper and lower UTI.[7] The association between VUR and serum procalcitonin concentration has also been shown by previous studies.[3-6] These studies have tried to show predictive ability of high serum procalcitonin concentration for diagnosis of high-grade VUR.

Leroy and colleagues reported in a retrospective cohort study a strong relationship between VUR and high procalcitonin level (odds ratio, 2.4; $P = .001$). Procalcitonin, with a threshold of 0.5 ng/mL and greater, had a sensitivity of 92% and specificity of 44% for diagnosis of high-grade VUR.[6] Bressan and colleagues found a significantly higher level of procalcitonin in patients with VUR, but they did not show any correlation between serum procalcitonin level and the grade of VUR.[3]

Leroy and coworkers assessed 12 articles in a recent meta-analysis with 526 children with UTI.[6] They showed a strong independent association between serum procalcitonin level and high-grade VUR. The best cutpoint of serum procalcitonin concentration for prediction of high-grade VUR with high sensitivity was 0.5 ng/mL in this study.[6,8,9] They suggested performing VCUG or RNC in children with the first febrile UTI and high procalcitonin concentration. The combination of high procalcitonin level and abnormal early renal parenchyma increased the possibility of high-grade VUR in this meta-analysis. Procalcitonin levels of 0.5 ng/mL and higher and abnormal early DMSA scan had a sensitivity of 93% and a specificity of 27% for the diagnosis of high-grade VUR. Urinary tract dilation was also associated with high-grade VUR, but with less sensitivity than high procalcitonin level. Sandrine and colleagues have also shown that most patients with low-grade VUR had low procalcitonin concentration and did not need VCUG or RNC in the first episode of febrile UTI.

We showed that serum procalcitonin level was significantly higher in patients with high-grade VUR than that in patients with low-grade VUR or patients without VUR. We determined a serum procalcitonin level of 0.31 ng/mL as a threshold for diagnosing high-grade VU (sensitivity of 90% and specificity of 32%). This threshold was lower than that determined by previous studies (0.5 ng/mL). Although the association between high-grade VUR and the level of serum procalcitonin was significant in our study, this association was not as strong as values reported by other studies. However, small number of our patients especially those with high-grade VUR limited us to establish a cutoff value for the test.

CONCLUSIONS

High serum procalcitonin may predict high-grade VUR, and consequently may recognize high-risk children with UTI who need VUR assessment and antibiotic prophylaxis in the future. We need more studies with greater numbers of cases, especially those with high-grade VUR, for more precise determination of the predictive ability of serum procalcitonin concentrations for high-grade VUR and the best values of serum procalcitonin level as cutpoint. Future studies can also combine procalcitonin concentration and DMSA scan scoring to increase sensitivity and specificity and avoid cystography with no diagnostic and therapeutic benefits.

CONFLICT OF INTEREST

None declared.

FINANCIAL SUPPORT

This study was sponsored by Tehran University of Medical Sciences.

REFERENCES

1. Albert Bensman, Olivier Dunand, Tim Ulinski, Urinary tract infections, Chapter 54, In Pediatric Nephrology, Ellis D Avner, sixth edition, Springer, 2009, 1300-1310.
2. Roussey-Kesler G, Gadjos V, Idres N, et al. Antibiotic prophylaxis for the prevention of recurrent urinary tract infection in children with low grade vesicoureteral reflux: results from a prospective randomized study. J Urol. 2008;179:674-9.
3. Bressan S, Andreola B, Zucchetta P, et al. Procalcitonin as a predictor of renal scarring in infants and young children. Pediatr Nephrol. 2009;24:1199-204.
4. Prat C, Domínguez J, Rodrigo C, et al. Elevated serum procalcitonin values correlate with renal scarring in

children with urinary tract infection. Pediatr Infect Dis J. 2003;22:438-42.

5. Benador N, Siegrist CA, Gendrel D, Greder C, Benador D, Assicot M, Bohuon C, Girardin E. Procalcitonin is a marker of severity of renal lesions in pyelonephritis. Pediatrics. 1998;102:1422-5.
6. Leroy S, Adamsbaum C, Marc E, et al. Procalcitonin as a predictor of vesicoureteral reflux in children with a first febrile urinary tract infection. Pediatrics. 2005;115:e706-9.
7. Mantadakis E, Plessa E, Vouloumanou EK, Karageorgopoulos DE, Chatzimichael A, Falagas ME. Serum procalcitonin for prediction of renal parenchymal involvement in children with urinary tract infections: a meta-analysis of prospective clinical studies. J Pediatr. 2009;155:875-881.
8. Leroy S, Romanello C, Galetto-Lacour A, et al. Procalcitonin is a predictor for high-grade vesicoureteral reflux in children: meta-analysis of individual patient data. J Pediatr. 2011;159:644-51.
9. Leroy S, Romanello C, Galetto-Lacour A, et al. Procalcitonin to reduce the number of unnecessary cystographies in children with a urinary tract infection: a European validation study. J Pediatr. 2007;150:89-95.

Correspondence to:
Rozita Hoseini, MD
Division of Pediatric Nephrology, Shahid Labafinejad Medical Center, 9th Boustan, Pasdaran Ave, Tehran, Iran
E-mail: rozitahoseini@yahoo.com

Received October 2012
Revised August 2013
Accepted August 2013