Survey of Relationship Between Changes in Serum levels of Procalcitonin with Response to Treatment in Patients with SIRS Positive Acute Pyelonephritis

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Abstract

Introduction: Urinary tract infection (UTI) is a common human illness. Patients with acute pyelonephritis may progress to septicemia and septic shock. Disease complications are significantly associated with increased mortality. Rapid and timely diagnosis of sepsis and differentiating it from non-infectious causes with similar symptoms is very important; because timely initiation of antibiotic therapy in patients with sepsis is vital in reducing mortality and improving final outcome. Serum procalcitonin level increases in patients with sepsis and bacterial infection. The aim of this study is measuring serum levels of procalcitonin in patients with Systemic Inflammatory Response Syndrome (SIRS) positive acute pyelonephritis before and after treatment and a survey of the relationship between changes in serum levels of procalcitonin with response to treatment in patients with SIRS positive acute pyelonephritis.

Materials and methods: This study was carried out on 30 patients older than 18 years with SIRS positive acute pyelonephritis who were admitted to Shahid Beheshti Hospital in Yasuj, Iran, in 2016. Before initiation of antibiotic treatment, procalcitonin levels were measured. Then 5and ten days and two weeks after treatment simultaneous urine sample and a blood sample was taken. In cases with negative culture in each of their urine cultures, serum levels of procalcitonin were measured and the results were compared.

Results: This study included 30 patient (15 males, 15 females) with SIRS positive acute pyelonephritis. The mean and standard deviation of participant´s pre-treatment serum procalcitonin level and post-treatment serum procalcitonin level were 8/88±1/24 and 0/05±0/01 ng/ml respectively, (p value= 0/001). The mean and standard deviation of pre-treatment serum procalcitonin level in patients with complicated and uncomplicated pyelonephritis were 10/97±1/46 and 0/54±0/08 respectively, (p value= 0/001).

Conclusion: The procalcitonin can be used in patients with urinary tract infections to evaluate their response to treatment and duration of hospitalization and duration of antibiotic therapy.

Key words: sepsis, pyelonephritis, procalcitonin, systemic inflammatory response syndrome, SIRS

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Introduction

Urinary tract infection is a common and painful disease in humans (1). Urinary tract infections include cystitis (bladder infection), pyelonephritis (kidney infection) prostatitis (prostate infection) and urethritis (urethra infection) (1, 2 and 3). Following a urinary tract infection, the patient may have septicemia and septic shock. The incidence of disease complications is clearly associated with an increase in mortality (4). Currently, there are no strong inflammatory markers useful for determining the severity of the disease in febrile urinary tract infections (5, 6). Rapid and timely diagnosis of sepsis and its differentiation from non-infectious causes that manifest themselves with similar symptoms is very important because the timely start of antibiotic therapy in sepsis patients is to reduce mortality and improve the outcome of many patients (7). Many studies have been done in the last decade to access markers that can be used to detect early sepsis (8). Procalcitonin is produced during sepsis by macrophages and monocytes of various organs and released into the bloodstream (9 and 10). One of these studies has been conducted on the serum procalcitonin level in patients with sepsis, which results in an increase in the serum level of procalcitonin in these patients (11). Procalcitonin has a half-life of 20 to 15 hours in the blood and its concentration is related to the severity of infection in ICU patients (12, 13). Urinary tract infections cause more than 7 million referrals to doctors in the United States each year. These infections are detected in 1-3% of girls in school age and 2 to 8% of pregnant women. Symptomatic upper urinary tract infections are commonly prevalent in pregnancy and 20-30% of pregnant women with asymptomatic bacteriuria have pyelonephritis (4). Almost all women experience urinary tract infections during their lifetime (14). According to estimates, 10% of men and 30% of women after age 60 have bacteriuria, of which 30% are pyelonephritis (15).

The microbial spectrum of acute uncomplicated cystitis and pyelonephritis mainly consists of Escherichia coli (75 to 95%) and other Enterobacteriaceae species such as Proteus mirabilis, Klebsiella pneumoniae and Staphylococcus saprophyticus (2 and 3). The microbial spectrum of the UTI is wider and includes the above, as well as Pseudomonas, Sarasia, Enterococcus, Staphylococcus and fungus (16 and 17). Clinical manifestations of urethritis include: diarrhea, frequency, urgency and hematuria (18). Clinical manifestations include purulent discharge from the penis with irritation (1). Clinical manifestations of pyelonephritis include: high temperature symptoms associated with high fever (more than 38.5 degrees), chills, abdominal pain, tenderness of the vaginal corvus and vomiting (19). Pyelonephritis may cause complications including renal scarring and papillary necrosis and urinary tract obstruction and peri nephritis abscess, amphysematous pyelonephritis and chronic renal failure. Patients with urinary tract infections may also have septic septicemia and shock. The incidence of disease complications is clearly associated with increased mortality (4).

Diagnosis of acute pyelonephritis begins with taking a history and physical examination including body temperature measurement, tenderness of the costovertebral angle and examination of the abdomen and pelvis (20). The gold standard for diagnosis of urinary tract infection is urinary culture. Unfortunately, however, the results are not available until 24 hours after referral. Under the following conditions, growth of less than or equal to 10^{5} micrograms can indicate a real infection:

1) Patients who received recent antibiotics.
2) Patients who have growths less commonly found in their urine culture such as Pseudomonas, Klebsiella, Sarasia and Enterobacteria (21).

Sepsis is a leading cause of worldwide mortality, accounting for 26% of hospitalized patients and 16% of patients hospitalized in intensive care units (22 and 23). It is also responsible for 18- 28% of hospital deaths (24). Rapid and timely detection of sepsis and its differentiation from non-infectious causes that manifest themselves with similar symptoms is very important because timely antibiotic treatment in sepsis patients is vital in reducing mortality and improving the final outcome of patients (25).

Materials and methods

This cross-sectional and descriptive-analytic study was conducted on patients with acute pyelonephritis.

15 patients were male and 15 were female. Data were gathered and analyzed by SPSS 9.1 software. To examine the t-test, paired t-test and one-way variance analysis in the case of normal variables were used. In all statistical tests, the level of significance was less than 5%.

In this study, which was performed at Shahid Beheshti Hospital in Yasuj in 2016, patients over the age of 18 who had fever and at least one of the symptoms of dysuria and frequent urination, pain and tenderness of costovertebral angle were diagnosed with acute pyelonephritis. After explaining the goals of the study, they indicated their willingness to cooperate. After receiving informed written consent, the urine specimen was collected in a sterile container and cultured on an agar culture medium, and patients who, after 48 hours of urination, had more than 100,000 colonies of bacteria per milliliter were considered as urinary tract infection (UTI), and among these patients, those with two or more criteria of SIRS, were included in the study. Before starting antibiotic treatment, 2 ml of blood sample was taken and after centrifugation and separating the serum, the specimen was transferred to a freezer and stored at a negative temperature of 40 ° C until all samples were maintained under the same conditions. From patients on day 5 and on day 10 and two weeks after the start of treatment, urinal culture and blood samples were taken simultaneously. If urine culture in each of the cultures was negative, the serum sample of the same day was used to measure the serum Procalcitonin level. Sample serum freeze was deciphered at room temperature after completion of the sampling, and the Procalcitonin serum titre was measured using electrochemiluminescence

method based on the electron velocity in the circuit with ELEXIS.

Results and Conclusion

The results of this study showed that Procalcitonin serum level in patients with acute pyelonephritis is associated with response to treatment, and with the onset of antibiotic therapy and negative urine culture, its level is significantly reduced. These results, with the study of Mobin et al. (2010), correspond to the relationship between Procalcitonin and response to treatment (29).

The results of this study showed that patients with serum Procalcetonin before treatment had a higher serum Criteria SIRS score. In a study by Fardin Asadi et al, in 2014 comparing CRP and Procalcitonin in children with SIRS and septic shock, it was shown that the Procalcitonin and CRP levels in patients with septic shock was significantly higher than patients with SIRS and sepsis. Procalcitonin is more sensitive in differentiating them (32). From these findings, it can be concluded that patients with acute SIRS-positive pyelonephritis, with higher Procalcitonin levels, are at increased risk of septic shock.

This study also showed a significant relationship between the Procalcitonin serum level before treatment in patients with acute SIRS positive acute pyelonephritis and the number of admission days, and patients with serum Procalcitonin before treatment had higher the number of days in hospital. Sugimoto et al. (2013) in a study on acute pyelonephritis patients showed that patients with high Procalcetonin levels (greater than 10 ng / ml) had more severe complications than other patients (27).

Ahmadinejad et al. (2009) conducted a three-year study on the procalcitonin role in the differential diagnosis of infectious and noninfectious systemic inflammatory response syndrome that showed a significant difference between serum Procalcitonin (greater than 10 ng / ml) and death; there was a meaningful relationship between patients with infectious sepsis (30). In a study by Levy MM et al. (2003) on patients with sepsis admitted to the intensive care unit, the survival rate of these patients was reported to be closely correlated with a reduction in procalcitonin serum levels between two to three days (28). From these findings and the results of previous studies, it can be concluded that patients with acute SIRS-induced acute pyelonephritis with a higher serum procalcitonin level will have longer hospitalizations.

In this study, patients with serum Procalcitonin before treatment were shown to have a longer urine culture negativity. The results of Hladík et al. (2005) in the study of procalcitonin and its role as an inflammatory bio-marker correspond to the results of our study (26).

From the findings, it can be concluded that in patients with acute pyelonephritis, SIRS-positive Procalcitonin can be used as a biomarker for rapid assessment of response to treatment, and in patients with a low serum Procalcitonin antibiotic treatment can be stopped.. This can reduce the long-term use of antibiotics and reduce the growing trend of microbial resistance to antibiotics. Future studies are suggested separately for each infectious disease with a larger sample size and the results should be compared.

The results of the study showed that there was no significant difference between Procalcitonin level before treatment and type of microorganism grown in urinary culture. Of the 30 patients, 22 patients were positive for urinary culture with E. coli. The mean and standard deviation of Procalcitonin level before treatment in this group of patients was 5.56 ± 4.15 ng / ml, whereas in one the patient had positive urine culture with an Acinetobacter. The mean and standard deviation of Procalcetonin serum level in this patient was 22.67 ± 12.12 ng / ml. It is recommended that more studies be done with a larger sample size to compare the type of bacteria grown in urine culture and Procalcitonin levels and compare the results.

In this study, it was also shown that in patients with complicated urinary tract infection, the serum Procalcitonin level before treatment is higher than patients with uncomplicated acute pyelonephritis. Therefore, the duration of antibiotic treatment and the length of hospitalization should be carefully considered in these patients.

In this study, only Procalcitonin was used to evaluate the response to treatment. Mitaka C reported that Procalcitonin and CRP increase in sepsis and inflammatory diseases. The study, which was conducted in 2005 on differentiated clinical trials between infectious and non-infectious SIRS, showed that Procalcitonin and CRP increased in infectious and non-infectious SIRS, but Procalcetonin was more closely related to the severity of sepsis (31).

In this study, Electrochemiluminescence (ECL) method was used to measure Procalcitonin level and it is based on the latest laboratory methods. On the contrary, the ELISA method used to determine the Procalcitonin level based on changes in particle color Latex. In this method, the serum level of Procalcitonin is quantitatively titrated, which will be more valuable than the semi-quantitative ELISA method to assess the response of patients to treatment. Most of the previous studies have been done on Procalcitonin using semi-quantitative ELISA and further studies are recommended using the new ECL method and the results to be compared.

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