

Procalcitonin in diagnosing the diabetic foot infection

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Abstract

Objectives: Diabetic foot infection is a debilitating disease that requires prompt diagnosis and treatment. In this study, we assessed inflammatory markers; serum Procalcitonin (PCT), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and leukocyte counts in two groups of patients with infected and non-infected diabetic foot ulcer.

Patients and Methods: A descriptive cross-sectional study was carried out on diabetic patients during 18 months in Firoozgar Hospital. Patients were divided in two groups according to Infectious Disease Society of America (IDSA) guideline for diagnosis and treatment of diabetic foot infections. Blood samples were drawn from venous lines for measurement of complete blood count (CBC), ESR, CRP, and PCT. Diagnostic values of serum PCT Levels were determined by immunoluminometric assay. SPSS version 15.0 software was used for analysis.

Results: Sixty adult patients were considered for this study. Thirty patients with infected ulcer with mean age of 57.5 ± 2.09 years and 30 with non-infected ulcers with mean age of 61.1 ± 1.9 years were evaluated.

Patients with infected ulcers had significantly elevated levels of CRP, ESR and leukocyte counts in comparison with the non-infected ulcers. Serum PCT levels did not differ between the two groups.

Conclusion: Our study suggests CRP, ESR and Leukocyte counts can be used to diagnose of infected ulcers. The role of PCT in localized infections should be determined in further studies.

Keywords: Diabetes, Diabetic Foot infection, Inflammatory markers, Procalcitonin

Introduction

Foot infection is the most common complication in diabetic patients. Peripheral arterial diseases, secondary to diabetes, predispose these patients to foot infection. Trauma and pressure accompanied by diabetic neuropathy and the disease of the small vessels are also among the main factors which may lead to ulceration and diabetic foot infection (1).

Foot infection in diabetic patients has a wide spectrum from cellulitis to chronic osteomyelitis of which management is very difficult due to the limited access of

phagocytic cells to the infected tissue (2). Since these infections have potential risk of gangrene and limb amputation (3,4), detecting and diagnosing the infection in diabetic patients is critical and life-saving. However, predicting the infection's status and identifying the extent and severity of diabetic ulcers (differentiating the abscess with osteomyelitis) is difficult for inexperienced physicians (5). Inflammatory signs and symptoms may not be evident due to the diabetes effects on the vascular and immune systems which can compromise the local response to infection. Due to the progressive nature of these types of infections, prompt diagnosis and treatment is crucial (6,7).

Procalcitonin (PCT) is a 116-amino acid peptide, which has been recently introduced as an inflammatory marker in order to detect bacterial infections. PCT releases from the thyroïdal C cells and is the precursor of Calcitonin. Liver, lungs and kidneys' parenchymal cells are also the principal source of circulating PCT in sepsis (8).

There are controversial data about the role of PCT in the diagnosis of local infections such as soft tissues, bones and joints (9,10). The diagnostic role of PCT in diabetic foot infection (DFI) is uncertain as well and limited number of studies is available in this regard. A study performed by Uzun and colleagues in Turkey, revealed the potential role of PCT in detecting the diabetic foot infection (11).

In this study, serum PCT, c-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and leukocyte counts are being compared within the two groups of patients with infected and non-infected diabetic foot ulcer.

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Patients and Methods

In this analytical and cross-sectional study, total number of 60 patients with documented diabetes and diabetic foot ulcer, referring to the Endocrine Institute of Firoozgar Hospital, from October 2008 to June 2009, were enrolled in the study. Diabetic foot infection was diagnosed using the IDSA (Infectious Disease Society of America) guideline (5) in which the infection severity was categorized to four distinct groups: 1- Uninfected ulcer (wounds without purulent discharge or any evidence of inflammation) 2-Mild infection (presence of ≥ 2 signs of inflammation including erythema, swelling, warmth and tenderness, cellulitis/erythema with ≤ 2 cm diameter around the ulcer and limited infection of the skin and superficial subcutaneous tissues, without evidence of systemic infection) 3- Moderate infection (cellulitis extending > 2 cm, lymphangitic streaking, infection extension beneath the superficial fascia, deep-tissue abscess, gangrene, and muscle, tendon, joint or bone involvement) 4- Severe infection (systemic manifestation of infection including fever, chills, tachycardia, hypotension and acidosis).

Considering the above mentioned criteria, patients were categorized in two groups; 1- Uninfected (those with the first group characteristics) and 2- Infected (including each of the mild, moderate and severe infection groups).

Those with other infectious diseases such as urinary tract infection, pneumonia, patients with hematologic malignancy, and patients receiving antibiotics during the previous month were excluded from the study.

Blood samples were obtained from patients in order to measure white blood cells (WBC), ESR, CRP and PCT level. CRP was assessed by a semi-quantitative latex agglutination method (Bionik slide agglutination test kit) measuring the CRP levels of 6, 12, 24, 48, and 96mg/l. ESR was quantified by an Electra auto-analyzer for one hour.

The blood sample for the analysis of PCT level was centrifuged for 20 minutes and the resulted serum was subsequently kept at the temperature of -18°C . The PCT concentration in serum was measured by Immunoluminometric method using B.R.A.H.M.S procalcitonin kit (LIAISON B.R.A.H.M.S PCT, Germany[®]). WBC $>12000/\mu\text{l}$, PCT $>0.5\text{ng/ml}$, ESR $>17\text{mm/h}$ for men and $> 25\text{ mm/h}$ for women and CRP $\geq 12\text{ mg/l}$ were considered as the cut off levels, considering the manufacture company and laboratory references.

Statistical analysis was performed by SPSS for Windows version 15 using descriptive indices (mean, median, mode and standard deviations) and also chi-square and Mann-Whitney U tests. Two-tailed significant level of 0.05 was used to detect the difference between variables.

The study was approved by the research deputy of Tehran University of Medical Sciences, faculty of Medicine (Pardis Hemmat).

Results

From the 60 patients who were enrolled in the study, 30 patients had uninfected ulcers (Group 1), however, the rest 30 patients were suffering from infected ulcers (Group 2). In the first group, 12 patients (40%) were male and 18 (60%) were female with mean age of 61.6 ± 1.9 years. In the second group, 20 patients (66.7%) were male and 10 patients (33.3%) were female and their mean age was 57.5 ± 2.09 years.

There was significant difference regarding gender (P value =0.03) and duration of diabetes ($p=0.04$) between the two groups (Table 1). Furthermore, the mean level of WBC (P value =0.005), CRP (P value =0.002) and ESR (P value <0.001) were significantly different in the two groups as well (Table 2). In contrast, no significant difference was observed regarding mean age and the PCT level (P value > 0.3) between the two groups.

Table1. Characteristics of patients in two groups

		Group 1 n(%)	Group 2 n(%)	P Value
Gender	Male	12(40)	20 (66.7)	0.03
	Female	18(60)	10 (33.3)	
Duration	$<5\text{ y}$	10 (37)	4 (17.4)	0.04
	5-10 y	9 (33.3)	4 (17.4)	
	$>10\text{ y}$	8 (29.6)	15 (65.2)	

Table2. Comparison of mean values within the two groups

	Group 1	Group 2	P Value
WBC (Cells/ μl)	7540 ± 412.4	9938 ± 881.6	0.005
ESR (mm/h)	36.4 ± 5	68.9 ± 6.06	<0.001
CRP (mg/l)	12.4 ± 2.4	21.8 ± 2.9	0.002
PCT (ng/ml)	0.1 ± 0.001	0.1 ± 0.00	0.3

Discussion

Foot infection is one of the leading causes of morbidity and mortality in diabetic patients and its assessment needs clinical and paraclinical evaluations (1).

In this study, serum inflammatory markers including WBC, ESR, CRP and PCT were compared in two groups of patients with and without infected foot ulcer. In contrast to Uzun et al. study, our findings demonstrated that WBC, ESR, CRP, but not PCT, are valuable inflammatory markers in detecting DFI. Although, the sensitivity of serum PCT to identify DFI was not noticeable in the Uzun's study (PCT $> 0.06\text{ng/ml}$, sensitivity: 78%) (11).

Jeandrot et al. revealed that the measurement of CRP and PCT might be noteworthy to distinguish between infected and uninfected diabetic foot ulcers (12). However, the role of PCT as a diagnostic marker in local infections such as soft tissues, bone and joints is uncertain and demands more studies to confirm its diagnostic value (9,10,13,14).

Leukocytosis is another diagnostic marker for inflammatory and infectious diseases (15). In our study, although total leukocyte count was less than $12\ 000/\mu\text{l}$ in both groups, a significant rise was observed.

Additionally, Jeandrot et al. presented CRP as the best diagnostic factor to detect infection in DFI (Sensitivity 70%, Cut-off point= 17 mg/l), however, they did not find WBC and neutrophil counts as valuable diagnostic factors (12). In the study performed in Turkey, WBC counts and

ESR revealed a moderate sensitivity and specificity to detect DFI (11).

Apart from the mentioned factors, diagnostic role of ESR to detect the bacterial infections, especially in osteomyelitis is well known. Ertugrul et al. reported that ESR, CRP, wound size and positive history of diabetic foot ulcer may be helpful in diagnosing osteomyelitis in diabetic patients (16). Moreover, Kaleta et al. showed that an ESR greater than 70mm/h had 89% sensitivity and 100% specificity in diagnosing osteomyelitis in diabetic patients (17). Although diagnosing the osteomyelitis and joint involvements were not among the aims of our study, the mean ESR was significantly higher in the infected group.

Furthermore, during an inflammatory process and as a consequent upon cytokine stimulation, CRP is synthesized in liver and therefore, the rise in CRP may be an indicator of a bacterial infection (18). In addition and in comparison with normal individuals, CRP level is higher in diabetic patients (19) and diabetic patients with ulcer have a higher CRP level in comparison with those of non-ulcerative extremities (20). Weigelt et al. demonstrated that acute foot ulcers may lead to a rise in the level of acute-phase proteins, cytokines and chemokines even without concomitant infection (21). In contrast to Uzun study (11), our findings demonstrated that CRP concentration was higher in infectious diabetic ulcers than non-infectious ones, however, no comparison to normal individuals was performed.

And last but not least, consistent with other studies (22), the infection was found more in males, which can be due to more serious attention of women to health issues, and the duration of diabetes was positively related to the incidence of DFI.

Absence of control group, lack of definite diagnosis using radiologic and microbiologic modalities and insufficient follow-ups were among the limitations of our investigation.

In conclusion, WBC, ESR and CRP can be helpful parameters in diagnosing DFI, however, determination of definite diagnostic role of PCT in DFI needs further thorough studies.

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Conflict of interest

None declared.

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