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Role of Procalcitonin in 3 to 36 Months Old Children with Fever without Focus

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ORIGINAL ARTICLE

ABSTRACT: Fever without a source (FWS) is a condition that may be created by infectious or noninfectious etiologies. Discrimination between these two groups is challenging. Various studies show the efficacy of some inflammatory markers in order to better diagnosis. This study investigates the diagnostic value of procalcitonin (PCT) as an inflammatory marker in detecting serious bacterial infection in the patient with FWS and whether PCT –guided antibiotic therapy can be helpful. In a randomized intervention trial, 200 consecutive patients 3 to 36 month of age with FWS (≥ 39 ℃) were included; this study was performed at tertiary care hospital in Bandar Abbas. Data were assessed at baseline, after 1, 3 days and when fever improved. The control group (n=100) received Antibiotic according to usual practice while in the PCT group (n=100) Antibiotic treatment was based on serum PTC concentration, a careful past medical history and some laboratory tests were obtained. The mean age of the patients in PCT group and control group was 20.12±10.80mo and 18.23±10.99mo, respectively. There was not any significant statistically difference for age and sex between two groups. By PCT use, antibiotic prescription was significantly reduced in PCT -guided group in comparison with control group (66% VS 86%, P Value= 0.001). The rate of overall outcomes that included the final diagnosis the duration of fever and any morbidity or mortality was similar in both groups. In this study PCT-guided antibiotic prescription reduced antibiotic prescription with no significantly change in overall outcomes.

Keywords: Procalcitonin (PCT), Antibiotic, Fever without Source (FWS)

INTRODUCTION

Fever is a common symptom among children and account for about one third of pediatric visits (Finkelstein et al., 2000; Nelson et al., 1992; Krauss et al., 1991). Fever is common presentation of pediatric infectious disease but can´t predict its severity (Behrman et al., 2007). Fever Without Focus (FWF) is defined as fever ≥ 39 ℃ less than one week in children who seems well, weren´t toxic and without other disease which decrease the sensitivity to infection, without an obvious source after complete history taking and physical examination. Although these children often have self-limited viral infections but some may have occult bacteremia (McGowan et al., 1973; Teel et al., 1975). Also sever local infections such as pneumonia and meningitis is reported. (Shapiro et al., 1986; Baraff et al., 1993).Early diagnosis and distinguish between self-limited viral infectious disease and early stages of infectious disease which may develop to sever local infections is very important in management of patients with FWF.Procalcitonin is pro-hormone for calcitonin, which is secreted by parafollicular cells of the thyroid gland. The biological activity of procalcitonin is significantly different from calcitonin and is believed to be part of the complex inflammatory cascade of the immune system. Procalcitonin has been shown to be elevated in bacterial infections but not in viral infection or other inflammatory conditions. The early initiation and appropriate use of antibiotics are crucial factors in managing critically ill pediatric patients with bacterial infections. Some studies reported that procalcitonin is more specific and sensitive test than other tests such as White Blood Cells (WBC) count, Absolute Neutrophil Count (ANC) and C-Reactive Protein (CRP).(Philipp et al., 2004). In children PCT has a sensitivity of 93% and Negative Predictive Value (NPV) of 96% in diagnosis of sever bacterial infection.PCT show a favorable kinetic profile for use as a clinical marker, it promptly increases within 6 to 12 hours upon stimulation and circulating PCT levels halve daily when the infection is controlled by the host immune system or antibiotic therapy (Becker, 2004).In children with low PCT level the patients can be managed without antibiotic therapy. We hypothesized that PCT test lowers the antibiotic usage in 3 to 36 months old children with FWF.

METHODS AND MATERIALS

A total of 200 children in 3 to 36 months of age with FWF referred to Bandar Abbas pediatric hospital were enrolled in our study. Inclusion Criteria was :1-Core body temperature assessed rectally ≥ 39 ℃ 2- No sign and symptoms Compatible with specific local infection.3- Less than 7 days in fever duration.4- patients who seems well and aren't toxic. There pediatric Specialists evaluated the patients. Complete history including: previous hospitalization, Prematurity, low birth weight and also complete physical examination was done.

Patients were randomly assigned into two groups either to receive treatment according to their serum PCT level or receive standard treatment according to their physical examination and history taken by the physician. Exclusion criteria was: 1-Patient who avoided to sign informed consent form. 2-Antibiotic use in previous two days. 3- Congenital or acquired two days. 4- duration of Fever more than 7 days.5- Vaccination in previous 2 days. PCT level was assessed with Minividas and with Enzyme Link Fluorescent Assay in PCT group. Also for all patients Complete Blood cells and differention (CBC diff) Erythrocyte Sediment rate (ESR) and CRP and urine analysis (UA) and urine culture (UC) was tested. In PCT group, patients were divided into 3 subgroups. Patient with PCT level less than 0.1 ng/ml who didn't received antibiotic. Patients with PCT level between 0.1 ng/ml to 0.5 ng/ml received antibiotic according to deuton made by the physician according the patient situation. All patients with PCT level higher than 0.5 ng/ml received antibiotic treatment because of high Probability of bacterial infections. In standard treatment group antibiotic was used according to the history and physical examination done by physician. Patients were hospitalized and additional Laboratory tests were requested if needed. Patient was visited in first and third day and after Fever discontinuation. Hospitalized patients were visited daily. Duration of fever, antibiotic treatment and data regarding hospitalization and Final diagnosis was recorded.

Data was analyzed using SPSS16 software and descriptive statistics (Mean , standard Deviation , frequency and percentage) chi-square test and Independent samples T-test. P value less than 0.05 was assumed to be significant.

RESULTS

We evaluated 217 Patient and 17 were excluded. (One Patient had cystic fibrosis, 10 had antibiotic use in previous 2 days, 5 Patients avoided to Participate in the study and one had vaccination in previous two days.) Finally 200 Patients were enrooted in the study. 120 (60%) were female and 80 (40%) were male. Their average age was 19.17 10.91 .The baseline characteristic of patients in two groups is summonsed in Table 1. More patient in Control group treated with antibiotic (p=0.001) (Table 2). But there wasn't any significant difference (p=0.76) (Table 2).

Table 1. Baseline characteristic of patients in two groups

Items	PCT group	Control group	P value
Male	61 (61%)	59 (59%)	0.44
Age (months)	20.12 ± 10.80	18.23 ± 10.99	0.22
Low Birth weight	1 (1%)	4 (4%)	0.18
Prematurity	0 (0%)	2 (2%)	0.24
Previous hospitalization	19 (19%)	27 (27%)	0.12
WBC leukopenia	8 (8%)	9 (9%)	0.12
Leukocytosis	15 (15%)	65 (65%)	0.19
PMN dominancy	47 (47%)	56 (56%)	0.12
High ESR	58 (58%)	65 (65%)	0.19
CRP Negative	52 (52%)	42 (42%)	
CRP+1	21 (21%)	19 (19%)	
CRP+2	13 (13%)	14 (14%)	
CRP+3	14 (14%)	25 (25%)	

Table 2. Antibiotic therapy and duration of fever in two groups

Items		PCT group	Control group	P Value
Antibiotic Therapy	Yes	66 (66%)	86 (86%)	0.001
	No	34 (34%)	14 (14%)	
Duration of fever	< 3 days	18 (18%)	22 (22%)	0.76
	3-5 days	45 (45%)	44 (44%)	
	>5 days	37 (37%)	34 (34%)	

DISCUSSION

Early detection of infection is still a problem for physicians. This isn't logical to administer antibiotics for all patients with possible infection because of the problem of bacterial resistance. Current tendency is toward lowering antibiotic usage in viral and self-limited infection and decreasing the duration of antibiotic therapy in bacterial infections. Therefore finding a marker for detection of bacterial infections is valuable (Philipp et al., 2004). In this study our aim was to assess PCT role in lowering antibiotic usage in children 3 to 36 months. We Compared antibiotic usage and duration of fever in 100 patients according to their PCT level and 100 patient according to the history taking and physical examination done by a pediatric specialist.PCT test lowered the antibiotic usage but didn't altered the duration of fever in these patients. A study in 1359 Patient also showed that PCT can lower antibiotic usage (Philipp et al., 2004).Another study on 458 patients reported antibiotic use in 25 % of patients in PCT group in and 97 % of Patients in control group which was statistically significant (Matthias et al., 2008). Another study reported 85 % antibiotic usage in PCT group and 99 % in control group. Our results also showed that the duration of fever wasn't significantly in PCT and control group. Conclusion: Antibiotic use can be reduced without significant change in duration of fever in 3 to 36 months old children with FWF.

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