

SERUM C-REACTIVE PROTEIN AND INTERLEUKIN6 LEVELS IN NEONATAL SEPSIS

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Summary: In this article, we studied complete blood count, serum C-reactive protein (CRP) and interleukin (IL-6) levels in 30 newborn infants with sepsis at admission, in the 24th hour of admission and at the end of the treatment. Our purpose was to determine the relationship among these parameters in the early diagnosis of neonatal sepsis. In our study, there was not a significant difference in white blood cell (WBC) and thrombocyte count among the values of the first, 24th hour and end of therapy in the study group ($P>0.05$). However, there was not a significant difference in B/N ratio among the values at admission, 24th hour and end of therapy in the study group ($P>0.05$). Both serum CRP and IL-6 levels were found to be significantly higher than those of control subjects at the beginning ($P<0.05$). Similarly, the values obtained on the 24th hour were also elevated. However, at the end of therapy both decreased to normal level ($P<0.05$). Based on these data, we think that serum CRP levels only which is a simple method may be used in the diagnosis of neonatal sepsis. However, WBC and serum IL-6 levels may be useful to establish mortality, because there was a statistically significant difference for these parameters between the survivors and deaths ($P<0.05$).

Key words: C-reactive protein; Interleukin; Newborn; Sepsis

Introduction

The early diagnosis of sepsis in newborn infants is an important problem because the early signs and symptoms of septicemia in term or preterm infants are usually non-specific (2,3). Serum C-reactive protein (CRP), IL-6, IL-1ra (interleukin-1 receptor antagonist), tumor necrosis factor (TNF)-alpha, soluble TNF receptors (p55 and p75) and circulating intercellular adhesion molecule-1 (cICAM-1) concentration have been used in order to determine early diagnosis of sepsis (1,4,5,6,7,8,9,10,11,12,14,15). In this article, we studied complete blood count, serum CRP and IL-6 levels in newborn infants with sepsis to determinate the relationship among these parameters in the early diagnosis of neonatal sepsis.

Material and Methods

The study includes 30 infants with neonatal sepsis and 10 healthy age-matched control infants. In the diagnosis of sepsis, inclusion criteria included physical signs of infection and respiratory or cardiovascular dysfunction. Physical symptoms of infection were defined by the presence of at least two of the following: feeding intolerance, abdominal distension, lethargy, irritability, temperature instability, hyperbilirubinemia and hepatosplenomegaly (8).

In all patients complete blood count, serum CRP and IL-6 levels were determined at admission, in the 24th hour of admission and at the end of the treatment. In healthy infants these parameters were studied only at admission. Complete blood count was counted by electronic impedance method in the automatic counter (Medonic CA 610, Sweden). Serum CRP and IL-6 concentrations were measured by latex agglutination and enzyme linked immunosorbent assay methods, respectively. The normal ranges of hemoglobin, white blood count (WBC) and thrombocyte count were 14–18 g/dl, 5000–20,000/mm³ and 150,000–450,000/mm³ respectively (13). The values of >0.2 , >6 mg/dl and >8 pg/ml were accepted as positive for the band/neutrophil (B/N) ration, serum CRP and IL-6 levels, respectively.

A combination of cefotaxim plus ampicillin-sulbactam was initiated in all patients, but antibiotics were changed in required infants according to the antibiogram. Statistical analyses were performed by using Mann-Whitney U test, Kruskal-Wallis variance analysis and Chi Square test.

Results

Of 30 infants with sepsis, 21 were boys and nine were girls, and of the healthy infants six were boys and four were girls. There was no significant difference in age at admission, gestational age, weight and sex between the groups

($P > 0.05$) (Tab. 1). Blood culture was positive in 14 (47%) infants. The microorganisms isolated from blood cultures were as follows; coagulase negative *Staphylococcus* in four (28.5%) infants, *Enterobacter* in four (28.5%) infants, *Escherichia coli* in three (21.5%) infants, *Klebsiella* in two (14.5%) infants and *Serratia* in one (7%) infant. Four (13.3%) infants died in the study group.

Table 1 presents clinical and laboratory findings of the study and control groups. There was not a significant difference in age at admission, gestational age and weight between the study and control groups ($P > 0.05$). There was not a significant difference in WBC and thrombocyte count among the values at admission, 24th hour and end of therapy in the study group ($P > 0.05$). B/N ratio was higher in the study group than the control at the beginning ($P > 0.05$). However, there was not a significant difference in B/N ratio among the values at admission, 24th hour and end of therapy in the study group ($P > 0.05$). Both serum CRP and

IL-6 levels were found to be significantly higher than those of control subjects at the beginning ($P < 0.05$). Similarly, the values obtained on the 24th hour were also elevated. However, at the end of therapy both decreased to normal level ($P < 0.05$) (Tab. 1). When comparing the results of survivors and deaths, we found statistically significant difference in WBC count and serum IL-6 levels between the groups (Tab. 2).

Discussion

Numerous studies have been performed to determine the relationship between cytokines and neonatal sepsis in the literature (1,4,5,6,9,10,11,12,14,15). They showed that both serum CRP and IL-6 concentrations elevated in infants with sepsis, and some of them revealed that the best predictors of infection were the combination of the initial IL-6 value and CRP value after 24 h. (1,6,7,11). Kallman et al.

Tab. 1: Clinical and laboratory findings of the study and control groups.

Parameters	Study Group (n: 30)	Control Group (m: 10)	P
Age at admission (day)	10.6±1.8	4.9±0.5	>0.05
Gestational age (week)	38.1±0.34	38.5±0.52	>0.05
Weight (g)	2860±137	3260±217	>0.05
Hemoglobin (g/dl)	12.68±0.55	15.01±0.43	>0.05
WBC count (/mm ³)			
At the beginning	12,657±2518	11,370±1140	>0.05
On the 24 th hour	9466±1614		
At the end of therapy	9033±941		
Band/Neutrophil ratio			
At the beginning	0.14±0.03	0.08±0.008	<0.05
On the 24 th hour	0.12±0.01		
At the end of therapy	0.10±0.01		
Thrombocyte count			
At the beginning	199,710±22,798	225,500±31,617	<0.05
On the 24 th hour	197,440±45,144		
At the end of therapy	191,660±32,640		
CRP (mg/dl)			
At the beginning	20.58±6.96	2.92±1.31	<0.05
On the 24 th hour	29.56±8.3		
At the end of therapy	4.9±1.7		
Serum IL-6 (pg/ml)			
At the beginning	359.86±90.83	5.11±1.94	<0.05
On the 24 th hour	110.03±56.06		
At the end of therapy	3.96±2.10		

Tab. 2: Laboratory findings of the survivors and deaths.

	Sepsis Group (n:30)		
Parameters	Survivors	Deaths (n: 4)	P
WBC count (/mm ³)	11,184±973	4375±857	0.005
Band/Neutrophil ratio	0.12±0.01	0.28±0.12	>0.05
Thrombocyte count (/mm ³)	196,576±19,696	171,500±16,271	>0.05
CRP (mg/dl)	21.72±8.0	13.15±2.9	>0.05
IL-6 (pg/ml)	336.3±68.7	516.8±238.7	0.04

(9) noted that IL-6 contributes to the diagnosis of sepsis faster than CRP. Silveira et al. (15) and de Bont et al. (5) noted that the combination of TNF-alpha and IL-6 determinations appeared to be a good predictor of neonatal sepsis. In our study both serum CRP and IL-6 levels were found to be significantly higher than those of control subjects at the beginning ($P < 0.05$). Similarly, the values obtained on the 24th hour were also elevated and they were within normal ranges at the end of therapy.

Dollner et al. (7) compared six infalmmatorz mediators [CRP, IL-6, soluble TNF receptors (p55 and p75) and soluble adhesion molecules (ICAM-1, E-selectin)] as early diagnostic tests for neonatal sepsis, and studied the possible benefit of combining parameters. They noted that CRP performed best as a diagnostic test for neonatal sepsis. Diagnostic accuracy was further improved by combining CRP and IL-6, where as the other parameters (p55, p75, ICAM-1 and E-selectin) added no further diagnostic information (7). In the other study of the same authors similarly it was noted that used in combination with CRP, IL-6 seems to be a valuable parameter in the early diagnosis of neonatal infections (6). Kuster et al. (10) recorded that interleukin-1 receptor antagonist and IL-6 are superior to cICAM-1 and CRP as predictors of sepsis 1 or more days before clinical diagnosis (10). In our study we found similar findings in both serum CRP and IL-6 levels. Therefore, we think alone serum CRP levels which is a simple method may be used in the diagnosis of neonatal sepsis. However, WBC and serum IL-6 levels may be useful to establish mortality, because there was a statistically significant difference for these parameters between the survivors and deaths ($P < 0.05$).

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