Short Communication

The Relationship Between Scoring Systems and Cytokine Levels in Neonatal Sepsis

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Abstract

In this study, 20 newborn infants with sepsis were evaluated and scored according to the criteria of Töllner and Rodwell and associates. Leukocyte count, serum C-reactive protein (CRP), tumour necrosis factor (TNF)-alpha and interleukin (IL)-6 levels were also studied in all infants. The aim of this study was to determine if a relationship exists between the scoring systems and the cytokine levels in neonatal sepsis. The infants were divided into two groups as blood culture positive and negative. Blood culture was positive in 12 (60%) infants. We did not find a significant difference for leukocyte count, cytokine levels and scoring systems between the blood culture positive and negative groups. However, we found a positive correlation between the scoring systems and serum CRP and TNF-alpha levels (P <0.05), but no correlation with IL-6. In conclusion, we suggest that only serum CRP level without performing scoring and studying serum TNF-alpha concentration may be used in early diagnosis of neonatal sepsis. However, further studies are necessary to define this because of the small sample size of our pilot study.

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Key words: C-reactive protein, Interleukin-6, Newborn, Tumour necrosis factor

In newborn infants, the early diagnosis of sepsis is an important problem because the early signs and symptoms of septicaemia in term or preterm infants are usually non-specific.[1,2] Many clinical and haematological scoring systems have been developed in the early diagnosis of neonatal sepsis.[3-8] The aim of this study was to determine if a relationship exists between the scoring systems and the cytokine levels in neonatal sepsis. To our knowledge, this relationship has not been previously evaluated in the literature.

The study was carried out in Erciyes University Faculty of Medicine, Division of Neonatology. Neonates with physical signs of infection and respiratory or cardiovascular dysfuction were included. Physical symptoms of infection were defined by the presence of at least two of the following: feed intolerance, abdominal distension, lethargy, irritability, temperature instability, hyperbilirubinaemia and hepatosplenomegaly.[9] On admission, all infants were evaluated and scored according to the criteria of Töllner[3] and Rodwell et al[4] and the results were recorded. In addition, leukocyte count, serum C-reactive protein (CRP), tumour necrosis factor (TNF)-alpha and interleukin (IL)-6 levels were studied. Serum TNF-alpha and IL-6 concentrations were measured by enzyme-linked immunosorbent assay method. A combination of cephalosporin plus aminoglycoside was initiated in all infants, but antibiotics were changed in required infants according to the antibiogram. The infants were divided into two groups as blood culture positive and negative. The groups were compared for the clinical laboratory findings and scoring systems. Statistical analysis was performed by using the Mann-Whitney U test - Wilcoxon Rank Sum W and Spearman's correlation coefficient test.

The study comprised 20 infants (13 boys and 7 girls) with neonatal sepsis. Blood culture was positive in 12 (60%) infants. The microorganisms isolated from blood cultures included *Staphylococcus epidermidis* in 5 (41%) infants, *Eschericha coli* in 2 (16.5%) infants, *Enterobacter* in 2 (16.5%) infants, Klebsiella in 2 (16.5%) infants and *Enterococcus* in 1 (9.5%) infant. Three (15%) infants died. We did not find a significant difference for the leukocyte count, cytokine levels and scoring systems between the blood culture positive and negative groups (Table I). In determining whether there was a correlation between the

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TABLE I: CLINICAL AND LABORATORY FINDINGS OF THE INFANTS WITH AND WITHOUT CULTURE POSITIVE

Study group				
Parameters	Culture positive (n = 12)	Culture negative (n = 8)	Z	*P*
Age at admission (day)	5.75 ± 5.86	6.57 ± 6.96	-0.38	>0.05
Gestational age (week)	37.75 ± 2.26	37.75 ± 2.43	0.00	>0.05
Weight (g)	2630 ± 636	2602 ± 541	-0.07	>0.05
Leukocyte count (mm^3)	12.316 ± 7409	11.100 ± 3351	-0.46	>0.05
Serum CRP level (mg/dL)	74 ± 120	17 ± 29	-1.09	>0.05
Serum TNF-alpha (pg/mL)	148 ± 275	175 ± 336	-0.03	>0.05
Serum IL-6 (pg/mL)	292 ± 344	290 ± 424	-0.42	>0.05
Töller scoring system	10.0 ± 3.51	8.43 ± 1.84	-0.93	>0.05
Haematologic scoring system	4.50 ± 1.38	3.87 ± 1.55	-0.75	>0.05

CRP: C-reactive protein; IL-6: interleukin-6; TNF: tumour necrosis factor

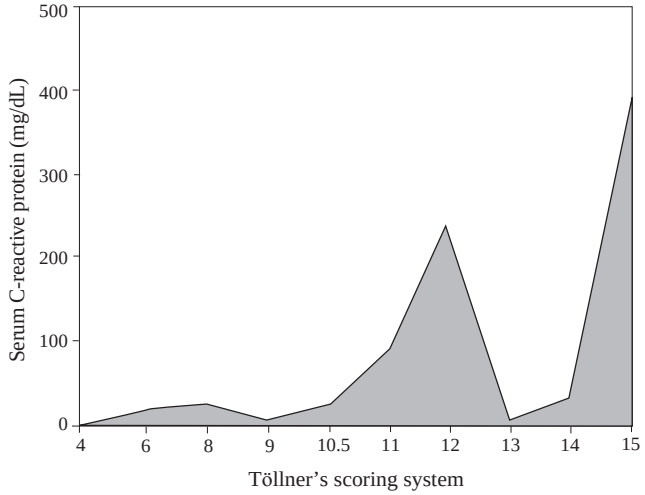

Fig. 1. A relationship between serum C-reactive protein and Töllner's scoring system.

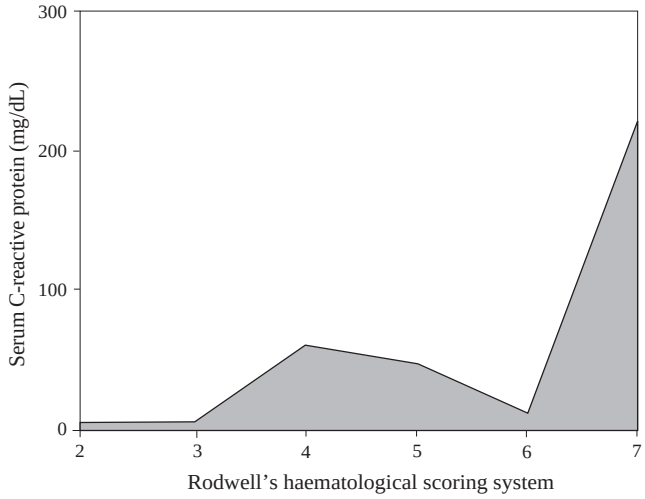

Fig. 2. A relationship between serum C-reactive protein and Rodwell's haematological scoring system.

scoring systems and the parameters, which included CRP, IL-6 and TNF-alpha levels, we found a positive correlation between Töllner's scoring system and CRP levels (r = 0.52; *P* = 0.01) (Fig. 1), and Töllner's scoring system[3] and TNF-alpha levels (r = 0.51; *P* = 0.02). However, there was no correlation with IL-6 level (*P* = 0.25). Similar findings were observed with Rodwell et al's haematological scoring system;[4] a positive correlation was found between haematological scoring and CRP levels (r = 0.54; *P* = 0.01) (Fig. 2), and haematological scoring system and serum TNF-alpha levels (r = 0.66; *P* = 0.001), but there was no correlation with IL-6 (*P* = 0.20).

In 1982, Töllner[3] developed a scoring system to determine the early diagnosis of septicaemia in the newborn in which both the clinical and laboratory findings such as skin color, complete blood count, blood gas analysis, and cardiac, respiratory and gastrointestinal findings were used. In 1988, Rodwell et al[4] composed three groups which included sepsis, probable infection and non-infected infants, and formulated a haematologic scoring system that assigned a score of 1 for each of 7 findings: abnormal total leukocyte count, abnormal total neutrophil (PMN) count, elevated immature PMN count, elevated immature to total PMN ratio, immature to mature PMN ratio $\geq$0.3, platelet count $\leq$150,000/mm^3, and pronounced degenerative changes in PMNs. In the last scoring system, clinical findings of the infants were not included.[4]

Several other scoring systems were also formulated.[5-8] For example, Mautone and associates[5] developed a scoring system including blood and blood chemical tests which were scored from 0 to 2. The results showed that neonates with scores <5 should be considered free from sepsis, those scoring 5-7 should arouse suspicion of sepsis, and sepsis should be considered definitely present in those scoring >7. This scoring system presented 100% sensitivity, 88.2% specificity, 100% positive predictive value and 88.2% negative predictive value. The authors of this study

concluded that the system was reliable and easy to use.[5] Mahieu et al[7] developed a scoring system composed of CRP, neutrophil fraction, thrombocytopenia, fever, and prolonged parenteral nutrition exposure to predict nosocomial sepsis in ill neonates.

In our study, we used the scoring systems of Töllner [3] and Rodwell et al[4] which were universal. Our findings showed that there was a positive correlation between scoring systems and serum CRP and TNF-alpha levels in both scoring systems. Recently, Dollner[10] compared 6 inflammatory mediators [CRP, IL-6, soluble TNF receptors (p55 and p75) and soluble adhesion molecules (ICAM-1 and E-selectin)] as early diagnostic tests for neonatal sepsis and studied the possible benefit of combining parameters. They noted that CRP was the single best diagnostic test. Diagnostic accuracy was further improved by combining CRP and IL-6, whereas the other parameters (p55, p75, ICAM-1 and E-selectin) added no further diagnostic information.[10]

In conclusion, we suggest that only serum CRP level without performing scoring and studying serum TNF-alpha concentration may be used in the early diagnosis of neonatal sepsis. However, further studies are necessary to define this because of the small sample size of our pilot study.

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