Hematologic Scoring System for Early Evaluation of Neonatal Sepsis

YENİ DOĞAN SEPSİ SİNİN ERKEN DEĞERLENDİRİLMESİNDE HEMATOLOJİK SKORLAMA SİSTEMİ

Ülkü TIRAŞ*, Şenay SAVAŞ*, Yıldız DALLAR**, Gülten TANYER***,
Ömer ERDEVE*, Rukiye UNSAL*

* MD., Ankara Education and Research Hospital, Pediatrics,
** MD.Assoc.Prof., Ankara Education and Research Hospital, Pediatrics,
*** MD.Prof., Ankara Education and Research Hospital, Pediatrics, Ankara, TURKEY

Summary

Neonatal sepsis is a clinical syndrome of first month of life characterized by signs and symptoms of systemic infection and bacteriemia. Presence of clinical signs differs this situation from temporary bacteriemia seen at healthy newborns. Early diagnosis of sepsis is an obligation due to its high morbidity and mortality.

Eighty four septic newborn seen in one year period were evaluated prospectively. Patients were evaluated for clinical outcome, laboratory data, etiologic agents and factors affecting mortality. The aim of the study was to establish a usable hematologic scoring system that makes the sepsis diagnosis earlier.

Thirty one of 84 patients (36,9%) were preterm versus 53 (63,1%) full term. Twenty eight of patients (33,3%) had early onset, 41 (48,8%) had late onset and 15 (17,8%) had nosocomial sepsis. Premature rupture of membranes, urogenital system infection and/or maternal fever at period of one week before delivery and perinatal asphyxia were determined as serious risk factors for early sepsis. Prematurity and low birthweight affected mortality significantly ($p<0,05$). Mortality rate for neonatal sepsis was 19% and mortality of preterms was significantly higher than terms ($p<0,05$). Hematologic scoring system was constituted by scoring five laboratory data separately and certain sepsis cases had 66,7% rate for a score >2.

A usable hematologic scoring system is necassary for early diagnosis of neonatal sepsis and a combination system rather than one test result was found more diagnostic.

Key **Words:** Hematologic scoring system, Neonatal sepsis

T Klin J Med Res 2002, 20:55-59

Özet

Neonatal sepsis, yaşamın ilk ayında, sistemik enfeksiyon ve bakteriyeminin bulguları ile karakterize klinik sendromdur. Klinik durumun varlığı, bu durumu bazı sağlıklı yenidoğanlarda görülen geçici bakteriyemiden ayırır. Yüksek mortalité ve morbiditesinden dolayı yenidoğan sepsisinin erken tanısı bir zorunluluktur.

Bir yıllık periyotta görülen 84 septik yenidoğan prospektif olarak değerlendirildi. Hastalar klinik sonuçları, laboratuar verileri, etyolojik ajanları ve mortaliteyi etkileyen faktörleri yönünden değerlendirildiler. Çalışmanın amacı; sepsis tanısını daha erken sağlayabilen bir hematolojik skorlama sistemi oluşturmaktı.

Seksendört olgunun 31'i (%36,9) pretermken, 53'ü (%63,1) termdi. Olguların 28'i (%33,3) erken sepsis, 41'i (%48,8) geç sepsis ve 15'i (%17,8) hastanede edinilmiş sepsis idi. Erken meınbran rüptürü, ürogenital sistem enfeksiyonu ve/veya doğumdan bir hafta öncesinde annede ateş ile perinatal asfıksi erken sepsis için ciddi risk faktörleri olarak değerlendirildi. Prematürite ve düşük doğum ağırlığı mortaliteyi istatistiksel olarak etkiliyordu ($p<0,05$). Yenidoğan sepsisinde mortalité oranı %19 idi ve prematürelerde mortalité hızı teorilere göre belirgin yüksekti ($p<0,05$). Ayrı beş laboratuar verisinden oluşan hematolojik skorlama sistemi kuruldu ve kesin sepsis olgularında skorun >2 olma oranı %66,7 idi.

Yenidoğan sepsisinin erken tanısında kullanılabilir bir hematolojik skorlama sistemi gereklidir ve tek testten ziyade bir kombinasyon sistemi daha tanısaldır.

Anahtar Kelimeler: Hematolojik skorlama sistemi, Neonatal sepsis

T Klın Araştırma 2002, 20:55-59

Neonatal sepsis is a clinical syndrome of first month of life characterized by signs and symptoms of systemic infection and bacteriemia. Presence of clinical signs differs this situation from temporary bacteriemia seen at healthy newborns(l). Sepsis can be divided into two groups named as early (first 72 hours of life) and late onset sepsis (>72 hours). Sepsis developing after 48 hours of hospitalization is accepted as nosocomial one(2). Due to high mortality and morbidity of newborn sepsis,

early diagnosis and treatment gains importance(3). Certain diagnosis of sepsis only by clinics is difficult because of non-specific clinical symptoms, so that some microbiological and laboratory methods are used (4).

In this study, 84 septic newborn seen in one year period were evaluated prospectively. The aim of this study was to evaluate patient's clinic and laboratory data, find out etiologic agents and the factors affecting mortality and try to establish a hematologic scoring system that makes neonatal sepsis diagnosis as possible as earlier.

Material and Methods

Eighty four sepsis diagnosed patients at Ankara Education and Research Hospital Neonatology Unit were evaluated prospectively. Gestational ages were determined by Dubowitz criteria and patients were subgrouped as premature (gestational age <37 weeks) and term. Hypoactivity, hypothermia or hyperthermia, pallor, cyanosis, jaundice, lethargy, apnea, cyanosis, poor peripheric circulation, hepatosplenomegaly, hypo/hyperglysemia, gastrointestinal symptoms (vomiting, abdominal distention and diarrhea), cutis marmoratus and poor sucking were determined as clinical signs and symptoms of sepsis. Gestational risk factors (urinary infection of mother, chorioamniotis, premature rupture of membranes, fever, antibiotic usage, preterm labor, perinatal asphyxia, multiple gestation, alcohol or nicotine usage, chronic disease) were investigated for all cases. All patients were evaluated by urine, cerebrospinal fluid and venous blood cultures. Bactec automatized technique was used for blood cultures. Complete blood count and peripheral smears were obtained. Total leukocyte count <5000 /mm^3 or >24000 /mm^3 (5), low or high absolute neutrophil count according to Monroe's reference range (6), immature/mature neutrophil rate >0,3, immature/total neutrophil rate >0,2 and platelet count <150,000 /mm^3 (5,6) were accepted as laboratory data supporting sepsis. Hematologic scoring system (HSS) was constituted by scoring each laboratory data separately by one point. Sensitivity, specificity, negative and positive predictive values were obtained for all parameters. Blood culture positivity was accepted as certain sepsis at evaluation. Statistical analysis was made by Chi-square and Fisher certain Chi-square test with help of Instat software program.

Results

Thirty one of 84 patients (36,9%) were preterm whereas 53 (63,1%) were term. Twenty eight of patients (33,3%) had early onset, 41 (48,8%) had late onset and 15 (17,8%) had nosocomial sepsis. General mortality rate for sepsis was 19% (16/84). Mortality rate for early and late sepsis were 26,7% and 19,5% in order .Only two patients (13‰) were lost due to nosocomial infection. No statistically significant difference for mortality rate between early and late onset sepsises was determined ($p>0,05$). Although prematures constitute almost 18‰ of hospitalized patients, mortality rate for prematures (35,5‰) was higher than one for terms (9,4%) ($p<0,05$). Birth weight lower than 2500 grams increased mortality rate to 35,1%) when compared to 6,4‰ rate of >2500 grams weighted neonates ($p<0,001$).

The distribution of signs and symptoms are listed on Table 1. Poor sucking, hypoactivity, lethargy, jaundice, pallor and apnea were most common symptoms of our cases. Gestational risk factors rate was 56,7‰ for early sepsis and 12,2% for late sepsis, and their presence was statistically significant ($p<0,05$). Premature rupture of membranes, urogenital system infection and/or maternal fever at period of one week before delivery and

Table 1. The percentage of sign and symptoms seen at sepsis

Clinical situation and percentage			
Poor sucking	82,1%	Poor peripheric circulation	26,2%
Hypoactivity	78,6%	Gastrointestinal symptoms	23,8%
Jaundice	58,3%	Hepatosplenomegaly	22,6%
Lethargy	53,6%	Hypothermia	17,9%
Pallor	52,4%	Skin manifestations	14,3%
Apnea	38,1%	Hypoglycemia	9,5%
Hyperthermia	34,5%	Hyperglycemia	6%
Cyanosis	32,1%		

Table 2. Distribution of microorganisms obtained by blood culture for sepsis subgroups

	Early unset	Late unset	Nosocomial	Total percentage
K.pneumonia	5	6	3	38,8 %
S.aureus	6	3		25%
S.epidermidis	1	•($•)		5,5 %
C.freundi		1		2,7 %
Streptococcus B		1		2,7 %
E.coli		2		5,5 %
S.pneumonia		?Jrf		2,7 %
S.marcescens			5	13,8%
P.aeruginosa			1	2,7 %

perinatal asphyxia were determined as serious risk factors for early sepsis. Positive blood culture ratio was %42,9 (36 cases). No positive cultures were obtained from cerebrospinal fluid and urine. The etiological agents isolated from blood cultures were as follows; Klebsiella pneumonia (14), Staphylococcus aureus (9), Serratia marcescens (5), Staphylococcus epidermidis (2), E. Coli (2) and Pseudomonas aeruginosa, Citrobacter freundi, Streptococcus pneumonia and Group B Streptococci (Table 2).

The sensitivity, specificity, negative and positive predictive values of hematologic data were determined (Table 3). Each result was estimated by one point, and score >2 was indicating diagnosis of sepsis. The most sensitive test was immature/total neutrophil ratio >0,2. The highest negative predictive value was again for this test, and when it was negative possibility of non-sepsis state was 60,3%. HSS >2 point was accepted as border for sepsis diagnosis and certain sepsis cases had 66,7% rate for HSS>2. A non-sepsis state possibility rate was 64,7% for scores not exceeding one point.

Discussion

The increased development at neonatal intensive care and treatment modalities could not decrease the incidence and mortality of sepsis (7). The mortality rates for neonatal sepsis change between 20-50% at reported articles and rate at our unit (19%) was almost same with reported articles(7,8). Most of studies show that early sepsis incidence is higher than late sepsis; the higher rate (48,8%) for late sepsis at our unit was related to majority of cases accepted by different centers at Middle Anatolia Region. The mortality rates were not significantly different when compared for both early (26,7%) and late (19,5%) sepsis cases (p>0,05). This was not parallel with majority of reports obtained (7,8). Mortality rates reported for <1500 gram weighted patients are almost 60%>. It decreases to 28% for 1500-2500 gram weighted and 10% for >2500 gram weighted ones (8). Also our study significantly showed that the lower birth weight increases mortality rate at septic neonates for almost five times (p<0,001). Again mortality rate increased almost four times for prematures (p<0,05).

The most important risk factors for sepsis at prenatal period are premature rupture of membranes, maternal fever or urogenital infection of mother before labor, major congenital anomalies, prematurity and intrauterine growth retardation (9). Seventeen of

Table 3. Sensitivity, specificity, negative and positive predictive values of separate tests constituting HSS

Hematologic Test	Sensitivity %	Specificity %	Positive predictive Value %	Negative Predictive Value %
lmmature/Mature>0,3	61	50	63,2	47,8
Immature/Total>0,2	66,7	43,8	47,1	63,6
Thrombocytopenia	30,6	79,2	52,4	60,3
Leukopenia/Leukocytosis	22,2	79,2	44,4	57,6
Neutropenia	47,2	47,9	40,5	54,8

30 early sepsis (56,7%), and five of 41(12,2%) late sepsis had these risks at our unit. Symptoms of sepsis at neonatal period are non-specific (10). Poor sucking, hypoactivity, lethargy, jaundice, pallor and apnea were most common signs of our cases. Majority of septic cases developed thermal irregularity at our study; hyperthermia and hypothermia rates were %34,5 and %17,9 in order.

Gold standart for proof of sepsis is positive blood culture, but early diagnosis should be suspected by clinic progress and other laboratory data, because of the fatality of situation (10). There are studies reported concerning hematologic parameters that support early diagnosis of sepsis. It was shown that immature/mature ratio of neutrophils is the most sensitive one. Sensitivity rates of %>90-95 were reported (6). At our study, it was again the most sensitive (66,7%>) test, but with lower rate. The highest negative predictive value was again for immature/total neutrophil rate >0,2. Hematologic scoring system used for early diagnosis of sepsis do not significantly increase the positive predictive value, but negative predictive value may reach upto hundred percent. Rodwell and collègues had formulated a HSS including elevated immature polymorphonuclear neutrophil (PMN) and degenerative changes in PMNs in addition to our scoring system and showed that the higher the score the grater was the likelihood of sepsis. At their study; with score <2, the absence of possible sepsis was ***99%*** (11). Our study showed that negative predictive value for hematological scoring system was 64,7%o but because its easiness and cheapness, it is still a usable method for early evaluation. This shows that HSS should be improved and standardized by addition of some simple tests. Yurdakôk (10) and Franz (12) showed that C reactive protein has a low sensitivity at the onset of clinical signs but the sensitivity improves with the course of infection. Marigold and colleagues showed that the presence of neutrophils more immature than bonds and the absolute neutrophil count are the two values that best separate infected patients. They also claimed that the band count had minimal value for identifying infected patients (13).

The most common isolated bacteria was Klebsiella pneumonia (38,8%>) at our unit, differing than reports from Europe and United States showing Group B Streptococci as most common (14). Ihkkan and colleagues fom Turkey has also reported Klebsiella pneumonia as leading agent for neonatal sepsis (15). These results were also concordant with developing countries' reports (7,14).

Neonatal sepsis has high mortality rate and concerning its spread velocity, it should be evaluated as early as possible. HSS might be used as supportive parameter for early diagnosis of sepsis because it is easy and inexpensive and these make it valuable for a developing country such as Turkey.

REFERENCES

1. Klein JO, Marcy SM. Bacterial Sepsis and Meningitis. In: Klein R, ed. Infectious Diseases of the Fetus and Newborn Infant, 4 ' ed. Philadelphia: WB Saunders Co, 1995: 835-90.
2. Gotoff SP. Infections of the Neonatal Infant. Pathogenesis and Epidemiology. Behrman RE, Kliegman RM, Jenson HB, Nelson WE, eds. Nelson Textbook of Pediatrics, 16th ed. Philadelphia: WB Saunders Co. 2000: 538-44.
3. Stoll BJ. The Global Impact of Neonatal Infection. Clin Perinat 1997; 24(1): 1-21.
4. Boyer KM. Infectious Diseases. Burg Ingelfinger Wald Polin Gellis and Kagan's, ed. Current Pediatric Therapy. Saunders, 1996; 565-71.
5. Philip AGS, Hewith JR. Early diagnosis of neonatal sepsis. Pediatrics 1980; 65:1036-41.
6. Rodwell RL, Leslie AL, Tudehope DI. Early diagnosis of neonatal sepsis using a hematologic scoring system. J Pediatr 1988; 112:761-7.
7. Simon C, Schroder H, Beyer C, Zerbst T. Neonatal Sepsis in an Intensive Care Unit and Results of Treatment. Infection 1991; 19(3): 146-9.
8. Vesikari T, Janas M. Neonatal Septicaemia. Arch Dis Child 1985;60:542-6.
9. Barruch W. Neonatal Sepsis: Patogénesis and Supportive Therapy. Seminar Perinat 1997; 21: 28-38.
10. Yurdakök M, Erdem G, Tekinalp G. Prematüre Bebeklerde Neonatal Sepsisin Erken Tanısında Serum CRP Değeri. Çocuk Sağlığı ve Hastalıkları Dergisi 1992; 35:289-93.
11. Rodwell RL, Taylor KM, Tudehope DI, et al. Hematologic scoring system in early diagnosis of sepsis in neutropenic newborns. Pediatr Infect Dis J 1993; 12:372-6.

12. Franz AR, Pohlandt F. Diagnostic tests for bacterial infections. Arch Dis Child Fetal Neonatal ED 1999; 80:F78-9.

13. Ardron MJ, Westengard JC, Dutcher TF. Band neutrophil counts are unnecessary for the diagnosis of infection in patients with normal leukocyte counts. Am J Clin Pathol 1994; 102:646-9.

14. Stoll BJ. The global impact of neonatal infection. Clin Perinat 1997; 24(1): 1-21.

15. Ilıkkan B, Vural M, Özbek S ve ark. Yenidoğan ünitesinde sepsis olgularının değerlendirilmesi. 8. Ulusal Neonatoloji Kongresi, Kongre Kitabı, 1997: 100.

Received: Nov. 14, 2001

Correspondence:: Ömer ERDEVE
Ankara Education and Research Hospital
Pediatrics, Ankara, TURKEY
omercrdeve@yahoo.com