Role of procalcitonin and CRP in diagnosis and follow-up of neonatal sepsis

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We aimed to investigate the role of procalcitonin in the diagnosis and follow-up of neonatal sepsis, and to compare it with C-reactive protein (CRP) in this context.

Between April and October 2002, a total of 67 neonates were randomly recruited into the study and were divided into four groups as: those with highly probable sepsis (group 1), probable sepsis (group 2), possible sepsis (group 3), and no sepsis (group 4; controls).

When the initial procalcitonin levels of the groups were compared, the results were statistically significant ($p<0.05$) except for the comparison between groups 3 and 4 ($p>0.05$). When the initial CRP levels were compared between the groups, the levels measured in groups 1 and 2 were significantly higher than the levels measured in groups 3 and 4 ($p<0.05$). In addition, the decreasing levels in procalcitonin were statistically more significant than the decreasing levels in CRP in showing the response to antibiotic treatment ($p<0.01$ and $p<0.05$, respectively).

In conclusion, serum procalcitonin levels seemed to be superior to serum CRP levels in terms of early diagnosis of neonatal sepsis, in detecting the severity of the illness, and in evaluation of the response to antibiotic treatment.

Key words: newborn, sepsis, procalcitonin, C-reactive protein.

The clinical findings of sepsis are uncertain in newborn infants, and these findings may be associated with multiple conditions besides infection. Therefore, antibiotics are started immediately in newborn infants who have nonspecific findings of infection and are continued until the final result of the blood culture is obtained[1,2]. Blood culture is the most valuable diagnostic method, but it may yield false-positive results because of contamination. Also, blood culture can remain negative despite generalized bacterial infection[3]. Body fluid cultures, determination of bacterial antigens, white blood cell count, acute phase proteins [C-reactive protein (CRP), haptoglobin, fibrinogen, α1-antitrypsin], interleukin and procalcitonin (PCT) are the other laboratory studies which support the diagnosis[4,5].

Procalcitonin (PCT) is the precursor protein of calcitonin and has no hormonal activity. It is a 116 amino-acid protein with a molecular mass of 14.5 kDa[6]. It was shown in healthy volunteers that PCT is detectible in the plasma two hours after the injection of a small amount of bacterial endotoxins, increasing rapidly in 6-8 hours, and reaching a plateau and then decreasing to normal levels after 24 hours[6,7]. PCT levels increase in severe sepsis and its plasma concentration is related to the patient's clinical condition and capacity of immune reaction. Serum PCT levels appeared to correlate with the severity of microbial invasion and decreased rapidly after appropriate antibiotic therapy. Some patients with localized bacterial or viral infection had a slight rise in PCT. Normal serum and plasma levels of PCT are less than 0.5 ng/ml. Levels above this value have been accepted as pathological[6-9].

Increases in PCT levels have been reported after the intravenous injection of bacterial endotoxins in laboratory conditions. This increase has been observed after the elevation

of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), but before the rise in CRP. PCT increases a few hours later than TNF-α and IL-6, and it declines after the fall in IL-6, but before CRP at the end of the inflammation in clinical conditions[6]. CRP is one of the acute-phase proteins. Although it is a classical and sensitive marker of inflammation, it cannot be used to differentiate between bacterial and other infections[10]. It is a disadvantage that CRP increases after PCT for the follow-up of the progression of the infection[6].

Chiesa et al.[2] stated that an increase in PCT levels in early- and late-onset of neonatal sepsis is quite reliable. Monneret et al.[11] reported that elevated PCT levels correlate with sepsis and that appropriate antibiotic therapy lowers it rapidly. They also found that CRP did not show a similar correlation. In another study, Franz et al.[12] suggested that the combination of IL-8 and CRP appeared to provide a more reliable method in the early diagnosis of neonatal sepsis.

The aim of our study was to determine the role of PCT in the diagnosis of neonatal sepsis and in the evaluation of the clinical response to antibiotic therapy. In addition, we aimed to compare its efficiency with that of CRP.

Material and Methods

We prospectively studied the newborn infants born between April 2002 and October 2002 admitted to the Neonatal Intensive Care Unit of the Pediatric Department of Uludağ University Faculty of Medicine.

Infants who had clinical or laboratory findings of neonatal sepsis were enrolled in the study. The infants were classified into four groups according to the criteria defined by Gitto et al.[13]. Infants who had no signs of clinical and laboratory infection were included as the control group. Table I shows the criteria of the groups.

Exclusion criteria were administration of antibiotic therapy during admission and refusal of parental consent. The newborns who died during follow-up and who had exchange transfusion for neonatal hyperbilirubinemia were also excluded from the study.

Gestational age, birth weight and gender, admission time and time of the blood sampling were recorded.

The changes in the hematologic parameters were processed according to the Manroe[14] and Rodwell[5] scoring systems. Leukopenia is defined as leukocyte count <5,000/mm^3;

Table I. Criteria Employed for Defining the Sepsis Score

Groups	Criteria
Group 1 High probable sepsis	At least 3 sepsis-related clinical signs* CRP >1 mg/dl At least 2 other altered serum parameters in addition to CRP** Blood culture: positive or negative
Group 2 Probable sepsis	Less than 3 sepsis-related clinical signs* CRP>1 mg/dl At least 2 other altered serum parameters in addition to CRP Blood culture: negative
Group 3 Possible sepsis	Less than 3 sepsis-related clinical signs* CRP <1 mg/dl Less than 2 other altered serum parameters Blood culture: negative
Group 4 No sepsis	No sepsis-related clinical signs* CRP <1 mg/dl No altered serum parameters Blood culture: negative

*Sepsis-related clinical signs: Temperature instability, apnea, need for supplemented oxygen, need for ventilation, tachycardia/bradycardia, hypotension, feeding intolerance, abdominal distension, necrotizing enterocolitis.

**Serum parameters other than CRP: white blood cell count, absolute neutrophil count, platelet count.

leukocytosis is defined as leucocyte count >25,000/mm^3 at birth, >30,000/mm^3 at 12-24 hours and >21,000/mm^3 after the second day. Thrombocytopenia is accepted as platelet count <150,000/mm^3. Normal absolute neutrophil count is accepted as 7,800-14,500/mm^3 in the first 60 hours and 1,750-5,400/mm^3 after 60 hours.

Before starting the antimicrobial therapy, blood samples (sample 1) for whole blood count, CRP, PCT and culture were obtained. This procedure was repeated at 24-48 hours (sample 2) and at 7-10 days (sample 3) as is the standard practice in our unit for babies with suspected sepsis. Cerebrospinal fluid (CSF), urine, and tracheal and gastric material cultures were sent if obtained. The first samples were also obtained from the control group.

Whole blood count and cultures were studied immediately. Samples were stored at –20°C for determination of PCT and CRP. After centrifugation at 5,000 pm for 15 mins, serum samples were obtained for the prevention of hemolysis. Whole blood count was performed in an automatic counter, Cell Dyn 3700 (Abbott Diagnostics Division, USA). CRP was determined using an immunonephelometric method using BN II device (Dade Behring Marburg GMBH, Marburg, Germany). Using quantitative techniques, detection limit was 0.5 mg/dl. PCT was measured by monoclonal immunoluminometric assay (Lumitest PCT, Brahm Diagnostica GMBH, Berlin, Germany). This assay is specific for PCT molecule. In this assay, two different antibodies, one directed against calcitonin and the other directed to katacalcin were used. Levels greater than 0.5 ng/ml were accepted as pathological. Levels lower than 0.5 ng/ml for PCT and 0.5 mg/dl for CRP were accepted as zero for statistical analysis. Blood and CSF cultures were analyzed using fully automatic BACTEC method by BACTEC 9240 device (Becton Dickinson, Germany).

Infants presenting with suspected infection received antibiotic therapy. Infants born in our university and then admitted to our unit were treated with ampicillin and gentamicin. If there was no clinical or laboratory response to this therapy, it was changed to cefotaxime and amikacin. Infants born in another hospital or at home were given cefotaxime and amikacin as initial therapy. Neonates who had positive cultures were treated with antibiotics according to the culture antibiogram. The antimicrobial therapy was stopped after clinical and laboratory improvement.

The study protocol was approved by the Ethics Committee of Uludağ University Faculty of Medicine. Informed parental consent was obtained for all infants.

The statistical analysis was done with SPSS version 10 for Windows. Correlations between the variables and the statistical differences were analyzed using Pearson's chi-squared test, Kruskall-Wallis test and Wilcoxon sign rank test. Receiver operating characteristics (ROC) analysis was performed by NCSS statistical program. Values of $p<0.05$ were considered to be significant.

Results

Seventy-nine neonates were eligible for the study, but 12 were excluded (7 died, 3 due to exchange transfusion because of neonatal hyperbilirubinemia, and 2 due to parental refusal). Sixty-seven infants were included in the final statistical analysis. Table II shows the characteristics of the study group. Infants were classified into four groups according to the study protocol as: those with highly probable sepsis (group 1), probable sepsis (group 2), possible sepsis (group 3), and no sepsis (group 4; controls).

Serum PCT and CRP levels were evaluated separately in the groups. There were significant differences between group 1 and groups 3 and 4, and group 2 and groups 3 and 4 in initial CRP levels ($p<0.05$). However, there was no correlation between groups 1 and 2 and groups 3 and 4 ($p>0.05$). No significant difference was detected between the second and third CRP levels in the first three groups ($p>0.05$) (Table III).

The changes in the CRP levels in response to the antibiotic therapy in each group were also compared (Table IV). In group 1, there was no significant difference between the second and third CRP levels ($p>0.05$). However, a significant difference was detected between the first and third CRP levels ($p<0.05$). Also, there was no significant difference between the first and second CRP levels in group 2, but a significant difference was detected between the first and third, and second and third CRP

Table II. Characteristics of the Patients in the Study

	Group 1 (n=15)	Group 2 (n=14)	Group 3 (n=20)	Group 4 (n=18)	p
Gender (Male/Female)	10/5	6/8	8/12	10/8	NS**
Gestational age (weeks) Mean±SD*	33.6±4.8	32.4±3.9	32.7±2.9	34.8±3.3	NS
Birth weight (g) Mean±SD	1923±841	1822±1036	1763±800	2205±827	NS
Age (hours) Mean±SD	36±69	34±59	35±54	34±55	NS
2nd sample obtainment time (hours) Mean±SD	36±8	35±6	38±8		NS
3rd sample obtainment time (hours) Mean±SD	181±47	187±29	179±19		NS

*Mean±SD: Mean±standard deviation. **NS: Not significant (p>0.05).

Table III. Comparison of CRP (mg/dl) Levels Between Groups

	Group 1 (n=15)	Group 2 (n=14)	Group 3 (n=20)	Group 4 (n=18)	p
1st CRP Mean±SD	1.3±1.8	1.1±1.4	0.2±0.4	0.1±0.4	NS[a,f] 0.002[b,c] 0.008[d] 0.07[e]
2nd CRP Mean±SD	0.9±1.9	0.6±0.6	0.8±1.8		NS[g]
3rd CRP Mean±SD	0.3±0.7	0.1±0.2	0±0		NS[h]

Mean±SD: Mean±standard deviation. Significant (p<0.05; b,c,d,e). NS: Not significant (p>0.05; a,f,g,h).

a: Comparison of the first CRP levels between group 1 and group 2. d: Comparison of the first CRP levels between group 2 and group 3.

b: Comparison of the first CRP levels between group 1 and group 3. e: Comparison of the first CRP levels between group 2 and group 4.

c: Comparison of the first CRP levels between group 1 and group 4. f: Comparison of the first CRP levels between group 3 and group 4.

g: Comparison of the second CRP levels of groups 1, 2 and 3. h: Comparison of the third CRP levels of groups 1, 2 and 3.

Table IV. Comparison of CRP (mg/dl) Levels in the Groups

	Group 1 (n=15)	Group 2 (n=14)	Group 3 (n=20)	Group 4 (n=18)
1st CRP Mean±SD	1.3±1.8	1.1±1.4	0.2±0.4	0.1±0.4
2nd CRP Mean±SD	0.9±1.9	0.6±0.6	0.8±1.8	
3rd CRP Mean±SD	0.3±0.7	0.1±0.2	0±0	
p	NS[x,z] 0.017[y]	NS[x],0.012[y] 0.008[z]	NS[x,y] 0.028[z]	

Mean±SD: Mean±standard deviation. Significant (p<0.05). NS: Not significant (p>0.05).
x: Comparison of the 1st and 2nd levels in the group. y: Comparison of the 1st and 3rd levels in the group. z: Comparison of the 2nd and 3rd levels in the group.

levels (p>0.05 and p<0.05, respectively). In group 3, there was no significant difference between the first and second and first and third CRP levels, but a significant difference was detected between the second and third CRP levels (p>0.05 and p<0.05, respectively).

When the initial PCT levels were compared between the groups, there was no significant difference between groups 3 and 4, but there were significant differences between the other groups (p>0.05 and p<0.05, respectively). Regarding the second PCT levels in the first three groups, there were significant differences between groups 1 and 2, and groups 1 and 3, but no significant difference was detected between the second and third groups (p<0.05 and p>0.05, respectively). There were no significant differences for the third PCT levels among the first three groups (p>0.05) (Table V).

When the groups were compared for the PCT progression (Table VI), there were significant differences in group 1 between the first

Table V. Comparison of PCT (ng/ml) Levels Between Groups

	Group 1 (n=15)	Group 2 (n=14)	Group 3 (n=20)	Group 4 (n=18)	p
1st PCT Mean±SD	9.3±9.9	1.8±1.7	0.6±0.8	0.4±0.3	0.006[a] 0.000[b,c,] 0.041[d], 0.013[e], NS[l]
2nd PCT Mean±SD	1.7±1.6	0.5±0.6	0.4±0.4		0.046[g,] 0.018[h], NS[i]
3rd PCT Mean±SD	0.8±1.6	0.2±0.2	0.2±0.2		NS[k]

Mean±SD: Mean±standard deviation. Significant (p<0.05: a,b,c,d,e,g,h). NS: Not significant (p>0.05: f,i,k).

a: Comparison of the first PCT levels between group 1 and group 2. d: Comparison of the first PCT levels between group 2 and group 3.

b: Comparison of the first PCT levels between group 1 and group 3. e: Comparison of the first PCT levels between group 2 and group 4.

c: Comparison of the first PCT levels between group 1 and group 4. f: Comparison of the first PCT levels between group 3 and group 4.

g: Comparison of the second PCT levels between group 1 and group 2. h: Comparison of the second PCT levels between group 1 and group 3. i: Comparison of the second PCT levels between group 2 and group 3. k: Comparison of the third PCT levels of groups 1, 2 and 3.

Table VI. Comparison of PCT (ng/ml) Levels Between Groups

	Group 1 (n=15)	Group 2 (n=14)	Group 3 (n=20)	Group 4 (n=18)
1st CRP Mean±SD	9.3±9.9	1.8±1.7	0.6±0.8	0.4±0.3
2nd PCT Mean±SD	1.7±1.6	0.5±0.6	0.4±0.4	
3rd PCT Mean±SD	0.8±1.6	0.2±0.2	0.2±0.2	
p	001[x], 0.010[y] NS[z]	0.001[x,y] 0.045[z]	NS[x,] 0.002[y] 0.019[z]	

Mean±SD: Mean±standard deviation. Significant (p<0.05). NS: Not significant (p>0.05).
x: Comparison of the 1st and 2nd levels in the group.
y: Comparison of the 1st and 3rd levels in the group.
z: Comparison of the 2nd and 3rd levels in the group.

and second and between the first and third PCT levels, but no significant difference was detected between the second and third PCT levels (p<0.05 and p>0.05, respectively). The differences between the three PCT le vels were found significant in group 2 (p<0.05). In group 3, no significant difference was found between the first and second PCT levels, but there were significant differences between the first and third and between the second and third PCT levels (p>0.05 and p<0.05, respectively).

Blood cultures were positive in four patients and tracheal aspiration culture was positive in one patient in group 1. Gastric material cultures were positive in two and tracheal aspiration culture was positive in one patient in group 2.

Procalcitonin and CRP levels of the patients who had positive cultures were compared with the others in groups 1 and 2. No significant difference was found between the PCT and CRP values of the culture-positive and -negative groups (p>0.05).

Receiver operating characteristics (ROC) analysis was made according to the mean PCT and CRP values in the groups, and the best results were determined for CRP and PCT for a cut-off value of 1 mg/dl and 2 ng/ml, respectively (Table VII). From these data, values of area under the curve $(AUC)_{PCT}$ were higher than AUC_{CRP} values on the ROC curve (Fig. 1).

Discussion

New and efficacious laboratory tests are needed in the diagnosis of neonatal sepsis. Acute phase reactants have been used frequently as an early marker of bacterial sepsis. Previous studies have shown CRP to be a useful marker of bacterial sepsis in the neonate[15-17]. There is

Table VII. ROC Analysis of the Mean PCT and CRP Levels

	Cut-off value	Sensitivity	Specificity	PPV	NPV	AUC
CRP	1	48%	87%	74%	69%	0.64
	2	17%	92%	63%	59%	0.66
PCT	1	59%	89%	74%	69%	0.71
	2	48%	100%	100%	72%	0.77

PPV: Positive predictive value. AUC: Area under the receiver operating characteristics (ROC) curve. NPD: Negative predictive value.

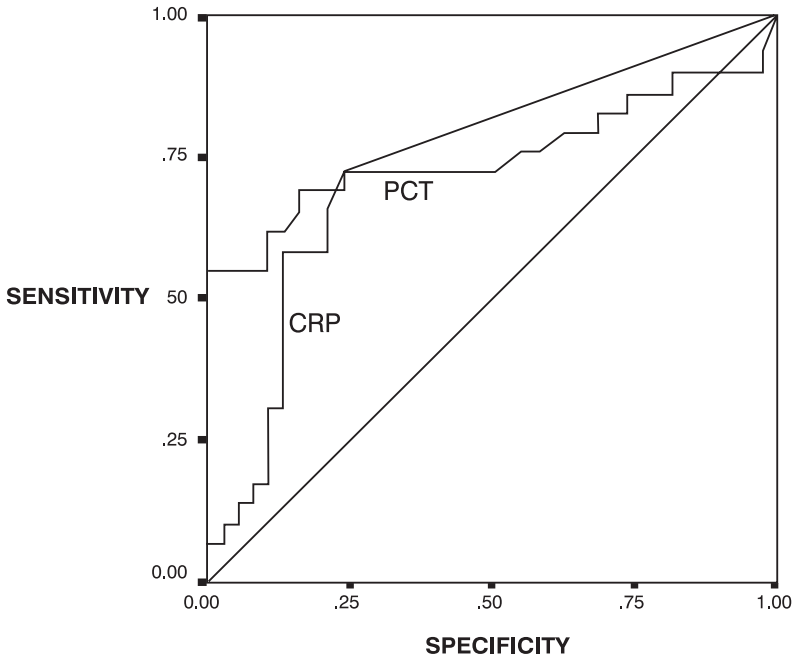

Fig. 1. The graphics of ROC according to mean CRP and PCT levels.

no single reliable test for the early confirmation of definite neonatal sepsis. Therefore, there is a continuing search for a new infection marker, including investigation of PCT and the other cytokines[2,18].

The previous studies had shown high PCT levels in all neonates with proven or clinically diagnosed early- or late-onset neonatal sepsis[2,11,18-20]. Monneret et al.[11] compared the CRP and PCT levels between the two groups of infants at two different periods (in the first 3 days of life and at 4-28 days). In patient groups, the infants had proven or clinically diagnosed sepsis. The control group involved the infants between 32 and 36 gestational weeks who had no suspicion of sepsis. They found slight PCT increase in the control group in the first three days of life but it was normal at 4-28 days. However, they found high PCT and CRP levels at both times in the sepsis group. The increase in PCT concentration was higher than that of CRP. Also, the decrease in PCT levels with the antibiotic therapy occurred faster, earlier, and to a more significant extent than in CRP. Chiesa et al.[18] compared 23 infants who had nosocomial infection (mean 14.7+-9.1 days) with 92 infants as controls. They found that PCT levels were slightly elevated, although within the normal range, in the control group. They also reported that PCT levels decreased with antibiotic therapy in the infected infants. In our study, we found that the infants with suspected or proven sepsis had higher PCT levels than the infants who were normal or had little infection suspicion.

When we analyzed the initial CRP levels, there was no difference between groups 1 and 2. Infants in group 1 had high suspicion

of sepsis. In group 2, sepsis was not proven, but probability of sepsis was high with clinical and laboratory findings. Initial CRP levels were insufficient to distinguish the degree of bacterial invasion, whereas PCT levels provided more useful information. Our results are similar to the data in the literature[23,24]. Gendrel et al.[21] concluded that CRP is released later than PCT in the early stages of sepsis.

It was reported in the previous studies that serum PCT levels correlated with the severity of microbial invasion and decreased rapidly after appropriate antibiotic therapy[2,11,21]. Monneret et al.[11] reported that both CRP and PCT levels increased in the infants with early-onset neonatal sepsis, but the rise in PCT levels was higher than in CRP. They also showed that both CRP and PCT decreased with the treatment of sepsis. However, they did not compare the rate of decline in PCT and CRP. They found no significant difference between CRP and PCT levels in late- onset neonatal sepsis, but PCT was found to peak and return to normal earlier than CRP. They concluded that PCT returned to normal with appropriate therapy earlier than CRP because of PCT's short half-life. We evaluated the responses of PCT and CRP to the antibiotic treatment, and found a significant decrease in PCT levels in groups 1 and 2 at 48 hours as an early response, but the decrease in CRP levels were found to be nonsignificant. However, both CRP and PCT levels decreased as a late response at 5-10 days and PCT levels decreased more than CRP. The early response to appropriate antibiotic therapy can be evaluated by PCT in the septic neonates, but not by CRP. On the other hand, the late response to treatment can be evaluated by both CRP and PCT. These findings correlate with the previous studies mentioned above.

Different results have been reported comparing the sensitivity and specificity of PCT and CRP[12,21]. Lapillonne et al.[19] studied the efficacy of PCT in neonatal sepsis in 19 septic infants with 131 non-infected infants (66 had respiratory distress syndrome (RDS), 12 had hemodynamic insufficiency and 53 were healthy) in the first 10 days of life (mean 2.3±2.4 days). They found that the sensitivity and specificity of PCT was 84% and 50%, respectively, using a cut-off value of 5 ng/ml. They concluded that the specificity was low because infants with RDS and hemodynamic insufficiency had higher PCT levels than the healthy infants. We also compared the sensitivity and specificity of CRP and PCT and made ROC analysis. We found the specificity, positive predictive value (PPV), sensitivity and negative predictive value (NPV) of PCT as 100%, 100%, 48% and 72%, respectively, using a cut-off value of 2 ng/ml. This means that none of the infants had diagnosis of infection if they did not have sepsis (100% specificity) and also that all of the infants who had positive tests were really infected (100% PPV). We found that the sensitivity, specificity, PPV and NPV of CRP using a cut-off value of 1 mg/dl were lower than those of PCT using a cut-off value of 2 ng/ml.

Chiesa et al.[2] studied the reliability of PCT concentrations in 28 infants who had severe early-onset of neonatal sepsis. They found sensitivity, specificity, PPV and NPV as 92.6%, 97.5%, 94.3% and 96.8%, respectively. They also found that 24 infants (85.7%) had PCT levels higher than normal at the time of diagnosis. However, at that time, only 13 of them (46%) had high CRP levels. These results are consistent with our findings. We found high PCT levels in 12 infants (80%) in group 1, which included the infants with high sepsis suspicion.

In a recent study, Corona et al.[25] studied 35 newborns and classified them into three groups according to their Sepsis Score. They found that CRP did not differ between the groups at 24 hours and became significant in the probable sepsis group at 48 hours of life. But PCT was significantly different between the groups, and the highest peak was observed in the first 24 hours and was confirmed at 48 and 120 hours of life. Our results support their conclusion that PCT concentrations might be used as a new marker for early and accurate diagnosis of neonatal sepsis.

In another study including 37 infants of less than 1500 g and 31 weeks gestational age, Janota et al.[23] found the sensitivity and specificity of PCT in the diagnosis of early-onset neonatal sepsis as 75% and 85%, respectively, using a cut-off value of 2 ng/ml. In the same study, they reported the sensitivity and specificity of CRP as 25% and 90%, respectively. They concluded that lower specificity of PCT can be

related to the multi-organ dysfunction of the infants who did not have sepsis. Similarly, we found that the sensitivity was lower than the specificity in our study.

Bonac et al.[24] compared the levels of CRP, PCT and IL-8 in the diagnosis of early-onset neonatal sepsis in 58 infants. They found that the sensitivity, specificity, PPV and NPV of PCT was 59%, 82%, 36% and 96%, respectively, using a cut-off value of 0.99 μg/L. They also reported that the sensitivity, specificity, PPV and NPV of CRP at the time of diagnosis was 36%, 92%, 43% and 89%, respectively, using a cut-off value of 14 mg/L. In ROC analysis, AUC_{PCT} (0.616) was found to be slightly higher than AUC_{CRP} (0.602) in their study. They did not state whether or not the difference was significant. Yıldız et al.[26] studied 97 term neonates admitted to hospital with the diagnosis of suspected sepsis. They found the specificity, sensitivity, PPV and NPV of PCT as 94.3%, 92.1%, 94% and 92%, respectively, and of CRP as 86.2%, 87.0%, 85.5% and 87.7%, respectively. They concluded that it would be useful to use PCT as an indicator in the early diagnosis of neonatal sepsis. In our study, we found that the sensitivity (48%) and NPV (72%) of PCT were lower than in Yildiz's study, although its specificity and PPV were both 100% using a cut-off value of 2 ng/ml. We found that AUC_{PCT} (0.77) was higher than AUC_{CRP} (0.64) although we used mean PCT and CRP levels in ROC analyses.

In contrast, Aygün et al.[27] compared PCT levels of 51 babies with suspected sepsis, respiratory distress syndrome, and meconium-stained amniotic fluid and 21 control babies (15 term, 6 preterm). They found that high PCT levels were present in all of the groups in the first days of life so they concluded that PCT was not a useful marker in the diagnosis of neonatal sepsis. Our results were not concordant with theirs. Their study and control groups were smaller and this may explain the different results.

In conclusion, our data confirm the data of other studies indicating that PCT is a more reliable marker of inflammation than CRP in the early diagnosis of neonatal sepsis, in determining the degree of microbial invasion and the severity of sepsis, and in evaluating the response to antibiotic therapy. The benefit of using PCT routinely in the diagnosis and follow-up of neonatal sepsis would be to decrease the use of unnecessary antibiotics and allow earlier discharge, with the related cost savings. However, we conclude that clinical evaluation must be the most reliable method in diagnosis, although all of the markers including PCT help us as supportive clues.

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