

Original Article

C-reactive protein in Neonates with Suspected Septicemia.

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Abstract

Objective: To evaluate the duration of antibiotic therapy in neonates with suspected septicemia.

Methods: The study was conducted prospectively on fifty consecutive neonates with suspected septicemia in the Department of Pediatrics, Prince Zeid Hospital, Tafila, Jordan, from January 2006 to June 2006. CRP was measured at various points.

Results: In 44% of cases therapy was stopped on 3rd day, as CRP was normal. In 8% antibiotics could be stopped within 5-7 days as CRP values returned to normal and in 48% therapy was extended beyond 7th day, as CRP values were high or rising persistently. Negative predictive value of serial CRP was 100% in deciding duration of antibiotic therapy in suspected neonatal septicemia up to 7 days.

Conclusion: The correlation between positive CRP, raised micro ESR and positive blood culture was significant ($p < 0.005$). (Rawal Med J 2007;32:25-27)

Keywords: C-reactive protein, Newborn, Sepsis.

INTRODUCTION

Sepsis is a significant cause of morbidity and mortality in neonates.¹ Neonatal sepsis (NS) may have subtle, diverse and nonspecific symptoms and signs; moreover, a delay in the diagnosis and commencement of treatment results in a high morbidity and mortality.² Its clinical manifestations vary from being specific to subtle, testing the very skills of a pediatrician. C-reactive protein (CRP), an acute phase reactant, is synthesized in the liver in response to inflammatory cytokines and may rise more than 1000 times during an acute phase response. It falls quickly after efficient elimination of microbial stimulus, due to its short half-life of 19 hours (3). In recent years, haematological and biochemical markers such as immature total neutrophil ratio⁴⁻⁶ platelet count⁶ CRP^{5,7} and various cytokines⁷⁻⁹ have all been suggested as being useful indicators for early identification of septic infants. CRP may be used as a parameter to identify the time period when antibiotics therapy can safely be discontinued in case of suspected neonatal septicemia, which was the aim of the present study.

SUBJECTS AND METHODS

The study was conducted in the Department of Pediatrics, Prince Zeid Hospital; Tafila, Jordan from January 2006 to June 2006. It was approved by the IRB of the hospital and informed consent was taken from parents or guardian. Fifty consecutive neonates up to 4 weeks of age with birth weight more than 1500 g and suspected septicemia were studied prospectively. Septicemia was suspected with "sepsis score" which included clinical features such as refusal for feed, abdominal distention, vomiting, lethargy, jaundice, poor cry, seizures, diarrhea, apnea, tachypnea, poor capillary refill, hypo-thermia, fever or umbilical discharge.¹⁰ If baby had three or more than three of above septicemia was suspected. Neonates who had undergone

surgery and those with diagnosis of meningitis were excluded from the study because they require longer duration of treatment regimen.

Serum CRP, micro ESR, blood culture and sensitivity were done in all the cases along with other investigations such as hemogram, X-ray chest, swabs for culture and sensitivity as and when required. CRP was measured by latex agglutination method (SPAN Diagnostics Ltd.). A value of more than 6 mg% was taken as abnormal. CRP was measured again 48 hours after initiation of therapy. If it was less than 6 mg%, antibiotics were stopped and patients were assigned to Group 1. Neonates with CRP more than 6 mg% were assigned to Group 2. Group 2 was further subdivided into 2a and 2b depending upon whether CRP was done every other alternative day (2a) or only on the 7th day after commencing of antibiotic therapy (2b). Antibiotics were stopped when CRP levels returned to normal. After stopping the treatment babies were observed for 48 hours in the hospital and followed upto 4 weeks for any relapse. A p value of <0.05 was considered significant.

RESULTS

Out of fifty neonates, 11 weighed between 1500-2000 g, 8 between 2001-2499 g and 31 were >2500 g. Fifty eight percent (n = 29) of the total neonates were male; 20% (n = 10) were preterm. Twenty six percent (n = 13) presented within 72 hours of life (early onset septicemia) and 74% (n = 37) after 72 hours (late onset septicemia). Refusal for feeds, lethargy, and jaundice were the main presenting features of NS followed by poor cry, pyoderma and hypothermia (table 1). Incidence of blood culture positivity was 42%, out of which 47.62% were gram positive and 52.48% gram negative. Amongst gram negative, Klebsiella was the commonest organism (23.8%) followed by E. coli (19.04%) and Acinetobacter (9.52%). Amongst gram positive,

coagulase positive Staphylococci accounted for 28.27% cases. CRP was positive in 50% and raised micro ESR in 48% cases.

Table 1. Clinical features of Neonatal Septicemia (N = 50).

Feature	N.	%
Refusal for feed	33	66
Lethargy	21	42
Poor cry	10	20
Diarrhea	3	6
Vomitting	3	6
Fever	3	6
Excessive crying	1	2
Jaundice	15	30
Pyoderma	8	16
Hypothermia	7	14
Cyanosis	6	12
Abdominal distention	5	10
Seizures	4	8
Conjunctivitis	4	8
Vomiting	3	6
Fever	3	6
Apnea	2	4
Tachypnea	2	4
Excessive crying	1	2
Poor capillary refill	1	2

Out of 50 cases of suspected neonatal septicemia CRP was negative after 48 hours in 44% (n=22) cases and antibiotics were stopped, no relapse was observed within 4 weeks (Group 1). In remaining 56% (n=28) cases where CRP was raised after 48 hours antibiotics were stopped on the 5th day in 2% (n=1) and continued for more than 7 days in 26% (n =13) cases as CRP was raised even on the 7th day (Group 2a). In Group 2b antibiotics were stopped in 6% (n=3) on 7th day and in 22% (n=11) continued for more than 7 days. CRP was not done beyond 7 days in any group (table 2). There was no relapse in any group within 4 weeks of discontinuation of antibiotics

(negative predictive value of 100%). The anti-biotics were required for more than 7 days in all neonates with raised CRP and positive blood culture.

DISCUSSION

Assay of CRP has been shown to be useful in the diagnosis and management of neonatal sepsis, with a higher likelihood ratio for the prediction of sepsis than many other tests.¹¹ It has been frequently used in the investigation and monitoring of neonatal sepsis.¹² The incidence of blood culture positivity was 42% in the present study, which is similar to other studies.¹³ Positive CRP and raised micro-ESR in our study was similar to that reported by Bhartia.¹³ Similarly, CRP was positive in all culture positive cases. The comparison of both CRP and micro-ESR with positive blood cultures was statistically significant ($p < 0.05$). There was no relapse in any of the cases in which antibiotics were stopped following normalization of CRP giving a negative predictive value of 100%.

Table 2. Level of CRP, Treatment, Relapse Rate in Various Groups and Correlation with Blood Culture

CRP Value	Groups (n)	Duration of treatment (n)	Blood culture positive (n)
<6 mg%	Group 1 (22)	<3days(22)	Nil
		5 days(1)	Nil
	Group 2a (14)	>7 days(13)	11
>6mg%	Group2(28)	7 days(3)	Nil
		Group 2b (14)	>7 days(11)

Twenty-one out of 24 (87.5%) cases that required longer duration of antibiotic therapy (>7 days) had positive blood culture suggesting that, those with positive blood culture and raised CRP needed longer duration of antibiotics therapy. No study comparing the blood culture positivity and raised CRP with duration of treatment is available. Further studies are required to determine the duration of antibiotics therapy in neonatal septicemia with raised CRP levels even after 7 days of therapy. In Conclusion, negative predictive value of serial serum CRP was 100% in our study in deciding duration of antibiotics therapy in neonatal septicemia up to 7 days. Newborn with suspected septicemia having raised CRP levels and positive blood culture need longer duration of antibiotics therapy (more than 7 days).

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