IJAM

RESEARCH PAPER

RELIABILITY OF SERUM PROCALCITONIN LEVEL FOR THE DIAGNOSIS OF LATE ONSET SEPSIS IN NEONATES

Dr. Javeri Aarti Harish Post Graduate, Department of Paediatrics, Sree Balaji Medical College and Hospital

Dr. Krithika AP Assistant Professor, Department of Paediatrics, Sree Balaji Medical College and Hospital

ABSTRACT

INTRODUCTION: Sepsis is one of the most common causes of neonatal sepsis, especially in developing countries. There are several investigations available that may be used as indicators to identify sepsis, however, the inability of a single laboratory investigation for rapid detection and diagnosis of sepsis, calls for the need of a specific investigation. It has been recently reported that procalcitonin can be used as a reliable predictor for diagnosis and to determine severity as well as outcome of neonatal sepsis.

Objective: To evaluate the reliability of serum concentrations of procalcitonin for the diagnosis of late-onset sepsis in a neonatal intensive care unit (NICU).

Methods and Materials: A cross-sectional study was conducted between the June 2018 to November 2018 at Sree Balaji Medical College and Hospital. Serum procalcitonin levels were determined for 25 neonates of age between 3-30 days.

Results: Distinct elevations of procalcitonin lvels in neonates with late-onset infection due to coagulase-negative staphylococci. Currently nosocomial infection due to coagulase-negative staphylococci is a frequent occurrence in NICUs.

Conclusion: Serum procalcitonin is an effective marker for diagnosis of Late Onset of Sepsis.

KEY WORDS : Late Onset Sepsis, Serum Procalcitonin, serum concentrations,

INTRODUCTION:

Incidence of sepsis in neonatal intensive care units (NICUs) is often high [1]. Early detection of neonatal sepsis is often difficult owing to nonspecific and minimal signs, which may be observed in various other non infectious conditions and definitive blood sample results, including blood culture may not be available immediately and easily. Furthermore, culture negative sepsis is now emerging, especially in cases of maternal antibiotic usage [2]. Hence, the availability of a single laboratory investigation is necessary for early detection as well as to predict the outcome of neonatal sepsis, also to minimize unnecessary treatment of non infected NICU cases [3].

As per recent reports, procalcitonin, a propeptide of calcitonin, undergoes posttranslational proteolysis into its hormonal derivative and increases significantly in sepsis [4-10]. However, the cellular source and mechanisms underlying the increase in sepsis and infective conditions is not yet identified. Two studies have demonstrated that procalcitonin is of significant importance in neonatal sepsis. In a study by Gendrel et al. [11] it was illustrated that serum procalcitinin levels were elevated in neonates with sepsis, compared to those who were noninfected and asymptomatic. In an investigation by Monneret et al. [12] it was demonstrated that procalcitonin levels were performed in both NICU babies and those admitted in regular nurseries, done after 72 hours. It was observed that procalcitonin levels were significantly raised.

METHODS AND MATERIALS:

A Cross-sectional study was conducted over a period of six months from June 2018 to November 2018 at Sree Balaji Medical College and Hospital. 25 babies admitted in the NICU during the study period were taken as the study subjects. Babies between 3 days and 30 days of age who presented with systemic infectious conditions during their NICU stay had blood drawn for serum procalcitonin levels at the onset of signs of infection and after complete recovery. Neonates who had had a documented episode of systemic infection within the previous 7 days were excluded. Venous blood samples were obtained using a sterile technique, following the universal precautions, after obtaining consent and centrifuged for 30 minutes after collection of sample. Serum procalcitonin levels were determined using the immunoluminometric assay.

The objective was to determine reliability of serum procalcitonin for diagnosis of late onset neonatal sepsis. All statistical tests were based on a significance level of <0.05

RESULTS:

During the study period, 25 cases with late-onset infection (mean post natal age being 15.72 days), were available for determining the sensitivities and specific concentrations across the range of 3 – 30 days of age.

Twenty two of the 25 cases were proved positive for sepsis by blood culture, three cases had necrotizing enterocolitis, but were culture negative. All cases positive for coagulase negative staphylococci, had clinical signs of sepsis, and also demonstrated positive sepsis screens. Four of the 12 neonates with late-onset sepsis due to coagulase-negative staphylococci had more than one blood culture positive for the same species.

All the twenty five cases had elevated levels of procalcitonin levels (mean level being 39.524, P value being approximately 0.0001). The procalcitonin ranged from 2.0 ng/ml to 249.1 ng/ml. Two of the 25 cases died, and 23 survived. There was no decline in procalcitonin levels in the babies who did not survive, until death. Whereas in those who survived, procalcitonin levels were within the normal range (approximate level being 1 ng/ml) in 3-7 days after administration of the appropriate antimicrobial therapy.

When CRP levels considered, seven out of twenty five cases were missed. In these seven cases, sepsis was caused by coagulase negative staphylococci.

DISCUSSION:

In the present study, the procalcitonin concentration after the first 48 hours of life proved to be an ideal marker for identifying late onset sepsis in its early course. After excluding the subpopulation of nonsurvivors, whose elevated procalcitonin levels were also correlated with outcome, distinct elevations of procalcitonin in infants with late-onset infection due to coagulase-negative staphylococci, and we suspected that these levels, which were distinctly lower than those found in cases with other systemic

Article History	Received	Accepted	Published
	15/01/2018	02/04/2018	20/05/2018

***Corresponding Author** Dr. Javeri Aarti Harish

Post Graduate, Department of Paediatrics, Sree Balaji Medical College and Hospital aarti.javeri.aj@gmail.com

infectious conditions, which might reflect a systemic response to the typically indolent course of infection with these organisms [13]. Nosocomial sepsis due to coagulase-negative staphylococci is currently an important and frequent event in NICUs [14]. Although this study included small numbers of patients and more stringent data are needed, the results prove the importance of serum procalcitonin lvels. DaSilva et al. [15] studied the diagnostic value of leukocyte indices in late neonatal sepsis and found that these indices, interpreted either independently or in combination, were of low diagnostic accuracy for evaluating neonates with suspected late sepsis caused by coagulase-negative staphylococci. Schmidt et al. [16] studied the pathogenicity of coagulase-negative staphylococci in newborns and found that CRP levels were abnormal at the time of initial evaluation in 64% of subjects (mean postnatal age, 25 days) with sepsis due to these pathogens. This finding is in keeping with our finding that when CRP levels are used alone for diagnosis, a significant proportion of patients with nosocomial systemic disease caused by coagulase-negative staphylococci will be missed in the early phase.

Clinical and laboratory findings for newborns with late-onset infection.

Case no.		Blood isolate	Times of sampling (postnatal d)	PCT level (ng/mL)	CRP level (mg/dL)	Outcome
1	Sepsis	*Staphylococcus aureus*	3	12.4	1.8	Survived
2	Sepsis	*Staphylococcus epidermidis*	4	4.3	1.6	Survived
3	Sepsis	*Klebsiella pneumoniae*	6	249.1	5.9	Survived
4	NEC (IIIa)*	. . .	6	50.5	4.5	Died
5	Sepsis	*Staphylococcus haemolyticus*	7	8.8	0.2	Survived
6	Sepsis	*S. epidermidis*	7	2.0	1.4	Survived
7	NEC (IIa)*	. . .	7	8.1	2.8	Survived
8	Sepsis	*K. pneumoniae*	7	59.7	1.9	Survived
9	Sepsis	*S. aureus*	8	57.3	5.0	Survived
10	Sepsis	*S. epidermidis*	9	5.0	0.4	Survived
11	Sepsis	*S. epidermidis*	10	2.0	0.1	Survived
12	Sepsis	*S. epidermidis*	12	2.7	1.6	Survived
13	Sepsis	*S. haemolyticus*	14	235.7	3.2	Died
14	Sepsis	*S. epidermidis*	15	3.3	0.1	Survived
15	Sepsis	*Candida albicans*	17	15.6	3.9	Survived
16	Sepsis	*S. aureus*	19	62.9	8.6	Survived
17	Sepsis	*S. epidermidis*	20	6.7	0.3	Survived
18	Sepsis	*S. epidermidis*	21	2.4	0.3	Survived
19	Sepsis and meningitis	*Pseudomonas aeruginosa*†	25	101.4	4.2	Survived
20	Sepsis	*K. pneumoniae*	27	39.7	10.4	Survived
21	Sepsis	*S. epidermidis*	29	2.2	7.8	Survived
22	NEC (IIb)*	. . .	30	22.8	20.9	Survived
23	Sepsis	*S. epidermidis*	30	9.4	0.5	Survived
24	Sepsis	*S. aureus*	30	10.3	6.8	Survived
25	Sepsis	*K. Pneumoniae*	30	13.8	0.6	Survived

CONCLUSION:

It can be concluded that procalcitonin appears to be an effective laboratory marker for accurately identifying late onset sepsis in the NICU setting. The amount of blood required to perform the investigation is small, and the results are available in a couple of hours.

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