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Original Research Paper

Paediatrics

PROCALCITONIN AS A MARKER OF NEONATAL SEPSIS

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ABSTRACT

Objective :- Early diagnosis of neonatal sepsis and appropriate treatment decreases the mortality and morbidity of these infants. The aim of this study was the assess the role of Procalcitonin (PCT) as a marker in the early diagnosis, treatment and follow-up of neonatal sepsis. **Methods :-** 80 neonates with clinical [n=15], suspected [n=38] and proven sepsis [n=27] were evaluated. The PCT levels were measured by immunoluminoassay before and on day 5 of treatment. PCT levels of 0.5-2 ng/ml, 2-10ng/ml and >10ng/ml were considered as weakly positive, positive and strongly positive, respectively. The sepsis screen tests and cultures of blood or other sterile body fluids in these three groups of infants were recorded. **Findings:** The levels of PCT in proven sepsis group were higher than that in other groups. Strongly positive. PCT level was seen in 2 of 15 cases of clinical sepsis, 6 of 38 suspected and in 25 of 27 cases with proven sepsis. PCT levels were dramatically decreased in three groups on day 5 of treatment. **Conclusion:** The results show that the serum Procalcitonin levels seen to be significantly increased in proven sepsis and decreases dramatically in all types of sepsis after appropriate treatment.

KEYWORDS : Neonatal sepsis; Procalcitonin; infection. CRP.

Introduction

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the First Month of Life. The overall incidence of Primary Sepsis is 1-5/1000 Live birth. The Incidence is much higher for very low birth weight infant (birth weight <1500gm)[1]. Since the clinical signs and symptoms of sepsis in neonates are non-specific and associated with high [28-50%] morbidity and mortality, early suspicion and treatment before blood culture confirmation of it is crucial[2]. An inflammatory marker such as C-reaction protein (CRP) does not reliably differential between the systemic inflammatory response and sepsis[2,3]. Procalcitonin (PCT), an precursor of calcitonin is a 116 amino acid protein secreted by the C cells of thyroid gland in normal situation but its levels man increase during septicemia, meningitis pneumonia and urinary tract infection[3,4]. This marker also is produced by macrophage, and monocyte cells of various organs in severe bacterial infection and sepsis[5,6]. The results of recent studies suggest the usefulness of PCT for early diagnosis of neonatal sepsis[7-19], although other investigation have observed lack of accuracy for this marker[20,21,22].

Since a kit for quantization of PCT is available for rapid quantitative measurement, we carried out this study was evaluate the serum level of PCT on neonatal sepsis in relation to our classification of neonatal sepsis.

SUBJECTS AND METHODS

This prospective study was conducted on neonates admitted for sepsis work in Neonatal intensive care unit (NICU) at Patna Medical College & Hospital, Patna from March 2019 to Feb. 2020. Sepsis work up including completed blood count (CBC), blood culture, erythrocyte sedimentation rate (ESR), CRP, urine analysis (UA), urine culture (UC), chest X-ray, cerebro-spinal fluid (CSF) analysis and culture was performed in all neonates. Three distinct groups were defined; proven sepsis, suspected sepsis and clinical sepsis (Table-1).

Exclusion criteria were administration of antibiotic therapy prior to admission, birth asphyxia, aspiration syndromes, laboratory finding suggestive of inborn error of metabolism and congenital anomalies. Before starting the antimicrobial therapy, blood samples (Sample1) for complete blood count, CRP, ESR, PCT and culture were collected. This procedure was repeated at day 5 after treatment with antibiotics (sample2). CSF, urine, tracheal and gastric aspirate cultures were obtained. Serum PCT level was measured using quantization immune-luminometry method by lumitest kit (Brahms Diagnostic, Berlin, Germany). In this assay a PCT level of 0.5ng/ml was accepted as pathological. PCT level 0.5-2ng/ml, 2-10 ng/ml and >10ng/ml considered as weakly positive, positive, and strongly positive, respectively.

We used SPSS version for statistical analysis. Correlation between variables and statistical differences were analyzed using Fisher exact, ANOVA, Monte Carlo and Wilcoxon tests. P values of <0.05 were considered to be significant.
Findings:-

Table 1: Criteria employed for defining the sepsis score

Group	Criteria	
Group I	Proven sepsis	Clinical signs and symptoms plus a positive bacteria culture.
Group I	Proven Sepsis	Clinical signs and symptoms with negative bacterial Culture
Group II	Suspected Sepsis	Clinical signs and symptoms with negative bacterial Culture but at least with 2 positive screening tests (ESR, CRP, CBC or CXR)
Group III	Clinical Sepsis	Clinical signs and symptoms with negative bacterial culture and negative screening test.

Table 2 : Relation between elevated Procalcitonin levels with normal sepsis screening tests.

Sepsis Group	Clinical sepsis	Suspected sepsis	Proven sepsis
Test	N=15	N=38	N=27
Normal ESR	7	8	10
Normal CRP	6	4	8
Normal WBC Count	15	10	12
Normal Chest X-ray			

WBC : White Blood Cell Count; CRP: C Reactive protein : ESR: Erythrocyte sedimentation rate

A Total 80 neonates were eligible for the study. These neonates are classified into three groups; proven sepsi (27 neonates), suspected sepsis (38 neonates) and clinical sepsis (15 neonates) according to the study protocol.

The mean gestational age, birth weight and the sex of the patients in these three groups were similar (P-value 0.096). Early onset sepsis was confirmed in 48(60%), late onset sepsis

in 22 (27.5%), Nosocomial sepsis in 10(12.5%) Causative pathogens and site of involvement were as follows: CSF in 2 patient positive for Escherichia coli, blood culture in 14 Patient positive for staphylococcus, Escherichia coli and Klebsiella; urine in two neonates for staphylococcus and Escherichia coli; and culture of the tip of chest tube was positive for Pseudomonas. Table 2 show the results of sepsis screening test including PCT in relation to three classified groups of patients.

If neonates with proven sepsis in spite of negative result for sepsis screening test, the result of PCT was positive. This result was seen also in some patients with clinical sepsis.

Table -3 : Serum Procalcitonin level (mg/ml) between groups before and after treatment

Group	Clinical Sepsis		Suspected Sepsis		Proven Sepsis	
	Before	After	Before	After	Before	After
Negative (PCT* <0.5 ng/ml)	2	12	9	24	0	0
Weakly Positive (PCT 0.5-2 ng/ml)	3	1	3	0	0	0
Positive (2-10 ng/ml)	8	2	20	12	2	1
Strongly Positive (PCT >10 ng/ml)	2	0	6	2	25	2

*PCT: Procalcitonin

Table 3 shows the serum concentrations of PCT in the studied groups. Comparison of serum PCT level before and after treatment reveals significant changes in clinical sepsis (P=0.001) and proven sepsis (P=0.003) groups of patients.

DISCUSSION

In the present study the PCT levels were remarkable high in neonates with proven sepsis and the levels dropped dramatically after treatment with antibiotics. Also in some cases of proven and suspected sepsis the levels of PCT were high in spite of negative, results for other sepsis screening tests.

Previous studies had shown high PCT levels in all neonates with proven of clinically diagnosed various types of neonatal sepsis [8,2,22,24,25].

In a recent study Koksal et al concluded that serum Procalcitonin level was superior to serum CRP level in terms of early diagnosis of neonatal sepsis, in detecting the severity of the illness and in evaluation of the response to antibiotic treatment[26].

In our study the serum PCT level was high in most of the patients before the initiation of therapy, but there was not a significant correlation between the serum PCT level and the type of sepsis.

In Koksal study, unlike our study, the level of serum PCT had a significant difference between the four study groups (no sepsis, probable sepsis, highly probable sepsis and possible sepsis). This difference may be due to the small sample size of our study. The serum PCT level in our study decreased significantly in all three sepsis groups which were most evident in proven sepsis group and like the same finding reported in other studies(26,27,28).

Athhan et al in their study revealed that at 7th day of therapy neonates who had achieved clinical recovery had a significant decrease of Procalcitonin levels compared to the initial values (P=0.000)[29]. This finding was reported also by Viallon and coworkers in 50 patients presenting with bacterial meningitis at day 2 after appropriate antibiotic treatment[30].

Carol et al in their study showed that Procalcitonin is more sensitive than the CRP in the diagnosis of septicemia, meningitis and urinary tract infection(28). In our study there were eight cases of culture positive sepsis accompanied with elevated levels of Procalcitonin while the CRP level was not high (table 2).

One of the limitations of the present study was the shortage of culture positive neonatal standard for sepsis to determine the sensitivity and specificity. For this reason was classified the neonatal sepsis into three groups and assessed the PCT level in relation to the class of sepsis before and after treatment.

CONCLUSION

The PCT concentration in our study was elevated in culture positive neonates and decreased with appropriate antibiotic therapy. In some cases of culture positive babies other sepsis screening tests were negative but the level of PCT was elevated. These findings support the usefulness of the PCT to establish an early diagnosis of neonatal sepsis.

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