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ASSESSMENT OF PROCALCITONIN AS AN ANALYTIC MARKER IN NEONATAL SEPSIS

Pediatrics

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ABSTRACT

OBJECTIVE: Neonatal sepsis is an early contamination happening within 28 days of the postnatal life. It has nonspecific signs and symptoms which make the diagnosis cumbersome. It inflicts an increase in morbidity and mortality among neonates. Procalcitonin (PCT) is acute phase reactant, which is synthesized by the C-cells of thyroid gland.

METHODS: A cross-sectional study was conducted at NICU, DMCH, Darbhanga, Bihar. The study was conducted over a period of 12 months from November 2018 to October 2019. The investigation incorporated all children with clinical indications of sepsis. The neonates were assigned into three groups as proven sepsis, suspected sepsis and no sepsis group. The CRP level and PCT level were compared between the three groups, and their sensitivity and specificity were calculated.

RESULTS: A total of 75 neonates were included in our study. There were 9 (12%) neonates with proven clinical sepsis, 47 (62.6%) neonates with suspected clinical sepsis, and 19 (25.3%) neonates with no sepsis. The mean and standard error of mean were calculated for CRP and PCT in all the three groups. The results showed a sensitivity of 88.90% for both CRP and PCT and specificity of 89.40% for CRP and 80.30% for PCT. The common organisms isolated from culture-positive group were Escherichiacoli(22.2%), Pseudomonasaeruginosa(22.2%), and Candida albicans (22.2%), followed by Klebsiellapneumoniae, Acinetobacterbaumannii, and methicillin-resistant Staphylococcus aureus.

CONCLUSIONS: PCT may not be adequately utilized as a sole marker of sepsis in children contrasted with CRP. PCT in conjunction with CRP and other tests for septic screen can aid in better diagnosis of neonatal sepsis.

KEYWORDS

C-reactive protein, neonatal sepsis, procalcitonin

INTRODUCTION

Neonatal sepsis is an early disease happening within 28 days of life. Neonatal sepsis is divided into two group as early onset neonatal sepsis (EONS) which happens within 3 days of birth and late-onset neonatal sepsis (LONS) which happens later [1]. It inflicts an increase in morbidity and mortality among neonates [2]. The estimated global neonatal death rates indicate 40% mortality due to sepsis. Further lack of accurate assessment and limited medical resources hamper accurate detection of neonatal sepsis among the developing countries [3]. Remarkably, it has nonspecific signs and symptoms which make the diagnosis cumbersome. It includes fever or hypothermia, cyanosis, apnea, lethargy, irritability, feeding difficulties, hypotonia, seizures, bulging fontanel, poor perfusion, bleeding problems, abdominal distention, and hepatomegaly. Even though blood culture is warranted as a gold standard method in identifying sepsis, the sensitivity varies based on the volume of blood and the bacterial load [4]. Total leukocyte count, absolute neutrophil count, immature-to-total neutrophil ratio, and C-reactive protein (CRP) are other parameters used to identify sepsis. Procalcitonin (PCT) is yet another acute phase reactant which is synthesized by the C-cells of thyroid gland. It is a peptide composed of 116 amino acids and a glycoprotein. It is also produced by hepatocytes and macrophages when there is an encounter by bacterial toxins [5]. Its utility as a marker in severe bacterial infection was first reported in 1993 [6]. PCT elevation is minimal in meconium aspiration, hypoxemia, and trauma on the contrary to CRP, which would be a better marker to identify neonatal sepsis[7] .The aim of our study is to evaluate PCT as a diagnostic marker of neonatal sepsis in comparison with CRP.

METHODS

A cross-sectional study was done at NICU, DMCH, Darbhanga, Bihar. The study was conducted over a period of 12 months from November 2018 to October 2019. The study included all neonates with clinical signs of sepsis such as fever or hypothermia, cyanosis, apnea, lethargy, irritability, feeding difficulties, hypotonia, grunting, seizures, bulging fontanel, poor perfusion, bleeding problems, abdominal distension, and hepatomegaly. The neonates were assigned into three groups as proven sepsis, suspected sepsis, and no sepsis group. The proven sepsis group included those neonates with both clinical signs and blood culture positivity. The clinically suspected sepsis group included those with clinical signs positive but culture negative. The no sepsis group was both culture and clinical signs negative. All neonates with positive blood culture were treated with appropriate antibiotic therapy at our Neonatal Intensive Care Unit. The CRP level and PCT level were looked at among the three group, and their affectability and explicitness were determined was submitted. C-reactive protein latex agglutination test the blood collected in discrete vials was permitted to clump. The serum was centrifuged and separated. A semi-quantitative test was carried out to identify the titer in positive cases. The sample was tested in dilutions of ½, 1/4, 1/8, 1/16, and 1/32. The CRP concentration was obtained by the formula: CRP concentration = sensitivity × titer, where the sensitivity is 0.6 mg/dl.

PROCALCITONIN

It was performed using PCT ELISA unit. All reagents, tests, and standards were set up as prepared. PCT was determined accordingly.

STATISTICAL ANALYSIS

The measurable examination was finished utilizing SPSS for Windows, Version SPSS 16. The mean, standard deviation, and standard mistake of mean were determined. The groups were compared using one-way ANOVA. The diagnostic test efficiency was evaluated by receiver operating characteristic (ROC) curve analysis. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

RESULTS

75 neonates were taken for examination. There were 9 (12%) children with demonstrated clinical sepsis, 47 (62.6%) neonates with suspected clinical sepsis, and 19 (25.3%) new-born with no sepsis. The mean and standard error of mean were calculated for CRP and PCT between all the three groups as shown in Table 1. P value was statistically significant ($P < 0.05$) in both CRP and PCT. The sensitivity, specificity, PPV, and NPV of the two diagnostic tests were calculated. ROC curve was elaborated for both CRP and PCT at 95% confidence interval. The cut off levels with optimum diagnostic efficiency derived from the curve for CRP was >0.3 mg/dl and PCT was >1.32 ng/ml. This yielded a sensitivity of 88.90% for both CRP and PCT and specificity of 89.40% for CRP and 80.30% for PCT [Table 2].

The common organisms isolated from culture-positive group were Escherichia coli (22.2%), Pseudomonas aeruginosa (22.2%), and Candida albicans (22.2%) followed by Klebsiella pneumoniae, Acinetobacter baumannii, and methicillin-resistant Staphylococcus aureus as shown in Table 3.

DISCUSSION

Sepsis includes a cascade of inflammatory process whose diagnosis is complicated due to the nonspecific signs and symptoms. It is a challenging task to establish an ideal diagnostic marker of sepsis as most of these makers rise in any kind of infective inflammatory process.

CRP is an acute phase reactant which rises following any tissue damage or infective process. It rises 6–8 h following any exposure with a half-life of 19 h,[8] whereas PCT is produced by monocytes and hepatocytes which rise in 4 h with a half-life of 25–30 h[5] .Comparatively, CRP rises late following any inflammation. There are several studies showing controversies on an ideal marker of sepsis. The aim of our study is to evaluate PCT as a diagnostic marker of neonatal sepsis in comparison with CRP.A multicenter study conducted in Spain revealed that PCT was not reliable and sufficient as a sole marker for sepsis [9]. On the contrary, Auriti et al. reported an increased diagnostic accuracy of PCT in neonates [10]. A study on perinatal influence on PCT showed that antibiotic therapy was associated with false-negative PCT results [11]. In our study, we found that both CRP and PCT were statistically significant in comparison between all the three groups. The sensitivity of both CRP and PCT was 88.90% each. The specificity for CRP was 89.40% and that of PCT was 80.30%. Park et al. reported that PCT had a sensitivity of 88.79% and specificity of 58.17%, while CRP had a sensitivity of 100% and specificity of 52.66% [12]. Other similar studies showed that PCT had a sensitivity of 66%–92% and specificity of 50%–97% [13-15]. In our study, the sensitivity was similar for both CRP and PCT whereas the specificity was lesser in PCT compared to CRP. This denotes that PCT as a separate diagnostic tool for neonatal sepsis can lead to more false-positive cases. The main problem with PCT is the physiological increase during the first 48 h of life which returns to normal on the 4th day [16]. Further studies have shown that premature birth is associated with rise in PCT without any bacterial infection. [17].

Table1: Mean and standard error of mean for C-reactive protein and procalcitonin in all the groups

Test	Group			P
	No sepsis (n=19)	Clinical sepsis (n=47)	Proven sepsis (n=9)	
CRP	0.063±0.043	0.460±0.246	2.2±0.959	0.007
PCT	0.416±0.311	1.275±0.344	5.737±1.009	0.001

CRP: C-reactive protein; PCT: Procalcitonin

Table 2: Sensitivity, specificity, positive predictive value, and negative predictive value of C-reactive protein and procalcitonin in neonatal sepsis

Test	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
CRP	>0.3	88.90	89.40	52.31	48.24
PCT	>1.32	88.90	80.30	55.01	45.57

CRP: C-reactive protein; PCT: Procalcitonin; PPV: Positive predictive value; NPV: Negative predictive value

Table 3: Organisms causing neonatal sepsis

Organism	Percentage (n=9)
Escherichia coli	22.2
Pseudomonas aeruginosa	22.2
Candida albicans	22.2
Klebsiella pneumoniae	11.1
Acinetobacter baumannii	11.1
MRSA	11.1

CONCLUSIONS

PCT may not be sufficiently used as a sole marker of sepsis in neonates compared to CRP. PCT in conjunction with CRP and other tests for septic screen can aid in better diagnosis of neonatal sepsis in the scenarios where this burden is high and other assays such as interleukin are expensive.

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