Research Article

Procalcitonin Level in Neonatal Sepsis

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ABSTRACT

A prospective study was conducted in a tertiary care centre from June 2015 to October 2016 to evaluate role of serum procalcitonin (PCT) level in predicting neonatal sepsis and comparison with CRP as a marker of neonatal sepsis. 100 neonates admitted in newborn intensive care unit (NICU) from the study group. These newborns were categorized into proven sepsis, suspected sepsis and control group based on symptoms and signs of infection and blood culture findings. Procalcitonin and CRP level were done for all these newborns. These levels were then statistically compared for all the groups. Out of 80 cases, 48 cases were of early onset sepsis and rest 32 were of late onset sepsis (LOS). 47(97.9%) out of 48 cases with early onset sepsis had positive procalcitonin level, while 30 (93.75%) out of 32 cases with LOS had positive procalcitonin value. 9 (18.75%) out of 48 cases with EOS had positive CRP value, while 15(46.87%) out of 32 cases with LOS had positive CRP value. Mean PCT was 33.75 + 13.75 ng/dl, 29.58 + 13.87 ng/dl and 0.335 + 0.4 ng/dl for proven sepsis, suspected sepsis and control groups respectively. Corresponding values for CRP were 1.33 ±1.74, 2.264 ±3.02 and 0.97 ± 2.87 ng/dl respectively for proven sepsis, suspected sepsis and control group. The sensitivity, specificity, PPV and NPV of procalcitonin was 96.25%, 85%, 96.25% and 85% and the sensitivity, specificity, PPV and NPV of CRP were 30%, 90%, 92.33% and 25% respectively. On comparing CRP and procalcitonin, there was statistically significant difference ($p < 0.005$) for early onset sepsis, while there was no significant difference ($p > 0.05$) for late of onset sepsis. Procalcitonin is highly sensitive marker in early onset sepsis with good positive and negative predictive value and high sensitivity.

KEY WORDS: CRP, neonates, procalcitonin, sepsis

INTRODUCTION:

Sepsis is the commonest cause of neonatal mortality. It is responsible for about 30-50% of total neonatal deaths in developing countries[1,2]. Early diagnosis of neonatal sepsis has been occupying the mind of paediatrician for a very long time. However, no single reliable test is available and a battery of tests are being used for this purpose[3]. This situation leads to empirical use of antibiotics because of high neonatal mortality rates[4]. Several leucocyte indices and acute phase protein levels have been evaluated for the diagnosis of sepsis. CRP in one of the acute phase reactant being used extensively for diagnosis of sepsis. Apart from infection, high CRP value is also seen in autoimmune diseases, surgery, meconium aspiration and recent vaccination. CRP value does not rise significantly until almost 14-48 hours after the onset of infection[5,6,7].

Serum procalcitonin has been reported as measurable laboratory marker of inflammatory response to infection. Macrophages and monocyte cells of liver increase procalcitonin secretion during the process of sepsis. Also, level of procalcitonin increases rapidly in 6-8 hours, reaching a plateau between 12 and 48 hours. This makes it a promising new marker for early identification of infected patient [8]. Another favourable point for procalcitonin is its increase in bacterial and fungal infection but no changes with viral infection and other inflammatory disease.

MATERIALS AND METHODS:

This prospective study was conducted in neonatal intensive care unit (NICU) of MLB Medical College, Jhansi from June 2015 to October 2016. Neonates with clinical features of sepsis such as refusal to feed, feeding intolerance, lethargy, excessive irritability, high pitched cry, seizures, temperature instability, apnea, respiratory distress,

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poor perfusion, tachepnea, bradycardia, abdominal distension, necrotizing enterocolitis, vomiting, sclerema, were included in this study. Neonates who were excluded were those who were already on antibiotics, who developed sign of sepsis within 72 hours of discontinuation of antibiotics and those with any congenital anomalies.

Detailed history was taken for risk factors in mother as well as in neonates like PROM, PV leaking, prolonged labour, multiple vaginal examinations. These neonates were thoroughly investigated. CBC, platelets, I/T ratio, ANC, micro-ESR, CRP, PCT, BT culture were done before starting antibiotics. Proclacitonin was measured by enzyme linked fluorescent assay using VIDAAS automated multiparametric immunoassay analyzer. Procalcitonin level of >0.5 ng/dl was taken as positive test for sepsis. Serum CRP value of > 1 ng/dl was taken as positive test for sepsis and measured quantitatively by nephlometry method.

All this data was accumulated and analysed. Statistical analysis was performed using Microsoft excel 2007 and Med Cal 9, 0.1 software, Microsoft word and Microsoft excel have been used to generate graph, tables. Chi-square test was used to compare between the groups and p value < 0.05 was considered to be significant.

RESULTS:

There were 100 neonates in our study group out of which 80 neonates had features of sepsis, while 20 newborns with no features of sepsis from control group. According to clinical symptoms of sepsis and blood culture results, neonates were classified into three groups: [1] Group A – Proven sepsis (32) positive blood culture and clinical symptoms of sepsis; [2] Group B – Suspected sepsis (48) with clinical symptoms but negative blood culture; and, [3] Group C – Control group (20) healthy neonates with no clinical and laboratory investigation suggestive of infection.

Out of 80 cases, 54 newborns (67.5%) were low birth weight as compared to 26 newborn with > 2.5 kg birth weight. Study group mostly consisted of preterm babies - 51 patient (63.3%) as compared to 29 term newborns (36.25%). Early onset sepsis was seen in 48 cases (60%), whereas there were 32 cases 940%0 of late onset sepsis. Among maternal risk factor 20 (41.7%) had PROM, 8(16.66%) had more than 3 vaginal examinations, 6 (12.5%) had meconium stained liquor, 9 (18.75%) had history of prolonged labour, 3 (6.25%) mothers had intra partum fever, while 2 (4.16%) mothers suffered UTI antenatally. Derangement and symptoms of CNS, GIT, CVS and haemotological system were seen in 14(17.5%), 3 (3.75%), 9(11.25%) and 7(8.75%) cases respectively. On comparing the positivity of procalcitonin in proven, suspected sepsis and control groups, it was found have statistically significant difference with p value of 0.001. Sensitivity, specificity, PPV, NPV value of CRP was 30%, 90%, 92.33% and 25% respectively while for procalcitonin these were 96.25%, 85%, 96.25%, 85% respectively.

Blood culture was positive in 32(40%) newborn and negative in 48(60%). Most common organism to be isolated was klebsiella, seen in 14(43.75%). Mean CRP was 1.33±1.74, 2.264±3.02 and 0.97±2.87 mg/dl respectively for proven sepsis, suspected sepsis and control group. CRP was observed to be positive in 24(30%) cases and negative in 56(70%) cases .One neonate of control group had positive CRP. Procalcitonin had positive value in 77(96.25%) cases while negative value in 3(3.75%) cases. 3 of the control group had positive procalcitonin

Table 1: Comparison of result of CRP in proven, suspected sepsis and control group.

CRP	Proven (n=32)	Control (n=20)	Suspected (n=48)
Positive	9	1	15
Negative	23	19	33
		p = 0.0897	p = 0.0390

Table 2: Comparison of result of procalcitonin in proven, suspected sepsis and control group.

PCT	Proven (n=32)	Control (n=20)	Suspected (n=48)
Positive	32	3	45
Negative	0	17	3
		p = <0.0001	p = <0.0001

Table 3: Comparison of Diagnostic performance of various laboratory parameters.

Variables	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV) (%)	Negative predictive value (NPV)
TLC	27.50	90	91.67	23.68
ANC	25.00	95	95.24	24.05
I:T Ratio	13.75	90	84.62	20.69
Micro-ESR	30	85	88.89	23.29
CRP	30	90	92.33	25
PCT	96.25	85	96.25	85

Table 4: Correlation of duration of onset of sepsis with CRP and procalcitonin (PCT) positivity

Gestational age	Total no. of cases (n=80)	No of cases with positive CRP	%	No. of cases with positive PCT value	%	p value
Early onset sepsis	48	9	18.75	47	97.91	0.0109
Late onset sepsis	32	15	46.87	30	93.75	0.3695

values. CRP was found to be of statistically significant difference when suspected sepsis group and control group was compared (p <0.05), but not of value when proven sepsis and control group were compared (p>0.05).

DISCUSSION:

Our study evaluated the role of PCT in neonatal sepsis and compared CRP with PCT as a marker of sepsis. Neonatal sepsis with its high mortality rate still remains a diagnostic and treatment challenge for neonatal health care providers.

On statistical analysis, CRP was found to be of value when suspected and control groups were compared (p <0.05) though it was not of much use when compared with regards to proven and control group (p>0.05). In our study, at a cut off value of > 1 mg/dl, CRP had sensitivity, specificity, PPV and NPV of 30%, 90%, 92.33% and 25% respectively. These results were comparable to those by Abdollahi A. et al who reported lower sensitivity and higher specificity of CRP in detecting sepsis[9]. Bonac B et al compared the levels of CRP, PCT and IL-6 in the diagnosis of neonatal sepsis in 58 infants. They 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[10]. These findings did not collaborate with our observation which may be due to difference in cut off value and laboratory method used.

Procalcitonin level was statistically highly significant (p<0.0001) when compared between proven sepsis and control group as well as with suspected sepsis and control group. PCT level were remarkable high in the neonates with proven sepsis and also in the suspected sepsis cases. This finding was comparable with that of the study which was conducted by Yadolla Zahedpasha et al[11] and Monerret G et al[12]. Another study demonstrated that in cases of proven and suspected sepsis the levels of PCT were high inspite of negative results for other sepsis screening test which is consistent with our result. Procalcitonin evaluation in this study demonstrated sensitivity of 96.25%, specificity of 85%, PPV of 96.25% and NPV of 85%. Claudio Chiesa et al studied the reliability of the PCT concentration in 28 infants who had severe early onset neonatal sepsis. They observed that the sensitivity, specificity, PPV and NPV were 92.6%, 97.5%, 94.3% and 96.5% respectively[13].

Yildiz et al 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%, 92% respectively. They concluded that it would be useful to use PCT as an indicator in the early diagnosis of neonatal sepsis[14].

CRP and PCT on comparison in cases of early onset sepsis showed procalcitonin to be better marker with p value < 0.05. However, when these parameters were seen with relation to LOS, no statistically significant difference was found (p >0.05). This led to the inference that PCT had a higher statistical value as a marker of EOS. Monneret G et al also reported that both CRP and PCT levels increased in infants with EOS, but the rise in PCT levels was higher than of CRP[12].

Naglaa F. Boraey et al in their study observed higher serum levels of PCT and CRP in neonates with EOS than those in neonates with LOS, with significant statistical difference (p value 0.002 and 0.009 respectively)[15]. Similar results were also reported by Jose B et al, who concluded that PCT is a useful marker of bacterial sepsis of vertical transmission, but is not sufficiently reliable to be the sole marker of neonatal sepsis of nosocomial origin[16].

Our study also showed that sensitivity of PCT for the diagnosis of neonatal sepsis was higher (96.25%) than that of CRP (30%) using a cut off value of 0.5ng/dl and 1 ng/dl of PCT and CRP respectively. In our study PCT as a marker of early onset sepsis exceeded CRP with a statistically significant difference (p<0.05). The higher sensitivity of PCT in comparision to CRP was also reported by other researchers like Naher B. S. et al[17], Vazzalwar R. et

al[18].

The considerable heterogeneity of the results among the studies evaluating these markers for detection of neonatal sepsis can be explained by the lack of a universally acceptable definition of neonatal sepsis, differences in the cut off values incorporated in the studied organism involved in sepsis and the laboratory methods used, which may all interfere in the result.

CONCLUSION:

Our study is a modest attempt to compare the role of procalcitonin in neonatal sepsis with other markers.The study group, though small by size, has illustrated that PCT is a highly sensitive marker with a good positive and negative predictive values. PCT was observed to be a better diagnostic tool in early onset as compared to CRP. Thus, it can be inferred that PCT is sensitive early marker of neonatal sepsis with a high yield. PCT levels done in all the neonates for early recognition of sepsis would lead to decrease in the number of patients unnecessarily treated as well as improve neonatal mortality rates.

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