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Studies On-going in the Search of a Novel Marker for Neonatal Sepsis

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Introduction

Esparcia employed a gene-based molecular technique using rDNA for diagnostic accuracy of bacterial meningitis and early-onset neonatal sepsis. Ng used a score based on proapolipo-protein CII and a des-arginine variant of serum amyloid to withhold antibiotics in infants with suspected infection and to discontinue antibiotics [1]. Kasper recently found that sensitivity of multiplex real-time PCR was 0.90 but specificity was low for late-onset nosocomial sepsis in premature infants. The limitations of these studies includes failure to provide information about antibiotic resistance, inability to differentiate the false-positive results because of potential contamination during blood sampling or processing from true positive cases and high cost. Prospective evaluation is needed to determine accuracy and safety of these exciting new approaches. Therefore, these are currently adjunctive methods with the exception, which remains gold standard for the diagnosis of HSV encephalitis [2]. None of the markers including hematologic indices, acute phase reactants, cytokines, and cell surface markers have shown sensitivity, specificity, positive and negative predictive value that are sufficiently powerful to guide the clinical management of neonatal sepsis. Different biomarkers have been used to diagnose neonatal sepsis, but with inconclusive results, because of small sample size, lack of clear reference values and lack of homogeneity in the study group [3]. Thus, there remains a need for a marker with high sensitivity, specificity, positive and negative predictive accuracy which is able to detect infection at an early stage. The inter alpha inhibitor family of proteins are serine protease inhibitors which provide protection from the increased protease activity associated with systemic immune system activation that accompanies sepsis and inflammation [4]. They are involved in extracellular matrix stabilization, inflammation, wound healing, and play an important anti-inflammatory and regulatory role in infection. Inter α inhibitor proteins is one of the important serine protease inhibitors secreted by the liver. Inter α inhibitor proteins is a hetero-trimeric, protein complex composed of two heavy chains and one light chain held together by glycosaminoglycan bonds [5]. The light chain, Bikunin, has a molecular weight and is the active, anti-protease component. In the presence of serine proteases, Bikunin is released and it provides protective effects. The half-life of Bikunin is very short and it is rapidly excreted by the kidneys. Inter α inhibitor protein concentration is independent of gestational age, postnatal age, and is similar to adult levels [6]. However, Inter α inhibitor proteins levels are significantly lower in septic neonates as compared with non-septic age matched controls. Receiver operating curve analysis has shown Inter α inhibitor proteins measurement to have sensitivity, a positive predictive value and a negative predictive value in a pilot study of neonates [7]. The levels of Inter α inhibitor proteins not only decrease in neonatal sepsis but also rise in response to antibiotic treatment. Yang and colleagues showed that low levels of Inter α inhibitor proteins are highly predictive of mortality in septic adult patients [8]. Because the levels of Inter α inhibitor proteins decrease with severe sepsis, measurement may also help to guide the prognosis as lower levels are associated with adverse outcome [9]. Chaaban demonstrated that the levels of Inter α inhibitor proteins also decrease significantly in patients with necrotizing enterocolitis and thus can be useful to diagnose patients with necrotizing enterocolitis at an early stage. Singh showed an immune-modulatory and protective role of administration of Inter α inhibitor protein in septic new-born mice. This underscores potential role of Inter α inhibitor proteins as a theranostic marker in infants with sepsis [10].

Acknowledgement

None

Conflict of Interest

None

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