La sepsi neonatale: ruolo emergente della ADM

Silvia Leonardi [1], Daniela Magri [2], Benedicta Maione [1], Sara Sarpa [1], Filomena Pisacane [1] , Federica Garziano [1] , Chiara De Falco [1], Ilaria Fierro [1], Giovanni Chello [2] , Rita Boenzi [1]

[1] *UOC Biochimica Clinica, Ospedale "Vincenzo Monaldi"*
[2] *UOC Terapia Intensiva Neonatale Ospedale "Vincenzo Monaldi", Napoli*

RIASSUNTO *La Sepsi Neonatale è un'infezione invasiva, spesso batterica, con alti tassi di ospedalizzazione e mortalità nei neonati. Può presentarsi come esordio precoce (SP), entro 6 ore dalla nascita, a causa di infezioni intra-partum, oppure come esordio tardivo (ST) dovuto a microrganismi ambientali o dispositivi intra-vascolari. La diagnosi precoce è critica ma difficile per i neonatologi. Recentemente, l'attenzione si è concentrata sulla MR-proAdrenomedullina (ADM) come possibile biomarcatore per la sepsi nei neonati, anche se i dati pediatrici sono limitati. Recenti studi indicano che i livelli di ADM sono più alti nei neonati con sepsi e diminuiscono rapidamente in quelli con sepsi controllata. Lo studio ha valutato i livelli plasmatici di ADM in 57 neonati ricoverati in TIN tra ottobre 2022 e marzo 2023. Dei 23 neonati con SP, i valori medi di ADM erano 1,82 nmol/L. Dei restanti 34 pazienti, 14 che presentavano valori di ADM elevati al T0 hanno sviluppato ST entro 72 ore dal ricovero. Questi risultati suggeriscono che ADM può essere un valido marcatore precoce per la sepsi, utile nella diagnosi e nel monitoraggio della sepsi neonatale.*

Parole chiave: *Sepsi Neonatale; Sepsi Precoce; Sepsi Tardiva; MR-proAdrenomedullina; Terapia Intensiva Neonatale*

ABSTRACT ***Neonatal Sepsis: emerging role of ADM. Background.*** *Neonatal sepsis is an invasive infection, usually bacterial, associated with high rates of hospitalization and mortality in pediatric settings. It can present as an early-onset sepsis (EOS), characterized by the development of symptoms within 6 hours of birth, caused by microorganisms acquired intra-partum due to premature rupture of membranes, chorioamnionitis, and preterm birth. There is also a late-onset sepsis (LOS), which can be caused by environmental microorganisms or, more frequently, by the use of central intravascular devices (catheters), as well as associated diseases. Early diagnosis of sepsis is thus a critical challenge for neonatologists, who must evaluate clinical signs that are difficult to distinguish from other non-infectious conditions in neonates. Various biomarkers have been studied to support clinicians in the rapid identification of patients at risk of sepsis progression and in evaluating the response to pharmacological treatment. Unlike adults, evidence for the use of new biomarkers for diagnosing and monitoring sepsis in neonates is lacking. Recently, the scientific community has focused on the use of MR-proAdrenomedullin (ADM) in Neonatal Intensive Care Units (NICUs), alongside markers used in common clinical practice. Despite extensive literature on ADM in the adult population, data on its performance in pediatrics are limited. It has been observed that ADM concentrations can be elevated in neonates, particularly preterm ones, due to low systemic vascular resistance. However, recent studies have highlighted that ADM levels can be significantly higher in neonates with sepsis compared to healthy controls and that ADM values decrease more rapidly in neonates with controlled sepsis. Therefore, based on these premises, ADM could be considered an early marker of sepsis in NICU patients****. Objectives.*** *The aim of our study was to evaluate whether ADM levels in neonates could serve as an early marker of sepsis, capable of stratifying the risk of mortality in young patients, alongside markers used in common clinical practice.* ***Materials and methods.*** *Our exploratory observational study aimed to assess plasma ADM levels in a cohort of neonates with gestational ages between 31 and 40 weeks at birth, admitted to the NICU. The study enrolled 57 neonates admitted to the Neonatal Intensive Care Unit at the AORN "Monaldi" in Naples, between October 2022 and March 2023. The average age of the patients was 1.4 months, with 22 males and 35 females. All underwent collection of clinical-anamnestic data and a blood sample at birth/admission (T0), and after 72 hours (T1), to measure ADM levels in addition to routine tests.* ***Results.*** *The screening involved 57 neonates, of whom 23 presented with EOS at T0. This group was considered the control group for ADM values (mean = 1.82 nmol/L). We chose to use values ≥ 1 as the cut-off, in accordance with current literature. Of the remaining 34 neonates admitted for reasons other than EOS, 15 had ADM values < 1 at T0 (mean = 0.77 nmol/L), while 19 had ADM values ≥ 1 (mean = 1.51 nmol/L). From the clinical evaluation of the patients combined with laboratory data at T0, it was found that of the 19 neonates with elevated ADM values, 14 developed LOS within 72 hours of admission. Of the 15 neonates with normal ADM values at T0, only 4 developed LOS.* ***Discussion.*** *Despite advances in pharmacological treatments, sepsis remains one of the leading causes of death in the neonatal period. In sepsis, Systemic Inflammatory Response Syndrome, and Septic Shock, where microcirculatory damage and endothelial dysfunction are associated with organ failure, there is a significant increase in ADM values due to its role, making it a valid early marker of organ failure capable of stratifying mortality risk in sepsis patients. The continuous advancement of laboratory diagnostics opens new perspectives for accelerating and improving patient assessment.* ***Conclusions.*** *In our study, we found that neonates with elevated ADM values at T0 were more susceptible to developing sepsis. Thus, measuring ADM in NICUs appears to be highly useful for the diagnosis and monitoring of neonatal sepsis.*

Key-words: *Neonatal Sepsis; Early-Onset Sepsis; Late-Onset Sepsis; MR-proAdrenomedullin; Neonatal Intensive Care Unit*