EARLY ONSET SEPSIS IN PRETERM NEWBORNS: RISK FACTORS AND BIOMARKERS

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Early-onset sepsis (EOS) remains one of the leading causes of morbidity and mortality among preterm newborns, with a global neonatal sepsis incidence of 2,824 per 100,000 live births and a case fatality of 17.6%. Its clinical signs (respiratory distress, apnea) are nonspecific, and risk factors include lower gestational age and birth weight, prolonged rupture of membranes (>18 hours was associated with a 9.67-fold higher risk), maternal chorioamnionitis, and low Apgar scores. Laboratory markers such as C-reactive protein, interleukin-6, and procalcitonin support decisions on starting or stopping antibiotics, but none is sufficiently sensitive and specific to be used alone; procalcitonin at 72 hours performed best (AUC 0.85), whereas CRP was not a significant predictor. Early recognition of EOS in preterm infants should therefore rely on risk-factor assessment and serial clinical examination, with inflammatory markers as supporting tools, which may allow a safer reduction of unnecessary antibiotic exposure.

Keywords: *early-onset sepsis, preterm newborns, risk factors, procalcitonin, C-reactive protein, antibiotic therapy*.

Early-onset sepsis (EOS) is an invasive bacterial infection that develops within the first 72 hours of life and remains one of the leading causes of morbidity and mortality among preterm newborns. A global systematic review estimated the incidence of neonatal sepsis at 2,824 cases per 100,000 live births, with a case fatality of 17.6%, and both incidence and mortality were higher for

early-onset than for late-onset sepsis [1]. In low-resource settings the incidence of EOS may reach 9.8% of live births, and mortality is highest in extremely low birth weight infants [2]. Clinical signs in preterm infants, such as respiratory distress and apnea, are nonspecific, which delays diagnosis and contributes to poor outcomes [2,3].

Risk factors for EOS include lower gestational age and birth weight, prolonged rupture of membranes, maternal chorioamnionitis and low Apgar scores. In a recent NICU cohort, rupture of membranes longer than 18 hours was associated with a 9.67-fold increase in the risk of neonatal sepsis, and hypoglycemia was linked to culture-negative EOS (OR 2.88) [3]. American Academy of Pediatrics guidance for infants born at ≤34 6/7 weeks recommends assessing risk on the basis of gestational age, circumstances of birth and clinical status, and weighing the benefits of empirical antibiotics against the harms of postnatal antibiotic exposure [4].

Laboratory markers are widely used to support the decision to start or stop antibiotics, but their performance is limited. Hematological indices, acute-phase reactants and cytokines lack sufficient sensitivity and specificity for diagnosing EOS, and newer markers such as presepsin and endocan are still at the research stage [2]. Interleukin-6 is regarded as an early marker, C-reactive protein (CRP) as a later one, and none of the current markers is sensitive and specific enough to justify withholding antibiotics without considering clinical findings, gestational age, maternal risk factors and the timing of sampling [5]. In the study by Vasilescu et al., CRP at 24 and 72 hours was not a significant predictor of confirmed EOS, whereas procalcitonin at 72 hours performed best (AUC 0.85; cut-off 0.27; sensitivity 93.8%, specificity 51.6%); the authors concluded that markers should be combined with repeated clinical evaluation [3].

In conclusion, early recognition of EOS in preterm newborns should rely on risk-factor assessment (gestational age, birth weight, prolonged rupture of

membranes, chorioamnionitis) and serial clinical examination, with inflammatory markers used only as supporting tools. Single biomarkers cannot replace clinical judgement, and combined, dynamic assessment may allow a safer reduction of unnecessary antibiotic exposure.

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