The Well-Appearing Newborn at Risk for Early-Onset Sepsis: We Can Do Better

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A common question in the newborn nursery is when to do a sepsis evaluation. When one considers pathogens such as group B *Streptococcus*, the risk of invasive infection is higher in the newborn than at any other time of life.[1] Overall, the incidence of early-onset sepsis (EOS, defined as a positive blood or cerebrospinal fluid culture within the first 72 hours after birth) in infants born at term is estimated to be ~1 per 2000.[2] Although case fatality rates are <2%, the incidence of long-term neurologic sequelae can be as high as 50%.[1,2]

A baseline risk of <1 per 1000 may be too low to justify routine evaluation for EOS, but perinatal factors can significantly increase that risk. Questions then arise: Whom to test, when to treat with antibiotics pending test results, when to perform a lumbar puncture, and how long to treat with antibiotics if cultures remain negative? In an effort to aid the clinician, guidelines[3,4] and risk-based tools[5,6] have been developed.

How does the newborn nursery provider use these available resources when managing the well-appearing term infant? The study by Mukhopadhyay et al[7] in this issue of *Pediatrics* examines this question. In a Web-based survey within a newborn outcome research network of 81 nurseries across the United States, they found wide variation in how well-appearing newborns are assessed and managed for EOS. Although the majority of respondents used 1 of the published guidelines or sepsis risk calculators, >25% relied on local protocols or individual provider discretion. Frequency of intervention varied from doing less to doing more than directed by published resources. Notably, 2 of the 81 responders reported that their site practice was to provide observation and routine newborn care to all well-appearing newborns, without consideration of perinatal sepsis risk factors.

In general, clinical practice guidelines are often not followed[8,9]; for the healthy-appearing newborn with a low risk of EOS there may also be concern that our current guidelines and risk-based calculators result in too many unnecessary evaluations and antibiotic exposures in infants who do not have EOS.[10,11] But what is more concerning in the study by Mukhopadhyay et al are the extremes of practice variation, from observation without regard to perinatal risk factors to intervention based solely on fetal tachycardia, neither of which is supported by any of the published guidelines or risk-based models.

The bugbear of chorioamnionitis also looms large in the findings of Mukhopadhyay et al. It was 1 of the 2 most common clinical risk factors that prompted evaluation and treatment; although this finding is consistent with currently published guidelines,[3,4] neither the guidelines nor the survey provides rigorous criteria for the diagnosis of chorioamnionitis, leaving it to individual interpretation. For respondents who primarily

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used risk-based calculators, most considered an obstetrical diagnosis of chorioamnionitis an additional risk factor, despite the fact that those calculators were specifically designed to avoid such subjective considerations.[6]

Earlier this year, a panel of experts in maternal, fetal, and neonatal care grappled with the vagaries of the term "maternal chorioamnionitis". In their summary report they recommended a more refined definition of intrauterine inflammation or infection (so-called Triple I), gave criteria for suspected and confirmed Triple I, and emphasized that isolated maternal fever was insufficient to make a diagnosis of Triple I.[12] However, this report is unlikely to change the findings of Mukhopadhyay et al, because almost all cases the newborn provider will have to struggle with will fall into the suspected category, a situation for which the panel recommends that "care should be individualized." Confirmation of Triple I requires either abnormal amniotic fluid laboratories or placental pathology; amniocentesis is rarely done, and pathology results typically are not available for several days after birth, leaving the newborn provider with no clear direction when evaluating the newly born infant.

The study by Mukhopadhyay et al has the usual shortcomings of survey research. In particular, it is limited by its sample size and depth of inquiry. Still, if such variation was evident among a limited sample, even wider variation is possible from a larger study. In a limited survey we also gain little insight into the barriers to guideline adherence or why providers choose an alternative approach.[9] What the survey by Mukhopadhyay et al does tell us is that assessment and management of the well-appearing newborn at risk for EOS have significant room for improvement, perhaps through a better understanding of the relative risks of harm and benefit for each of our treatment options (observation alone, evaluation and observation, or empirical treatment), the value and limitations of laboratory tests, the barriers that prevent providers from appropriately using available guidelines and risk-based tools, and how our current guidelines can provide better guidance.

ABBREVIATION

EOS: early-onset sepsis

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