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Editorial

A combination of ampicillin and aminoglycoside for early-onset neonatal sepsis

Streptococcus agalactiae, which is known as group B streptococcus (GBS), has traditionally been the leading cause of neonatal morbidity and mortality [1]. The gastrointestinal tract, especially the rectum, is considered as the major reservoir for the colonized vagina [2]. The Centers for Disease Control and Prevention issued recommendations for intrapartum prophylaxis to prevent perinatal GBS in 2010 [3]. This was also recommended by the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, the American College of Nurse-Midwives, the American Academy of Family Physicians, and the American Society for Microbiology [4]. With improved obstetrical management and evidence-based use of intrapartum antibiotics, early-onset neonatal sepsis caused by GBS is becoming less frequent [5]. However, early-onset sepsis remains one of the most common causes of neonatal morbidity and mortality in the preterm population.

Any strategy to identify the risk, confirm the diagnosis, and prevent the occurrence is welcome, although there are challenges for clinicians, including: (1) promptly identifying neonates with a high likelihood of sepsis and initiating antimicrobial therapy; (2) distinguishing "high risk" healthy-appearing infants or infants with clinical signs that do not require treatment; and (3) discontinuing antimicrobial therapy once sepsis is deemed unlikely [5]. In our previous reports, we developed a useful tool (chip-based multiplexed immunoassay using liposomal nanovesicles) which might provide an opportunity for early detection of the pathogens causing neonatal sepsis through an antepartum or intrapartum evaluation [6–8], because the identification of neonates at risk for early-onset sepsis is frequently based on a constellation of perinatal risk factors that are neither sensitive nor specific, and diagnostic tests for neonatal sepsis have a poor positive predictive accuracy [5]. Because of these challenges, clinicians often treat well-appearing infants for extended periods with an optimal treatment, such as broad-spectrum antimicrobial agents (ampicillin and an aminoglycoside), even when bacterial cultures are negative [5].

Research by Tsai et al, published in the *Taiwan Journal of Obstetrics and Gynecology* in 2012, showed that the incidence of non-GBS and antibiotic-resistant early-onset sepsis in preterm, low-birth-weight, or very low-birth-weight neonates was significantly increased [9]. The paper provided useful information that would encourage obstetricians and neonatologists to reconsider the severity of non-GBS neonatal sepsis.

First, *Escherichia coli* might be one of the most common pathogens in non-GBS neonatal infections, especially in preterm infants. Second, the overall incidence of *E. coli* neonatal sepsis remained stable after the introduction of intrapartum antibiotics prophylaxis, but increased in very low-birth-weight infants. Early-onset *E. coli* neonatal sepsis is more common in premature and very low-birth-weight infants and is more likely to be associated with intrapartum fever, preterm premature rupture of membranes, and sepsis onset on the first day of life than non-*E. coli* neonatal sepsis. Third, nearly 80% of *E. coli* neonatal sepsis was ampicillin-resistant and 16% was gentamicin-resistant, and all of these patients had a history of antepartum and intrapartum antibiotic exposure [9].

Based on the above finding, the guideline published in the journal *Pediatrics* in May 2012 can be argued against, because this guideline suggested that the optimal treatment of infants with suspected early-onset sepsis is broad-spectrum antimicrobial agents (ampicillin and an aminoglycoside) [5]. A combination of ampicillin and an aminoglycoside (usually gentamicin) is generally used as initial therapy, and it also has synergistic activity against GBS and *Listeria monocytogenes* [5]. If the report by Dr Tsai and colleagues [9] is reproducible in other hospitals in Taiwan, then other antibiotics should be used in place of the suggested optimal treatment. For example, third-generation cephalosporins (e.g., cefotaxime) represent a reasonable alternative to an aminoglycoside. However, this alternative treatment might not have any advantage, because several studies have reported rapid development of resistance when cefotaxime was used routinely for the treatment of early-onset neonatal sepsis [10], and extensive/prolonged use of third-generation cephalosporins is a risk factor for invasive candidiasis [5].

Neonatal sepsis is still the biggest challenge, not only for obstetricians, but also for neonatologists. One report might not change our treatment policy [9], but it is worthy of our attention.

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