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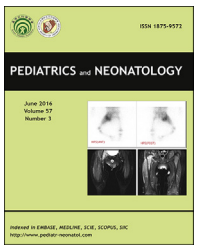

REVIEW ARTICLE

Bird's Eye View of a Neonatologist: Clinical Approach to Emergency Neonatal Infection

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Though the incidence of neonatal infection in term and near-term infants is relatively low, incidence of infection in preterm very low birth weight infants is as high as 20—30% and may result in neurodevelopmental impairment or mortality. Pediatricians should be familiar with recognition and emergency management of life-threatening neonatal infections, such as congenital pneumonia, early onset sepsis, late onset sepsis, bacterial and fungal meningitis, disseminated neonatal herpes simplex virus (HSV), and HSV meningoencephalitis. For the pediatrician, it is logical to approach the management of these infections by time of onset, i.e., early versus late onset of infection. Perinatal risk factors and simple laboratory tests, such as total white blood-cell count, immature/total ratio, and C-reactive protein are helpful in guiding the decision of antibiotics therapy. Successful management of these critical infections depends upon early diagnosis and timely administration of adequate antibiotics. Empiric antibiotic therapy must cover the most likely pathogens according to the risk factors of each individual neonate, and therapy duration is dependent upon culture results, clinical course, and the microorganism. Future research may focus on developing a practical neonatal sepsis score system based on risk factors and common biomarkers, which are readily available at bedside to make early accurate decisions and achieve better outcomes.

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1. Introduction

Although the incidence of neonatal infections in term and near-term infants is relatively low, neonatal infections have a significant impact on medical resource utilization. The incidence of health care-associated infections in preterm very low birth weight (PVLBW) infants is as high as 20—30%.[1] Furthermore, infection of PVLBW infants can result in death or neurodevelopmental impairment. Thus, pediatricians must be aware of the possibility of sepsis or health care-associated infections in any high-risk infants.

Life-threatening neonatal infections include congenital pneumonia with the possibility of development into persistent pulmonary hypertension of the newborn (PPHN) and/or septic shock and even mortality; early onset sepsis (EOS) in neonates, leading to high mortality rates and adverse neurodevelopmental outcomes in preterm infants; late onset sepsis (LOS) in neonates, resulting in moderate mortality rates and adverse neurodevelopmental outcomes in preterm infants. Bacterial or fungal meningitis is related to adverse neurodevelopmental outcomes, and neonatal disseminated herpes simplex virus (HSV) infection and HSV meningoencephalitis can both cause high mortality and high morbidity rates.

For the pediatrician, it is reasonable to approach the management of these infections by time onset, i.e., early versus late onset of sepsis, where EOS is defined as infection occurring within $<$ 3 days usually presenting with pneumonia or sepsis.

2. Congenital pneumonia

2.1. Pathogenesis

Congenital pneumonias result from intrauterine aspiration of infected amniotic fluid or aspiration of amniotic fluid during the birth process. Pediatricians need to be aware that congenital pneumonias sometimes progress to septic shock and can be associated with persistent pulmonary hypertension.

Pneumonia is caused by many of the same pathogens associated with neonatal sepsis, including EOS and LOS. In the area of antenatal chemoprophylaxis in developing countries, the pathogens responsible for congenital pneumonia include *Escherichia coli*, group B streptococcus (GBS), *Staphylococcus aureus*, *Klebsiella* spp, and *Streptococcus pneumoniae*.[2] HSV is the most common viral agent that causes pneumonia and has a very high mortality rate.[2,3] According to the recommendations of the Centers for Disease Control and Prevention (CDC), since 1996 early-onset GBS infection has been reduced by more than 85% after GBS prophylaxis protocol in the USA.

However, some reports showed that there were more *Escherichia coli* infections in neonates or more ampicillin-resistant organisms, although other reports did not have similar findings.[4]

2.2. Diagnostic approach

Any neonates who present with respiratory distress should be evaluated for pneumonia, with chest X-ray most helpful in its diagnosis and management. Pneumonia caused by GBS or other pathogens is difficult to distinguish from respiratory distress syndrome in the preterm infant. The most common abnormality identified was dense bilateral alveolar infiltrates with air bronchograms.[4]

2.3. Management

Successful treatment depends upon recognition of risk factors. Treatments include prompt diagnosis with administration of antibiotics and supportive therapy, including surfactant replacement[5] and nitric oxide inhalation for PPHN. Although clinical trials regarding surfactant replacement for congenital pneumonias are limited, surfactant replacement may reduce mortality, especially for PVLBW infants.[6]

Ampicillin and gentamicin are commonly used to treat infants with congenital pneumonias. Since Gram-negative bacilli rapidly develop resistance to cephalosporins, third-generation cephalosporins are not recommended routinely for suspected pneumonia[7] except when there is no improvement after 24 hours of treatment or if *S. pneumoniae* infection is highly suspected.[8] Once a specific organism is identified, therapy is modified according to the susceptibility pattern.

3. Early onset sepsis

3.1. Pathogenesis

EOS pathogenesis is the same as that of pneumonia. Organisms responsible for EOS reside in the birth canal and invade the amniotic cavity through the cervix. Given that the signs and symptoms of sepsis are also subtle and nonspecific, identification of infants at risk is critical for emergency intervention.[9] The neonate should be carefully evaluated for the presence of risk factors, including the following: intrapartum maternal temperature $\geq$ 38°C (100.4°F), chorioamnionitis, preterm infants at $<$ 37-weeks' gestation, Apgar scores $\leq$ 6 at 5 minutes, evidence of fetal distress, maternal GBS colonization, or membrane rupture of $\geq$ 18 hours.[9] Heart-rate analysis might also help the early diagnosis of late onset neonatal sepsis.[10]

Pneumonia is more common in EOS. If the classic signs of respiratory distress, including tachypnea, dyspnea, grunting, and cyanosis present within the first 4—6 hours of life, pneumonia should be considered.

3.2. Diagnostic approach

Low white blood cells ($<$5000/μL) (WBC), absolute neutrophil count less than 1000/μL (ANC), or proportion of neutrophils that are immature greater than 0.6 have been highly associated with culture-proven early-onset disease.[11]

Sequential assessment of C-reactive protein (CRP) may be helpful in guiding the duration of antibiotic therapy in suspected neonatal bacterial infection,[12] however, detailed physical examination with clinical symptoms is more important. Elevated procalcitonin ($>$ 0.5 ng/mL) is equally