

Neonatal Sepsis

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Abstract: Neonatal sepsis (NNS) is invasive infection, mostly bacterial, occurring during the neonatal period. NNS manifests with ill-defined symptoms, therefore, requires high index of suspicion for early diagnosis. Neonatal sepsis is becoming less frequent due to improved obstetrical management and evidence-based use of intrapartum antimicrobial therapy. However, early-onset sepsis remains one of the most common causes of neonatal morbidity and mortality in the preterm population.

Keywords: Neonatal Sepsis, Intrapartum

INTRODUCTION

Neonatal sepsis is one of the most common diagnosis made in the NICU [1]. The signs of sepsis are nonspecific. Most infants recover with supportive care (with or without use of antimicrobial therapy). Thus the challenges for pediatricians are to: (1) promptly identify neonates with a high risk of sepsis and initiate antimicrobial therapy; (2) distinguish "high-risk" healthy-appearing infants or infants with clinical signs who do not require treatment; and (3) to discontinue antimicrobial therapy once sepsis seems to be unlikely.

ETIOLOGY

Neonatal sepsis can be Early-onset sepsis (EOS) (within 72 hours of birth) or Late-onset sepsis (LOS) (after 72 hours of birth).

EOS

EOS most commonly occurs from vertical transmission of group B *Streptococcus* (GBS) from mother to infant. The rate of early-onset GBS invasive infection has declined from 0.6 per 1000 births in 2000 to 0.26 per 1000 in 2011 as per the reports of Centers for Disease Control and Prevention (CDC) [2, 3]. Early-onset sepsis caused by GBS has a fatality rate ranging from 5% to 20% [4]. Recently, *Escherichia coli* has emerged as the major pathogen responsible for sepsis in preterm infants and the second most common cause in full-term babies [5]. Both *E. coli* and GBS account for about 70% of cases of EOS.

LOS

Late-onset sepsis occurs between day 4 and 120, usually resulting from postnatal horizontal transmission of pathogens [6]. Preterm VLBW infants are particularly at high risk of LOS due to immature immune system and requirements for prolonged hospitalization. Late-onset sepsis is predominantly caused by Gram-positive pathogens (*Streptococcus pneumoniae*, *Streptococcus pyogenes*, *S. aureus* and GBS).

SIGNS AND SYMPTOMS

The signs and symptoms of neonatal sepsis are nonspecific which include fever or hypothermia, respiratory distress including cyanosis and apnea, difficulties in feeding, lethargy or irritability, hypotonia, seizures, bulging fontanel, poor capillary perfusion, bleeding problems, abdominal distention, hepatomegaly, guaiac-positive stools, unexplained jaundice. Infants with hypoxia-acidosis may gasp in utero and lead to pneumonia and meconium aspiration [7, 8].

INVESTIGATIONS

Blood culture

Blood culture is the gold standard for diagnosis of sepsis. It should be done in all cases before starting the treatment and should be observed for 72 hours before labelling it as sterile. Nowadays BACTEC or BACT/ALERT culture system can detect growth in 12-24hrs.

Sepsis screen

Sepsis screen is a panel of tests consisting of [9, 10]:

Component Abnormal value

TLC < 5000/mm³

ANC < as per Manroe chart for term and Mouzinho's chart for very LBL (VLBW) infants

Immature/ total neutrophil > 0.2

Micro-ESR > 15mm in 1st hr

CRP > 1mg/dl

Sepsis screen is considered positive if two of the above values are positive. If the screen is negative but clinical suspicion persists, then it should be repeated. If the screen is still negative, sepsis can be excluded.

Lumbar puncture (LP)

In Early onset neonatal sepsis, lumbar puncture is indicated in the presence of a positive blood culture or if the clinical examination is consistent with septicemia. While in cases of late onset sepsis, LP should be done in all infants prior to starting antibiotics.

Table-1: Normal values of CSF in newborn Period

| | Term | Preterm |
|-----------------------------|-------------|--------------|
| Cells | | |
| WBCs | 7 (0-32) | 9 (0-29) |
| PMN Cells | 61 % | 57 % |
| Protein (mg /dl) | 90 (20-170) | 115 (65-150) |
| Glucose (mg /dl) | 52 (34-119) | 50 (24-63) |
| CSF: blood (glucose) | 81 (44-248) | 74 (55-105) |

NEWER DIAGNOSTIC TESTS FOR DIAGNOSIS OF NEONATAL SEPSIS

Newer diagnostic tests can be grouped into:

- Acute phase reactants
- Cell surface markers
- Granulocyte colony stimulating factor
- Cytokines
- Molecular genetics
- Molecular cell proteomics

Acute phase reactants

These groups of endogenous peptides are produced by the liver as part of an immediate response to infection or tissue injury. These reactants are *C reactive protein, procalcitonin, fibronectin, haptoglobin, lactoferrin, neopterin* and *oromucosoid*

TREATMENT OF INFANTS WITH SUSPECTED EARLY-ONSET SEPSIS

The most common pathogens responsible for early-onset neonatal sepsis are GBS and *Escherichia coli*. A combination of ampicillin and an aminoglycoside (usually gentamicin) is generally used as initial therapy. Third-generation cephalosporins represent alternative to an aminoglycoside. But several

studies have reported rapid development of resistance with the use of cefotaxime and prolonged use of third-generation cephalosporins is a risk factor for invasive candidiasis [11]. Use of cefotaxime should be restricted for use in infants with meningitis attributable to Gram-negative organisms because of excellent CSF penetration [12]. Bacteremia without an identifiable cause of infection is usually treated for 10 days. Uncomplicated meningitis is treated for a minimum of 14 days. Other focal infections like cerebritis, osteomyelitis, endocarditis, are treated for longer durations. Gram-negative meningitis is treated for minimum of 21 days or 14 days after the culture turns to be negative, whichever is longer. Treatment of Gram-negative meningitis should include cefotaxime and an aminoglycoside till results of microbial susceptibility are known.

CONCLUSIONS

Neonatal sepsis is a major cause of morbidity and mortality during neonatal period. Diagnostic tests for neonatal sepsis apart from blood or CSF cultures are useful for identifying infants with a low probability of sepsis but not at identifying infants likely to be infected. Lumbar puncture is not required in all infants with suspected sepsis but should be performed in infants with signs of sepsis who can safely undergo the procedure, for infants with a positive blood culture, and infants who do not respond to antimicrobial therapy in the expected manner. The optimal treatment is broad-spectrum antimicrobial agents (ampicillin and an aminoglycoside). Once the pathogen is identified, antimicrobial therapy should be according to antimicrobial sensitivity and should be discontinued at 48 hours in clinical situations in which the probability of sepsis is low.

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