Management of Early Onset Neonatal Sepsis
Full Clinical Guideline

Reference no.: CG-NICU/4076/22

1. Introduction

Early onset neonatal infection (EONI) is a significant cause of mortality and morbidity in newborn infants. Infections account for 10% of neonatal mortality in the UK [1] and avoiding delays in recognising and treating infants at risk of infections is a priority for parents and health care providers. The updated NICE guideline (April 2021) for Neonatal infections[2] provides guidance "to reduce delays in recognising and treating infections and prevent unnecessary use of antibiotics."

This guidance is based on the recommendations made by the NICE guideline NG195 [2].

2. Aim and Purpose

- To reduce the risk of EONI
- To ensure early and adequate treatment of infants at risk of EONI
- To prevent unnecessary use of antibiotics

3. Definitions, Keywords

Early onset neonatal infection (EONI): neonatal infection less than 72 hours after birth

Late onset neonatal infection (LONI): neonatal infection 72 hours or more after birth

4. Main body of Guidelines

1.1 Identifying infants at risk of EONI

1.1.1 All infants

All infants should be evaluated for risk of factors for EONI within one hour of birth.

- Assess presence of any **risk factor for EONI** (Table 1)

Assess infant for any clinical indicators of EONI (

- Table 2)

If there are any risk factors or clinical indicators

- Perform an immediate clinical assessment
- Review maternal and neonatal history
- Conduct a physical examination of the infant including assessment of vital signs

1.1.2 Infants of mothers who have group B streptococcus identified within 72 hours after infant's birth

- Ask and document if those directly involved in the infant's care (family or healthcare professional) have any concerns
- Assess and identify any risk factor for EONI (Table 1)

Assess and identify and clinical indicator of EONI (

- Table 2)

Further clinical management decided on the presence of risk factors or clinical indicators

Table 1. Risk factors for early-onset neonatal infection, including "red flags"

Red flag risk factor
• Suspected or confirmed infection in another baby in the case of a multiple pregnancy.
Other risk factors
• Invasive group B streptococcal infection in a previous baby or maternal group B streptococcal colonisation, bacteriuria, or infection in the current pregnancy • Preterm birth following spontaneous labour before 37 weeks' gestation • Confirmed rupture of membranes for more than 18 hours before a preterm birth • Confirmed prelabour rupture of membranes at term for more than 24 hours before onset of labour • Intrapartum fever higher than 38°C if there is suspected or confirmed bacterial infection • Clinical diagnosis of chorioamnionitis

Table 2. Clinical indicators of possible early-onset neonatal infection (observations and events in the baby), including "red flags"

Red flag clinical indicators
• Apnoea (temporary stopping of breathing) • Seizures • Need for cardiopulmonary resuscitation • Need for mechanical ventilation • Signs of shock
Other clinical indicators
• Altered behaviour or responsiveness • Altered muscle tone (for example, floppiness) • Feeding difficulties (for example, feed refusal) • Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distention • Abnormal heart rate (bradycardia or tachycardia) • Signs of respiratory distress (including grunting, recession, tachypnoea) • Hypoxia (for example, central cyanosis or reduced oxygen saturation level)

- Persistent pulmonary hypertension of newborns
- Jaundice within 24 hours of birth
- Signs of neonatal encephalopathy
- Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors
- Unexplained excessive bleeding, thrombocytopaenia, or abnormal coagulation

1.2 Management decisions

In infants with any red flag or with 2 or more "non-red flag" risk factors or clinical indicators

- Perform investigations (See section 1.3)
- Start antibiotics (see section 1.4), without waiting for results of the investigations
- Give antibiotics as soon as possible and **always within one hour of making the decision**

In infants without red flags and only 1 risk factor or 1 clinical indicator,

- Withhold antibiotics and investigations unless other concerns
- Monitor infant for at least 12 hours using the newborn early warning system

In infants without any red flags, risk factors, or clinical indicators

- Provide routine postnatal care

1.3 Investigations before starting antibiotics in infants who may have EONI

- Take a **blood culture** sample before giving the first dose of antibiotics
- C-reactive protein (CRP)
- Full blood count (FBC)
- Lumbar puncture (LP) if
  - There is a strong clinical suspicion of EONI
  - There are signs or symptoms suggesting meningitis

Do not **routinely** perform

- Urine microscopy or culture
- Skin swab microscopy or culture

1.4 Antibiotics for suspected EONI

- Intravenous (IV) benzyl penicillin and gentamicin (see Table 3)
- Other antibiotics may be used, in discussion with the Service Consultant and microgeological advice e.g., suspected listeria; maternal chorioamnionitis with positive cultures with known organisms)

Table 3. Recommended doses for first line antibiotics for Early Onset Neonatal Infection

Drug	Dose	Age	Frequency
Gentamicin*	5mg/kg	< 7days	36 hourly

		≥ 7 days	24 hourly
Benzylpenicillin	25mg/kg (rounded **UP** to the nearest 10mg)	< 7days	12 hourly**
		7 – 27 days	8 hourly***
		≥ 28 days	6 hourly***
***See separate Gentamicin chart for more information (Derby site only)**			

** If baby appears very unwell, can shorten interval to 8 hourly, based on clinical judgement.

***increased if necessary to 50 mg/kg in severe infection. Where doses are prescribed at 50mg/kg, the dose must be rounded DOWN to the nearest 10mg to be given as a IV injection, or prescribed as an infusion.

1.5 Investigations during antibiotic treatment for EONI

- Repeat CRP 18-24 hours after presentation*
- Consider LP if
  - Blood culture is positive (other than coagulase negative staphylococcus)
  - Infant's clinical condition has not improved with antibiotic treatment
  - There is a strong clinical suspicion of infection
  - There are clinical symptoms or signs suggesting meningitis

*LP may be considered if the CRP is >30 or if there are clinical concerns.

1.6 Duration of antibiotic treatment

1.6.1 In infants given antibiotics for risk of EONI

Stop antibiotics at **36 hours** if

- Blood culture is negative
- Initial clinical suspicion was not strong
- Infant is well with no clinical indicators of possible infection
- CRP levels and trends are reassuring

1.6.2 In infants who have strongly suspected EONI but negative blood culture

Infants may be strongly suspected to have EONI despite a negative blood culture if there are strong clinical concerns or the CPR trend is worrying

- Give antibiotics for **7 days**

If antibiotics are continued longer than 36 h despite negative blood cultures, infant should be reviewed at least once every 24 h to consider if antibiotics can be stopped depending on the

- the level of initial clinical suspicion of infection *and*
- the baby's clinical progress and current condition *and*
- the levels and trends of C-reactive protein

1.6.3 Infants with blood culture positive EONI

- Give antibiotic as per the pathogen identified – seek advice from the microbiology team
- For EONI due to group B streptococcus (without meningitis), given antibiotics for 7 days

- If Gram negative sepsis is suspected, another antibiotic that is active against Gram-negative bacteria (for example, cefotaxime) should be added to the benzylpenicillin and gentamicin regimen. If Gram-negative infection is confirmed, benzylpenicillin should be stopped.

1.7 Meningitis

1.7.1 If meningitis is suspected but organism is unknown

- Treat with amoxicillin and cefotaxime

1.7.2 If meningitis is suspected to be caused by Gram-positive bacterium

- Continue treatment with amoxicillin and cefotaxime
- Seek expert microbiological advice

1.7.3 If meningitis is suspected to be caused by Gram-negative bacterium

- Stop amoxicillin, treat with cefotaxime alone

1.7.4 If meningitis is due to Group B streptococcus (blood or CSF culture)

- Treat with IV benzyl penicillin (50mg/kg every 12hours) for at least 14 days

AND

- Gentamicin for at least 5 days – as per Trust protocol

1.7.5 If meningitis is due to listeria (blood or CSF culture)

- Treat with amoxicillin or gentamicin

1.8 Discharge

- Consider prompt discharge after antibiotic treatment
- Ensure parents are informed about the treatment, further risk of infection and points of contact for advice

5. References (including any links to NICE Guidance etc.)

1 Office for National Statistics. Child and infant mortality in England and Wales: 2018. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/childhoodinfantandperinatalmortalityinenglandandwales/2018#neonatal-causes-of-death (accessed 13 Jul 2021).

2 NICE. Neonatal infection: antibiotics for prevention and treatment. 2021.https://www.nice.org.uk/guidance/ng195/resources/neonatal-infection-antibiotics-for-prevention-and-treatment-pdf-66142083827653

6. Documentation Controls

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