Screening for early onset neonatal sepsis in asymptomatic infants

Early onset neonatal sepsis (EONS) causes significant morbidity and mortality and, therefore, infants who are either at risk of infection or appear unwell are promptly screened and antibiotics commenced. The aim of this study was to determine whether nationally recognised maternal and neonatal risk factors, clinical indicators and laboratory results correctly identified infants with EONS.

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Keywords

early onset sepsis; neonatal; infection; C-reactive protein;

Key points

Kaltsogianni O., Nolan I., Hickey A., Greenough A., Kassim Z. Screening for early onset neonatal sepsis in asymptomatic infants. *Infant* 2017; 13(4): 152-53.

1. The NICE guideline provides a strategy for determining which infants undergo septic screening based on risk factors, and biochemical and clinical parameters.
2. This has led to investigations and prolonged courses of antibiotics in large numbers of healthy infants.
3. There is a need for more accurate predictors of sepsis so that unnecessary treatment procedures and antibiotics are avoided.

Early onset neonatal sepsis (EONS) represents a potential cause of significant morbidity and mortality. Therefore, infants who are either suspected to be at risk of infection because of maternal risk factors or appear unwell are promptly screened and antibiotics commenced. The optimum use of antibiotics remains a key priority in order to minimise the impact of treatment for healthy babies and their families and to avoid the development of antibiotic resistance, but are nationally recognised maternal and neonatal risk factors, clinical indicators and laboratory results correctly identifying infants with EONS?

Methods

Data were retrospectively collected from all infants who received antibiotics for suspected sepsis in a postnatal ward setting at King's College Hospital during a six-month period between September 2014 and March 2015. All infants who developed clinical symptoms requiring admission were excluded. The relevant risk factors and clinical indicators of EONS as defined by the National Institute for Health and Care Excellence guideline (NICE CG149) were reviewed.[1,2] Among others, these include:

- maternal risk factors, eg colonisation with Group B Streptococcus (GBS) in the current pregnancy, prolonged rupture of membranes (PROM) (>24 hours prior to birth) and maternal pyrexia (>38°C) in labour
- neonatal risk factors and clinical indicators, eg prematurity (<37 completed weeks' gestation), transient respiratory distress, irritability or poor clinical condition at birth.

C-reactive protein levels (CRP) and microbiology results from each patient were also recorded.

Results

During the six-month period, there were 2,699 live births; 244 (9%) of infants underwent a partial septic screen (blood culture and a minimum of two CRP levels) and were treated with antibiotics as per local policy (cefotaxime for at least 48 hours until the blood culture results were available). The outcomes of the screening for suspected EONS in asymptomatic infants can be seen in **TABLE 1**.

The majority (129) of infants were screened on the presence of a single risk factor or clinical indicator; 33 infants had a background of maternal GBS colonisation and 96 had one clinical indicator.

The other infants were screened and treated because of clinical suspicion of sepsis; they had 'soft markers' for sepsis but they were not unwell enough to require admission. These included transient tachypnoea and grunting, feeding intolerance and poor perinatal adaptation with quick recovery.

Overall there was only one positive blood culture, which was GBS. The indication for septic screening in this case was maternal pyrexia in labour. The baby's CRP level was 60.5mg/L.

Thirty-two babies had a lumbar puncture as their CRP levels were greater than 10mg/L, their mothers had sepsis or chorioamnionitis or the infants were perceived to have clinical signs of sepsis. There were no positive cerebrospinal fluid (CSF) cultures.

In 79 (32.4%) of the cases, inflammatory markers remained negative (CRP <2mg/L).

The main indications for screening were suspected maternal sepsis or chorioamnionitis followed by poor clinical condition at birth and maternal GBS colonisation with inadequate intrapartum antibiotic prophylaxis.

Overall, 25 (10%) infants received antibiotics for at least five days; one due to a positive blood culture and the remaining 24 in view of high CRP levels.

Indications for screening		Number of infants (n)	Microbiology results		Number of infants receiving antibiotics for >5 days	CRP <2mg/L
			Blood culture	CSF culture		
Maternal GBS colonisation	Inadequate IAP	33	Negative	Negative (n=4)	1	14
	Additional risk factor/ clinical indicator	17	Negative			
Maternal chorioamnionitis		59	GBS (n=1)	Negative (n=15)	15	28
Clinical indicators*	One clinical indicator	96	Negative	Negative (n=13)	9	37
	Two clinical indicators	39				
Total		**244**	**1**	**0**	**25**	**79**

TABLE 1 Outcomes of screening for suspected early onset neonatal sepsis in asymptomatic infants. Key: CSF = cerebrospinal fluid, CRP = C-reactive protein, GBS = Group B Streptococcus, IAP = intrapartum antibiotic prophylaxis, GBS. *Transient respiratory distress, feeding intolerance, poor perinatal adaptation.

Discussion

The incidence of EONS in the UK is around 0.9 per 1,000 live births and 0.9% of all neonatal admissions.[3] EONS accounts for 16% of all neonatal mortality.[4] Some studies have shown that, due to insufficient detection methods, culture-negative infection occurs frequently.[5] The fear of infection and its consequences has led to a majority of newborns receiving antibiotics unnecessarily.[6] For this reason, NICE created its guideline with an aim to prioritise the treatment of sick newborns and rationalise the use of antibiotics for healthy babies.[1-2]

This study aimed to examine whether nationally acclaimed maternal and neonatal risk factors and clinical indicators, and laboratory results (blood culture and C-reactive protein levels) correctly identified newborns with EONS at a postnatal ward setting of a tertiary teaching hospital. The data demonstrated variation in practice with regards to screening newborn infants for suspected EONS; in the majority of the cohort antibiotics were commenced on the presence of a single risk factor or clinical indicator. This may have been due to the concern of the clinician that the infant appeared unwell or diagnostic dilemma and fear of missing an underlying infection.

Microbiology, including blood and CSF cultures, remained negative in all but one of our patients regardless of the increase in CRP levels or the degree of clinical suspicion of sepsis. This is in agreement with previous evidence suggesting that microbial results are characterised by low sensitivity and specificity.[7-8] CRP levels increased in 68% of cases and guided decisions with regards to further investigations such as performing lumbar puncture and treatment duration.

Although CRP levels may be normal at the early stages of infection, normal values at 24-48 hours hold a high predictive ability for ruling out an infection.[9] Approximately 10% of the infants received antibiotics for a minimum of five days; this decision was based mainly on the presence of raised CRP levels (and positive microbiology in one case).

Diagnostic dilemmas and variation in management of healthy newborns with suspected EONS is due to a lack of rapid and reliable tests of sufficient sensitivity and specificity. The national guidance should be followed as it currently represents the most robust evidence available but future research should focus on the development of more accurate and reliable diagnostic tools that would assist the clinician in decision making. In the meantime, neonatal units should aim for earlier blood culture reporting and regular review of whether to continue antibiotic treatment.

Conclusion

Confirmed early onset sepsis in the postnatal ward setting is uncommon, yet a large number of newborn infants are screened and treated. Optimisation of intrapartum antibiotic prophylaxis, combined with more accurate predictors of infection and earlier reporting of blood culture results are required to minimise the impact of treatment on healthy babies and their families and avoid the development of antibiotic resistance. In addition, these steps will reduce unnecessary hospital stays with relevant cost savings.

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