A Less Invasive Approach to Screening for Early Onset Neonatal GBS

Abstract

S Glackin, J Miletin, AM Deasy
Combe Women & Infants University Hospital, Cork St, Dublin 8

Recent recommendations for the management of an asymptomatic term infant with one septic risk factor for Group B Streptococcus (GBS) invasive disease have advised a clinical approach. Following a previous audit in our unit which showed that high numbers of asymptomatic infants were receiving antibiotics, a new protocol was introduced which emphasised the importance of clinical examination. This study assessed the safety and efficacy of this new protocol through chart review of 1855 eligible infants. We found a statistically significant decrease (P<0.0001) from 444 (19%) to 121 (6.5%) in the total number of term infants who underwent septic evaluations and received antibiotics. 241 asymptomatic infants with one septic risk factor were managed conservatively. No eligible infants had GBS invasive disease during the three month study period. The new protocol is a safe and effective tool for evaluating infants at risk of GBS invasive disease.

Introduction

Neonatal sepsis is a devastating condition associated with significant morbidity and mortality most commonly caused by GBS. The incidence for early onset GBS (EOGBS) invasive disease varies from 0.35/1000 live births in the U.S to 1/1000 live births in the U.K and Ireland. 15-40% of pregnant women are colonised with GBS. Case fatality rate is approximately 2-3% for EOGBS disease in term infants. The risk of sepsis in an asymptomatic infant with risk factors for sepsis is low but clinically significant (0.5-1.0%). However, most infants (approx. 90%) who develop EOGBS invasive disease will be symptomatic within 24 hours after birth. Only 1% of these infants will have had at least one perinatal septic risk factor. In 2012 a survey of the different guidelines used in the UK showed little consensus on this issue with 125 different guidelines identified for 157 neonatal units. The RCOG guidelines recommend that infants with one GBS septic risk factor and no clinical signs should be carefully observed for the first 24 hours. In 2015 the Centre for Disease Control and prevention (CDC) changed their guidelines to improve the management of asymptomatic infants at risk for invasive EOGBS disease and thereby decrease unnecessary evaluation, antibiotic exposure and separation of mother and infant.

Many units use broad-spectrum intravenous (IV) antibiotics such as Penicillin to cover GBS and Gentamycin to cover E-coil. The toxic effects of Gentamycin are well known including ototoxicity and nephrotoxicity. A single dose of a Gentamicin can cause permanent hearing loss in genetically predisposed individuals.12 Broad-spectrum antibiotics can also increase the risk of resistant bacterija at a later stage. Early infant antibiotic exposures have also been linked to increased risk of wheezing in children, and can affect the developing intestinal microbiome, increasing the risk of gastrointestinal disease, as well as intussusception and autoimmune diseases. However in the case of suspected neonatal invasive disease, these antibiotics are the most effective. In 2011 a retrospective audit on septic evaluations was performed in our neonatal unit. Following this, a new protocol, Figure 1, was introduced for the management of asymptomatic term infants. The new protocol recommended that for suspected maternal chorioamnionitis or in a symptomatic infant, a septic evaluation and antibiotic exposure are always indicated. However, in infants with one septic risk factor who are asymptomatic, the new protocol recommended that four hourly clinical observations be performed by the nursing staff and that four and twelve hourly medical reviews be performed for 48 hours by the senior house officer (SHO).

The primary outcome of this study was the number of septic evaluations performed and antibiotic exposure in asymptomatic term infants at risk of GBS invasive disease and thereby decrease unnecessary evaluation, antibiotic exposure and separation of mother and infant.

Methods

Two independent reviewers (SG, AMD) performed a retrospective chart review of the babies born at term (≥ 37+0 weeks of gestation) from 1st July to 30th September 2012 in our tertiary maternity centre (Combe Women and Infants University Hospital). We excluded infants with significant congenital defects such as congenital heart disease, spina bifida, and surgical gastrointestinal conditions which would increase their risk of sepsis. Details of birth gestation, mode of delivery, presence or absence of septic risk factors, maternal antibiotics, Apgar scores, clinical symptoms, blood tests performed, blood results and duration of any antibiotics were recorded. The clinical symptoms observed and identified as symptoms of suspected sepsis are listed in Table 1. Neither written informed consent nor research ethic committee approval was sought as this was an audit of the changed clinical practice in our centre. The data was analysed using a PC-based statistics package (StatsDirect version 3.0.97). Descriptive statistics and Fisher exact test were used for the outcomes as appropriate.
Results

The results of the primary audit showed that 444 (19%) out of 2375 term infants born in the Coombe Hospital in the three month audit period in 2011 had septic evaluations which included an FBC, a serum CRP and a blood culture performed and received IV antibiotics. This was similar to international data (approx. 15%). Of these 444 septic evaluations, 242 (54.5%) were asymptomatic infants with one septic risk factor such as prolonged rupture of membranes (PROM) or maternal GBS positive high vaginal swab (HVS). The other 202 (45.5%) were performed on symptomatic infants with suspected invasive disease or those with multiple septic risk factors. Of the total septic evaluations performed, 2.5% (11) had positive blood cultures, 1.2% (5) of which were GBS positive and only one of whom had a septic risk factor. All of these GBS positive infants were clinically symptomatic. They concluded that the 4 (80%) of GBS positive infants had no known septic risk factors and that the 0% (0 of 242) asymptomatic infants who had septic evaluations and antibiotics for one septic risk factor had a positive blood culture or raised CRP. The annual incidence of EOGBS in our hospital ranged from 0.45/1000 live births to 0.68/1000 live births between 2009 and 2011. Following the introduction of the new protocol, Figure 1, a re-audit was performed. 1855 charts of infants who were eligible for inclusion were reviewed from the time period.

We found that 344 infants had septic risk factors and of these infants, 83 (4.5%) had septic evaluations and received IV antibiotics immediately after delivery. See Figure 2. Of the initial septic evaluations, two had a raised CRP while none had a positive blood culture. Of these infants, five were clinically unwell and received antibiotics for >48 hours despite their negative blood cultures. 261 infants with one septic risk factor were allocated as per the new protocol to four hourly observations for 48 hours if the mother had received adequate intrapartum antibiotics (IAP) (i.e. >2 doses or 1 dose > 4 hours before delivery) or four hourly observations and a four and twelve hourly medical review for 48 hours if the mother had received inadequate IAP. 241 infants remained asymptomatic. 20 infants were
identified as symptomatic on the postnatal ward. These infants all had septic evaluations performed on identification and received IV antibiotics.

None of these infants were blood culture positive however 6 had raised CRPs and received >48 hours IV antibiotics. See Table 1. All 241 infants in this time period had no septic risk factors. 18 infants were identified as having clinical symptoms of sepsis either at birth or during routine observations/ checks on the postnatal ward. None had a blood culture positive sepsis, however one had a blood culture positive suspected as contamination. Two other infants with rash had >48 hours IV antibiotics. We calculated that at least eleven thousand five hundred euro was saved by the unit in this three month audit period due to less on call blood tests being performed and analysed, which equates to annual savings of nearly fifty thousand euro.

**Discussion**

As previously mentioned, the RCOG and the CDC have recently changed their guidelines encouraging a more clinical and less invasive approach to infants with one septic risk factor. We confirmed our hypothesis that we are performing less septic evaluations and giving fewer courses of antibiotics. We reduced the numbers of septic evaluations performed and antibiotics given from 19% to 6.5% (p<0.001), of the total number of term babies born in those three months. In 2011, 242 (10%) of all term infants had septic evaluations and received antibiotics immediately after birth for one septic risk factor despite being asymptomatic, while in 2012, 241 (13%) asymptomatic infants with one septic risk factor were safely managed conservatively.

We also showed that four hourly clinical observations and four and twelve hourly medical reviews of infants with one septic risk factor successfully identified symptomatic infants. There was no difference between the numbers of infants with and without septic risk factors that were identified as symptomatic on the postnatal ward. No infants became significantly unwell and there were no known morbidity and no mortalities. We cannot calculate a sensitivity or specificity of our screening tool as we do not have any blood culture confirmed sepsis during this period. It was argued that we could not definitively state that no unwell infants had been missed, however as all infants get a postnatal check before discharge, a symptomatic infant would have been identified. In the US and in many European countries, all mothers are screened for GBS antenatally, with a positivity rate of 15-40%.

The policy is that these mothers should be covered with IAP, usually in the form of a Penicillin. However, it has been found that even with adequate IAP, EGBS infection in term infants in these countries is still a significant burden. In Ireland and in the UK, screening is not performed routinely. IAP are recommended in certain situations in our hospital such as intrapartum pyrexia >38°C, previous baby with GBS disease or delivery at < 37 weeks with PROM >18 hours. However, the evidence for this is inconsistent. Some centres perform 18 hour CRP measurement as an initial test. In our hospital, this is not performed. This has a 64% sensitivity and 56% specificity with a negative predictive value (NPV)of 93% and a positive predictive value (PPV) of 14%. However, many diagnostic tests for neonatal sepsis have a poor PPV. The use of procalcitonin can also be used in the evaluation of sepsis.

We did not evaluate late onset GBS (LOGBS) invasive disease, which has an incidence of 0.24 per 1000 live births for infants< 2000 grams at birth: a population-based study. Pediatrics. 2000;106:256-263.


Neonatal antibiotic treatment is unnecessary to well term infants with one septic risk factor. We emphasise the importance of clinical exam in all cases whether or not neonatal septic risk factors are known.

**Correspondence:** S Glackin
Our Lady's Childrens Hospital, Crumlin, Dublin 12

**References**


