CONGENITAL PNEUMONIA AND EARLY ONSET NEONATAL SEPSIS AT NORTHWICK PARK HOSPITAL

HAS OUR GBS SCREENING PROGRAMME MADE A DIFFERENCE?

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Stronger Together

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Introduction

- Congenital pneumonia (CP) and early onset sepsis (EOS) are important causes of neonatal morbidity and mortality
- GBS infection is the commonest cause of EOS
- Early onset Group B Streptococcal (EOGBS) infection most frequently presents with sepsis and pneumonia
- Intrapartum antibiotic prophylaxis (IAP) of maternal GBS carriers has reduced the incidence of invasive EOGBS infection in many countries

Background

- UK incidence of culture-proven EOGBS infection: 0.38 cases per 1000 live births in 2013 (PHE)

- Prospective UK data collected over 1 year for neonates who required a septic screen in the first 72 h of life indicated a combined rate of definite and probable EOGBS infection of **3·6 per 1000 live births***

- This estimate indicates a much greater disease burden in the UK than that suggested by figures of culture-proven sepsis, and lends support to the need for prevention strategies *

Estimated early-onset group B streptococcal neonatal disease

Suzanne Luck, Michael Torny, Katrina d'Agapeyeff, Alison Pitt, Paul Heath, Aoadhan Breathnach, Alison Bedford Russell. Lancet. 2003 Jun 7;361(9373):1953-4

Hypothesis

Universal maternal GBS screening + intrapartum antibiotics will reduce the incidence of not only invasive EOGBS, but also early onset neonatal sepsis and congenital pneumonia

Objective

To review the number of cases of CP and EOS pre and post the introduction of universal maternal GBS screening in March 2014

Methods

- Search criteria
  - All cases with a diagnosis of ‘sepsis’, ‘sepsis suspected’, ‘sepsis – presumed’, ‘unwell with negative microbiology’, ‘GBS sepsis’ or ‘congenital pneumonia’ on Badgernet (electronic neonatal database)

- Review of electronic and paper case notes of neonatal admissions from March 2011- April 2015

Inclusion criteria

- Born at NPH after March 2011 and admitted to NNU
- ≥35 weeks gestation
- Cases meeting criteria for EOS and CP

Case definitions of EOS and CP

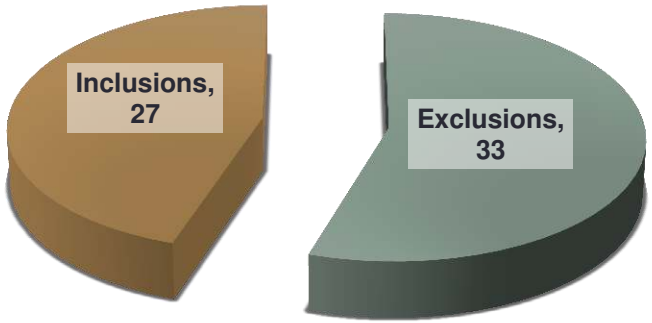
- EMEA definition of EOS
  - 2 clinical and 2 laboratory criteria in the presence of suspected or culture-proven sepsis (with onset <72h)

***European Medicines Agency Expert meeting on Neonatal and Paediatric Sepsis**, London, June 2010*

- CP defined as signs of respiratory distress + abnormal WCC/CRP + CXR changes consistent with infection

***Transient tachypnea of the newborn and congenital pneumonia: a comparative study.** Sandra Costa, Gustavo Rocha, Andreia Leitão & Hercília Guimarães. The Journal of Maternal-Fetal and Neonatal Medicine, 2012; 25(7): 992–994*

Total infections (EOS + CP)



n = 60

Screening

	Apr 2011-Mar 2012	Apr 2012-Mar 2013	Apr 2013-Feb 2014	Apr 2014-Mar 2015
Cases identified	20	14	19	7
Exclusions	10	6	13	4
Total infections	**10**	**8**	**6**	**3**
Total infections/ 1000 live births	**1.93**	**1.54**	**1.33**	**0.63**

Early Onset Sepsis (EOS)

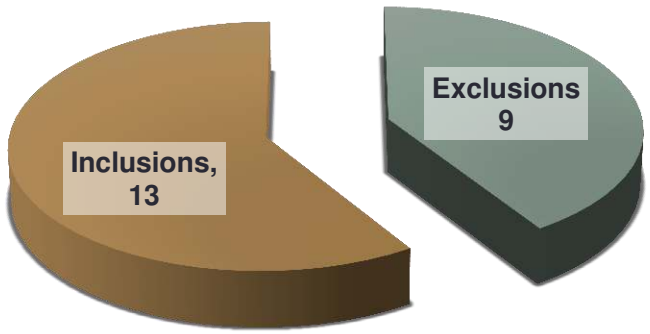
n = 38

Screening

	Apr 2011-Mar 2012	Apr 2012-Mar 2013	Apr 2013-Feb 2014	Apr 2014-Mar 2015
Cases identified	14	2	15	7
Exclusions	8	1	11	4
EOS cases	**6**	**1**	**4**	**3***
EOS cases / 1000 live births	**1.16**	**0.19**	**0.89**	**0.62**

*1 mother was GBS colonised and received adequate IAP

Congenital pneumonia (CP)



n = 22

Screening

	Apr 2011-Mar 2012	Apr 2012-Mar 2013	Apr 2013-Feb 2014	Apr 2014-Mar 2015
Cases identified	6	12	4	0
Exclusions	2	5	2	0
CP cases	**4**	**7***	**2**	**0**
CP cases/1000 live births	**0.77**	**1.35**	**0.44**	**0**

*2 babies GBS surface swab positive

The impact of screening so far

Category	Pre-screening rate (Apr 2011-Feb 2014)	Post-screening rate (Apr 2014-Mar 2015)	Ratio (95% CI) *	p-value
Total infections	1.61	0.63	0.39 (0.12, 1.29)	0.12
EOS	0.74	0.63	0.85 (0.24, 3.03)	0.8
CP	0.87	0	0.11 (0.01, 1.79)	0.12

(*) Calculated as post-screening rate/ pre-screening rate

Discussion

- The introduction of universal maternal GBS screening was associated with a reduction in the number of cases of EOS and CP
- No cases of CP so far post introduction of screening
- Rates of reduction not statistically significant
  - Small numbers
  - Only 11 months of post-screening data
- Confounding factors?

Conclusion

- Bradford Hill criteria for causation
  - Temporal association
  - Biological plausibility
  - Coherence

Sir Austin Bradford Hill, 1897 - 1991

- Preliminary data lacking power and statistical significance
- Further studies are necessary to confirm our observations
- Ongoing data collection in progress

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Table 1. Clinical and laboratory criteria for inclusion in neonatal sepsis clinical trials defined by the EMA

Clinical signs	Laboratory signs
Modified body temperature: • core temperature >38.5°C or <36°C **AND/OR** • temperature instability **Cardiovascular instability:** • bradycardia [mean HR <10th percentile for age in the absence of external vagal stimulus, β-blockers or congenital heart disease **OR** otherwise unexplained persistent depression over a 0.5–4 h time period] **OR** • tachycardia [mean HR >2 SD above normal for age in the absence of external stimulus, chronic unexplained persistent elevation over a 0.5–4 h time period] **AND/OR** • rhythm instability • reduced urinary output (<1 mL/kg/h) • hypotension (mean arterial pressure <5th percentile for age) • mottled skin • impaired peripheral perfusion **Skin and subcutaneous lesions:** • petechial rash • sclerema **Respiratory instability:** • apnoea episodes **OR** • tachypnoea episodes (mean respiratory rate over 2 SD above normal for age) **OR** • increased oxygen requirements **OR** • requirement for ventilatory support **Gastrointestinal:** • feeding intolerance • poor sucking • abdominal distension **Non-specific:** • irritability • lethargy • hypotonia	**WBCs:** • $<4\times10^9$ cells/L **OR** • $>20\times10^9$ cells/L **Immature to total neutrophil ratio (I/T):** • >0.2 **Platelet count:** • $<100\times10^9$/L **CRP:** • >15 mg/L **OR** **Procalcitonin:** • ≥2 ng/mL **Glucose intolerance** (confirmed at least twice): • hyperglycaemia (blood glucose >180 mg/dL or 10 mM) **OR** • hypoglycaemia (blood glucose <45 mg/dL or 2.5 mM) When receiving age-specific normal-range glucose amounts **Metabolic acidosis:** • base excess <−10 mEq/L **OR** • serum lactate >2 nM

HR, heart rate; WBC, white blood cell.