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The Neonatal Early Onset Sepsis Calculator; in Clinical Practice

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Abstract

Aims
To determine the impact of applying the Neonatal Early Onset Sepsis Calculator (NEOSC) to clinical practice. We evaluated this multivariable risk prediction model, used in the assessment of infants >35 weeks GA, at risk of neonatal sepsis.

Methods
A retrospective, cohort study comparing the rates of blood culture use in a large maternity hospital before and after the introduction of the NEOSC. Cases were ascertained from the records of the Department of Microbiology. The key variables were the number of blood cultures (all gestational ages, <72 hours old), infant antibiotic use and sepsis rates. Data for three years prior to NEOSC use (January 2015 – December 2017) were compared with 15 months (January 2018 – Q1 2019) after it was implemented.

Results
Pre- and post- NEOSC use, the total blood cultures taken annually were: 1,312 (2015), 1,149 (2016), 1,319 (2017) and 702 (2018), 192 (Q1 2019) respectively, a statistically significant reduction [$p < 0.00001$, 95% CI]. There was no significant difference in rates of either: culture-confirmed GBS-sepsis [p value 0.18, 95% CI] or other-pathogen sepsis [p value 0.32, 95%CI] in term infants between the two periods. There was a significant reduction in antibiotic use in the first 24 hours of life (average 11.3% pre-NEOSC and 5.9% after NEOSC was implemented) [$p < 0.00001$, 95% CI].

Conclusion
The introduction of the NEOSC has reduced blood culture and antibiotic use. This has been achieved without any increase in infection rates.

Introduction

Group B Streptococcus (GBS) is a recognised cause of perinatal sepsis. In Ireland in 2018, 51 cases of invasive GBS were reported (annual rate 0.84 per 1000 live births),[1] figures in line with European and internationally reported rates (0.3-1/1000 births).[2,3,4,5,6,7] Prior to the introduction of the calculator, annual incidence of GBS sepsis in term infants at our centre ranged from 0.71-1.13 per 1000 births (see Table 2).

GBS is the most common cause of infection in term infants.[7] A wide spectrum of risk factors have to be considered when deciding whether to screen, investigate or treat newborn infants for Early Onset Sepsis. Risk factors include GBS positive screening, GBS bacteriuria, Premature Rupture of Membranes (PROM) > 18 hours and maternal fever >38 degrees. [8,9,10,11] Prior to the introduction of the NEOSC at our centre (Epoch 1), all symptomatic infants >35 weeks gestational age had a septic work up performed and received treatment dose IV antibiotics. All infants >35 weeks GA who were asymptomatic but had risk factors had a septic work up performed and received prophylactic doses of antibiotics. This demonstrates that without a weighting system, there is a tendency to over-investigate and

treat.[5,12] The over-zealous use of antibiotics and subsequent alteration in the neonatal microbiome has been linked with childhood conditions such as atopy, asthma, allergy and obesity, although these associations remain unproven to date.[13] The NEOS calculator is a clinical decision support tool that uses a composite of risk factors (gestational age, highest maternal antepartum temperature, GBS status, local incidence of EOS, duration of ROM and details of intrapartum antibiotic cover) along with a clinical examination, to produce an individual risk and instruct whether investigation and treatment are warranted. During Epoch 2, the NEOSC was used to evaluate otherwise asymptomatic infants who were deemed to have the aforementioned risk factors. Infants >35 weeks GA were examined in the delivery ward and further management guided by the NEOSC suggested management. All symptomatic or high risk infants received treatment as per Epoch 1. Medium risk infants were monitored with vital sign observations for 36 hours on the postnatal ward. Low risk infants were discharged to the postnatal ward for routine care.

The NEOSC was developed at Kaiser Permanente Hospital Facility in California, USA. A cohort study was performed at the investigating facility, which included 204,485 infants and found that the calculator reduced investigation and antibiotic use by up to half, with no difference in subsequent sepsis rates.[14] These results have been reproduced internationally.[15]

Methods

This was a single centre, retrospective study examining data from 1st January 2015 to 31st December 2017, before the NEOSC was introduced and comparing with data from 1st January 2018 to 31st March 2019, the 15 months following introduction of the calculator. Infants of all gestational ages who had blood cultures taken within the first 72 hours of life were included.

Differences between the two groups were analysed using a Chi-squared (χ^2) test, available at: (https://www.socscistatistics.com/tests/chisquare/default2.aspx). The level of significance was set at $P < 0.05$.

Results

There were 37,514 infants born and 4,674 blood cultures drawn (all gestational ages) between 1st January 2015 – 31st March 2019.

Blood culture and antibiotic use before and after implementation of sepsis calculator

Prior to the introduction of the NEOSC the total blood cultures taken per year were: 1,312 (2015), 1,149 (2016), 1,319 (2017). After the introduction of the NEOSC the total number of blood cultures drawn were: 702 (2018), 192 (Q1 2019), a statistically significant reduction [$p < 0.00001$, 95% CI]. The rates of blood culture per 1,000 live births prior to NEOSC implementation were: 140 (2015), 127 (2016), 153 (2017) compared with 89 (2018) and 76 (Q1 2019) after its introduction. (See Table 1)

Table 1: Annual birth, numbers of blood cultures, antibiotic use within 24 hours and rate of blood culture draw.

Year	2015	2016	2017	2018	January-March 2019
Total Babies (>500g)	9389	9037	8619	7923	2546
>37 weeks	8735	8428	7983	7310	2393
< 37 weeks	636	609	636	568	145
Missing GA	-	-	-	45	8
Number of blood cultures taken within first 72 hours of life (All gestational ages)	1312	1149	1319	702	192
Antibiotics use within the first 24 hours of life	11.5%	10.4%	12.1%	6.7%	5.1%
Rate of Blood Culture Drawn / 1000 live births	140	127	153	89	76

There was a significant reduction in antibiotic use in the first 24 hours of life, where an average of 11.3% received antibiotics before NEOSC and 5.9% were treated after NEOSC was implemented [$p < 0.00001$, 95% CI]. This represents an average 48% reduction. (See Table 1)

Sepsis rates before and after implementation of sepsis calculator

During the study period, there were a total of 47 blood cultures reported positive in the first 72 hours of life, for infants of all gestational ages. The annual incidence of GBS positive cultures in term infants were: 7 (2015), 6 (2016), 8 (2017), 1 (2018) and 2 (Q1 2019). The annual incidence of "Other pathogen" positive cultures in term infants were: 1 (2015), 0 (2016), 1 (2017), 1 (2018) and 1 (Q1 2019). There was no significant difference in rates of either: culture-confirmed GBS sepsis [*p* value 0.18, 95% CI] or sepsis by other pathogen [*p* value 0.32, 95%CI] in term infants before and after the introduction of the NEOSC. (See Table 2)

Table 2: Rate of GBS positive term infants, rate of positive blood culture (other pathogens) in term infants.

Year	2015	2016	2017	2018	January – March 2019
Rate of positive culture / 1000 term infants (all pathogens)	0.8	0.71	1	0.68	0.84
Rate of GBS positive culture / 1000 term infants	0.91	0.71	1.13	0.82	1.25

Discussion

The objective of this study was to examine changes in the numbers of blood cultures taken in the first 72 hours of life and subsequent rates of positive blood cultures after introducing the NEOSC calculator into practice. We found an average reduction of 41% in the number of blood cultures taken, following implementation of the calculator. We also found that antibiotic use within the first 24 hours of life was reduced by an average of 48%. Following the introduction of the sepsis calculator, the restriction of investigation and treatment was not associated with an increase in sepsis rates within the first 72 hours of life.

Limitations of this study include its retrospective nature and our method of data collection. We collected our data from laboratory records of total numbers of blood cultures taken annually and records of positive cultures; clinical data, such as the indication for septic work-up (whether the patient was symptomatic or asymptomatic) was not available. Our annual figures for the total number of blood cultures included data for infants of all gestational ages, therefore we were unable to directly compare the changes in the target population for the whom the tool is validated (asymptomatic infants >35 weeks gestational age). We did not directly compare the clinical decision pathways used between the first and second epochs.

Our findings suggest that the inclusion of the sepsis calculator as a clinical decision support tool in an Irish teaching hospital has been safe and effective. When integrated with existing protocols, the sepsis calculator provides a pragmatic approach to the assessment of at-risk infants, reducing workload, laboratory investigation and, critically, promoting antimicrobial stewardship.

In conclusion, our findings support more widespread use of the sepsis calculator within Irish clinical settings and incentive for future prospective validation of the tool within these settings.

Declaration of Conflicts of Interest:
The authors have no conflicts of interest to declare.

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