Noa Fleiss, MD PGY-3
Mentor: Sudha Kashyap MD

Assessment of Antibiotics Administration in Late Onset Sepsis in the NICU- A Quality Assurance Project

Background and Study Rationale:

Neonatal sepsis is a leading cause of morbidity and mortality in Neonatal Intensive Care Units (NICUs). It is an ongoing public health challenge accounting for tremendous health care costs; an estimated $700 million annually in the US. [1,2] Despite several collaborations to improve the diagnosis of neonatal sepsis, it continues to be a significant healthcare problem requiring further attention. [1]

The Institute of Medicine (IOM) has determined that maintaining quality care and patient safety requires adherence to six practice attributes, among which, timeliness and effectiveness have been widely acknowledged.[3] It is therefore essential to recognize and diagnose neonatal conditions that mandate time-sensitive management. Neonatal sepsis is one example, where timely administration of appropriate antibiotic treatment would significantly reduce the incidence of mortality and neurodevelopmental sequelae in this population.[4,5]

Neonatal sepsis is divided into early-onset sepsis (EOS) and late-onset sepsis (LOS), based on age.[6] EOS typically occurs within the first 72 hours of life, and is associated with intrauterine or transplacental exposures, frequently secondary to ascending infections from the maternal genital tract. LOS occurs after the initial 72 hours of life, and is typically associated with nosocomial or community acquired infections.[7] The incidence of LOS has increased rapidly over the last decade, in contrast to EOS, and is inversely proportional to gestational age and birth weight. The very low birth weight (VLBW) infants, weighing less than 1500g, are exceptionally susceptible due to their relatively longer NICU stay, use of invasive life sustaining interventions, and previous exposure to broad spectrum antibiotics.[7,8] Additionally, inherent risk factors, such as impaired host defense systems, limited amounts of normal endogenous flora, and reduced barrier function of skin, are all contributing factors to the vulnerability of this group.[7]

Timely diagnosis of neonatal LOS can be challenging. The clinical signs are often non-specific and indistinguishable from normal physiologic disturbances.[7,9] Core temperature, blood biomarkers, high or low white blood cell count, high I/T ratio, and low platelet count are only some examples of confounding factors that make the clinical diagnosis difficult.[2] This explains why adhering to a checklist corresponding

to “signs of sepsis” may not apply to neonates, as it does in older children and adults.[9] Nevertheless, obtaining immediate blood cultures and initiating antibiotic treatment, in every case of clinical suspicion of neonatal LOS, continues to be the gold standard.[9]

The New York State Department of Health passed “Rory’s Sepsis Regulations” after a twelve-year-old patient named Rory Staunton died secondary to severe sepsis in 2013. The new regulations require hospitals to follow an evidence-based checklist in their clinical approach to early recognition and treatment of children with suspected sepsis.[10] While the law is meant to improve early recognition and treatment in patients with suspected sepsis, it does state that “protocols for children may exclude newborns and infants in the NICU.”[11] While there are distinct characteristics and differences in response to infections by neonates that make them a different clinical subgroup, sepsis and severe infection can still lead to rapid decompensation and death even in neonates and premature infants. It is because of this that we wanted to evaluate our own practices in recognition and timely administration of antibiotics for LOS in the NICU.

Study Objectives:

1. To conduct a quality assurance project determining if infants in the NICU are administered antibiotics within the first hour of suspected late onset sepsis recognition.

2. To compare time to antibiotic administration in two subgroups: a) infants suspected to have late onset sepsis in the NICU before Pediatric Sepsis Protocol was instituted and b) infants suspected of late onset sepsis after Pediatric Sepsis Protocol.

3. If antibiotic administration is greater than 1 hour from time of suspected late onset sepsis, then reasons as to why there was a delay in antibiotic administration will be evaluated.

Study Design and Methods:

This study is a retrospective cohort study. Data collected will include Birth weight, Gestational Age, date and time of blood culture, date and time of antibiotics ordered and given.

Inclusion Criteria:

- Term and Pre-term infants admitted to the NICU and suspected of late onset sepsis from July 2013 – December 2013 when Pediatric Sepsis Protocol was not in place

- Term and pre-term infants admitted to the NICU and suspected of late onset sepsis from October 2014 to March 2015 when Pediatric Sepsis Protocol was in place
- Late onset sepsis suspected - determined by blood culture ordered

Exclusion Criteria:

- Early Onset Sepsis
- Infants receiving daily blood cultures while on ECMO
- Infants who underwent a sepsis rule out but no blood culture was drawn

Statistical Analysis:

1. Approximately 500 infants are admitted to the NICU over a six-month period and it is anticipated that 200 (40%) of these will be evaluated for sepsis during their stay in the NICU. In total data will be collected from the medical records of approximately 400 infants (200 infants for every 6 month period).

    a. Unpaired T – test will be used to compare the mean for time to antibiotic administration in the two retrospective cohorts.

    b. Power - 0.80, with alpha of 0.05
    Assuming an N of 200 in each subgroup with a presumed standard deviation of 2.5 hours – an effect size of 0.7 is anticipated.

2. Reasons for late administration of antibiotics will be coded with a numerical value from 0-9.
    0 = No reason given
    1= No access
    2 = Awaiting specimen collection
    3 = Awaiting culture results
    4 = Something else running in the IV
    5 = Patient reason (i.e. apnea, decompensation)
    6= Antibiotics not ordered
    7= Waiting on imaging
    8= Change of shift
    9 = Pharmacy problem

    a. Description of continuous variables will be reported using means, medians and standard deviations. An ANOVA will be conducted to assess the variance of the means between these subgroups

Confidentiality of Study Data:

Data will be de-identified after extraction from the medical record and each subject will be assigned a unique study ID number. A separate password-protected and encrypted spreadsheet that can match patients to their study ID numbers will be maintained by one person (Investigator) on an encrypted, password protected computer. All data will be encrypted on a password-protected computer with plan to securely dispose of subject identifiers at the end of the study. All data and results that are published will be stripped of any identifiers.

Privacy Protection:

To protect health information all data collected will be maintained in secure facilities.

Potential Risks:

The research involves no more than minimal risk of loss of confidentiality as the study is a chart review. We have done other studies involving chart reviews and there have been no confidentiality breeches.

Data Safety Monitoring:

No DSMC is required as this is a non interventional study and essentially a chart review. Confidentiality will be assured as described above in the Confidentiality of study data section.

Potential Benefits:

There will be no direct benefit to subjects as the study is a chart review. However, the data evaluated could lead to improving antibiotics administration in the future for infants cared for in the NICU.

References:

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