



EDITORIAL

“Less is more”: decreasing antibiotic days in the NICU^{☆,☆☆}

“Menos é mais”: diminuindo os dias de antibiótico na UTIN

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Decreasing antibiotic days, mortality, and sepsis-related mortality are critical goals for our patients in the neonatal intensive care unit (NICU). In a prospective design, this small study in a single NICU evaluated the implementation of diagnostic criteria for early-onset sepsis (EOS) and late-onset sepsis (LOS), focused on stopping antibiotics early if hematologic and CRP tests were within the normal range for neonates.

The study by Pinto et al.¹ targeted stopping antibiotics after 48 hours versus treating for a full course in culture-negative “possible infections”. This is important, as “possible infections” likely drives antibiotic usage and days. This study reduced EOS antibiotic days primarily by defining fewer EOS evaluations as “possible infections”, which roughly translated into receiving two days instead of seven days of antibiotics in the first week after birth.

LOS antibiotic days and diagnosis of LOS were not affected. This remains a challenging area. These findings are similar to studies of CLABSI bundles, which while demonstrating lower CLABSI rates, have not lowered antibiotic usage.² This may be partially explained in that most studies examining antibiotics and sepsis in the NICU do not include information on the definition of sepsis used and data on

other infections that contribute to antibiotic usage. These include, in part, urinary tract infections (UTIs), ventilator associated pneumonia (VAP), necrotizing enterocolitis (NEC), and focal bowel perforation. While we still struggle with diagnostic criteria for VAP in neonates in the NICU, especially in those with chronic lung disease, the diagnosis of UTI, NEC, and focal bowel perforation are more clearly defined. Additionally, improvements to diagnosing viral infections are needed in the NICU. If we are able to make a diagnosis of a viral infection, antibiotics would more readily be discontinued and at times replaced with an antiviral.

Obtaining a urine culture during LOS evaluation is still not standard practice, despite studies reporting an incidence of approximately 8% in infants < 1,500 grams.^{3–5} Studies often claim that blood cultures are not sensitive enough; however, the infection may not be in the bloodstream. LOS evaluations should include a urine culture, but there is still variation in practice in this area.

Prevention of infections remains a key to reducing antibiotic days after the first week of life. In the area of fungal infections, antifungal prophylaxis has been shown to significantly reduce the number of antifungal days for empiric, presumed, and culture-positive *Candida* infections.⁶

While mortality appeared to initially decrease, logistic regression did not find significance between groups for both total and sepsis-related mortality. Other studies have reported an association with an increased risk for mortality when third generation cephalosporins are frequently used for EOS.⁷ Specifically with treatment of culture-negative early-onset sepsis, the risk for NEC is increased.⁸

In the article’s discussion, early diagnosis and antibiotic use was hypothesized as a way to lower neonatal mortality

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☆☆ See paper by Pinto MC et al. in pages 450–5.

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with sepsis. This has been demonstrated in a recent study using an electronic monitoring system, since an early detection system of LOS (12-24 hours prior to clinical symptoms) found a significantly lower overall and sepsis-associated (within 30 days of infection) mortality.⁹

Limitations of the study include reasons for selection of the different antibiotic regimens and the lack of a specific definition for sepsis-related mortality.

From this study, other NICUs can examine whether they have similar practices already in place or if this is an area for quality improvement. It is likely that the post intervention rate for possible EOS of 44% can be further lowered. It would be insightful for larger studies and/or data sets to explore some of the same questions in this article. As this group and others continue to study antibiotic usage patterns, it will be critical to link treatment changes with important clinical outcomes in prospective studies. If we are able to do so, we will be able to provide additional evidence for future best practices.

Conflicts of interest

The author declares no conflicts of interest.

References

1. Pinto MC, Bueno AC, Vieira AA. Implementation of a protocol proposed by the Brazilian National Health Surveillance Agency (ANVISA) for antibiotic use in very low birth weight infants. *J Pediatr (Rio J)*. 2013;89:450-5.
2. Schulman J, Saiman L. Metrics for NICU antibiotic use: which rate is right? *J Perinatol*. 2011;31:511-3.
3. Tamim MM, Alesseh H, Aziz H. Analysis of the efficacy of urine culture as part of sepsis evaluation in the premature infant. *Pediatr Infect Dis J*. 2003;22:805-8.
4. Bauer S, Eliakim A, Pomeranz A, Regev R, Litmanovits I, Arnon S, et al. Urinary tract infection in very low birth weight preterm infants. *Pediatr Infect Dis J*. 2003;22:426-30.
5. Downey LC, Benjamin Jr DK, Clark RH, Watt KM, Hornik CP, Laughon MM, et al. Urinary tract infection concordance with positive blood and cerebrospinal fluid cultures in the neonatal intensive care unit. *J Perinatol*. 2013;33:302-6.
6. Weitkamp JH, Ozdas A, LaFleur B, Potts AL. Fluconazole prophylaxis for prevention of invasive fungal infections in targeted highest risk preterm infants limits drug exposure. *J Perinatol*. 2008;28:405-11.
7. Clark RH, Bloom BT, Spitzer AR, Gerstmann DR. Empiric use of ampicillin and cefotaxime, compared with ampicillin and gentamicin, for neonates at risk for sepsis is associated with an increased risk of neonatal death. *Pediatrics*. 2006;117:67-74.
8. Cotten CM, Taylor S, Stoll B, et al. Prolonged duration of initial empirical antibiotic treatment is associated with increased rates of necrotizing enterocolitis and death for extremely low birth weight infants. *Pediatrics*. 2009;123(1):58-66.
9. Moorman JR, Carlo WA, Kattwinkel J, Schelonka RL, Porcelli PJ, Navarrete CT, et al. Mortality reduction by heart rate characteristic monitoring in very low birth weight neonates: a randomized trial. *J Pediatr*. 2011;159:900-6.