Empiric Treatment of Neonatal Early-Onset Sepsis: a Retrospective Analysis of the University of Utah Hospital Cases

Jadon S. Wagstaff[1], Michael G. Newman[2] , Elena Y. Enioutina[1]

[1]Division of Clinical Pharmacology, Department of Pediatrics, University of Utah, Salt Lake City, Utah

[2]University of Utah Health Science Center, Salt Lake City, Utah

Background

Neonatal sepsis remains a significant cause of morbidity and mortality among newborn. Early-onset sepsis is associated with microorganisms encountered at birth.

Neonates suspected of having early-onset sepsis begin treatment courses quickly – before blood culture results can be obtained. Because of the ambiguous symptoms and the danger of an untreated infection, most neonates treated for early-onset sepsis have negative blood culture results.

We aim to describe the choice and trends in empiric antibiotics used to treat early-onset sepsis and compare the outcomes of different treatment regimens.

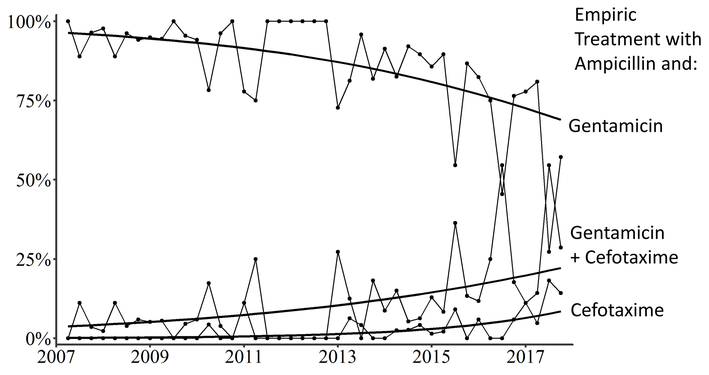
Methods

Electronic health records were obtained from neonates billed with ICD9 code 771.81 or ICD10 code P36 (sepsis of newborn) admitted to the University of Utah Hospital between June 23, 2007 and December 31, 2017.

Neonates that had a blood culture drawn within three days of birth and also started antibiotic therapy within three days of birth were analyzed as cases of suspected early-onset sepsis.

Severity of illness and risk of mortality were measured using All Patient Refined Diagnosis Related Groups (APR-DRG). Outcomes were modeled using multiple logistic regression.

Figure 1: Change in choice of empiric treatment over time. Trend lines fit with logistic regression.



Results

Figure 2: Mortality rate compared between neonates receiving and not receiving cefotaxime as part of empiric therapy. Un-circled graphs contain potential confounding variables controlled for in the multiple logistic regression model.

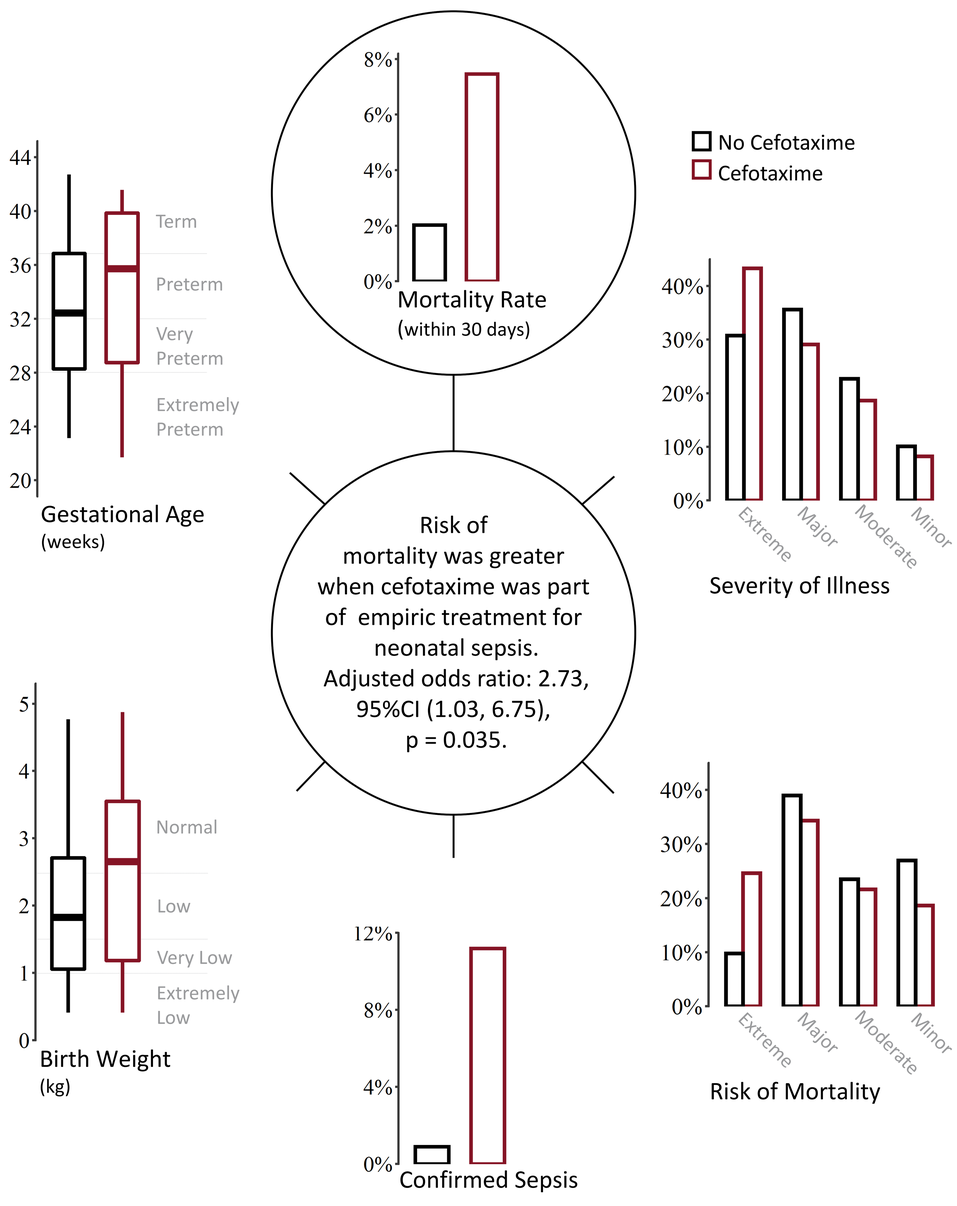


Table 1: Patient demographics and characteristics.

	No Cefotaxime	Cefotaxime
n	**890**	**134**
Mortality within 30 Days of Birth (% of n)	18 (2.0)	10 (7.5)
Blood Culture Confirmed (% of n)	8 (0.9)	15 (11.2)
Male Gender (% of n)	473 (53.1)	84 (62.7)
Length of Stay in Days (median [IQR])	25 [8, 59]	15 [8, 40]
Race (% of n)		
Caucasian	480 (53.9)	70 (52.2)
Other	153 (17.2)	26 (19.4)
Unknown	257 (28.9)	38 (28.4)
Ethnicity (% of n)		
Hispanic/Latino	156 (17.5)	25 (18.7)
Not Hispanic/Latino	428 (48.1)	67 (50.0)
Unknown	306 (34.4)	42 (31.3)

Findings/Conclusions

Including cefotaxime in a treatment regimen for early-onset sepsis is associated with an increased risk of mortality within 30 days of birth, even after adjusting for potential confounders (Figure 2, p = 0.035).

Clinicians used cefotaxime in patients with higher birth weight and gestational age; additionally, these patients had more severe morbidity and high risk of mortality (Figure 2, p < 0.05).

Cefotaxime may be preferred for gram negative infections; 13 of 15 neonates that cultured gram negative organisms started cefotaxime >12h after the first positive culture draw.

The use of cefotaxime as a replacement, or an addition to gentamicin has increased within this hospital system (Figure 1, p < 0.001).

These conclusions may not generalize to other hospitals.

Future Directions

Clark et al. discovered a similar relationship between cefotaxime administration and neonatal mortality in a large study of the Pediatrix network.[1]

In our study, the use of cefotaxime could be a surrogate for an unknown risk factor: we must further investigate the motivations for these clinicians to prescribe cefotaxime.

1. 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(1):67-74.