Comparison of outcomes in neonates receiving ceftazidime or cefepime

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Background: Given the national shortage of cefotaxime, healthcare institutions are challenged to select alternative antibiotics to manage infections caused by gram-negative organisms such as *Escherichia coli, Haemophilus influenzae, Klebsiella* spp., and more. Ceftazidime and cefepime are agents currently used as substitutions to cefotaxime within the neonatal population. However, neonatal outcomes from use of broader antibiotics remain unclear.

Objective: The primary objective of this study is the incidence of culture-positive sepsis after the first 72 hours of life requiring treatment for at least 7 days with targeted antibiotics between patients previously receiving ceftazidime or cefepime. Secondary objectives include outcome differences in multi-drug resistant organism infection, presumed culture-negative sepsis, respiratory infection, stage II or III necrotizing enterocolitis, urinary tract infection, length of hospital stay, postmenstrual age at discharge, all-cause mortality, and reported adverse events associated with ceftazidime or cefepime.

Methods: This was a single-center, retrospective study of neonates admitted to the neonatal intensive care unit from June 1, 2018 to June 1, 2021. Neonates were included in the study if they received at least twenty-four hours of either ceftazidime or cefepime during hospital admission and within the specified study period. Subjects were excluded if they received both ceftazidime and cefepime for greater than 24 hours during hospital admission. Moreover, subjects were excluded if transferred from outside hospital at greater than seven days of age or with missing medical history. Demographics were analyzed using descriptive statistics. Primary and secondary outcomes were analyzed with Fisher's Exact and Chi Square or Mann-Whitney U tests where appropriate.

Results: A total of 105 neonates were included in this study (ceftazidime = 55; cefepime = 50). Baseline characteristics were not significantly different between groups with the exception of fewer cumulative days of all antibiotics (9 [IQR 4-23.5] versus 25 [IQR 9.3-47] p = 0.01), fewer central line days (6.5 [IQR 0-11.5] versus 11 [IQR 6-40]), p = 0.001), and fewer ventilator days (4 [IQR 0-25] versus 13 [IQR 2.3-48]), p = 0.02) in the ceftazidime group compared to the cefepime group, respectively, during admission. There was no difference between culture-positive sepsis after initial course of study antibiotic (3.6% versus 8% in the ceftazidime and cefepime groups, respectively, p = 0.42). However, there were differences in treated respiratory infections after initial course of study antibiotic (1.8% versus 16%, p = 0.01), length of hospital stay (31 [IQR 12.5-85.5] days versus 77.5 [IQR 21-111.25] days, p=0.02), and all-cause mortality (9.1% versus 26%, p=0.02) in the ceftazidime and cefepime groups, respectively.

Conclusion: Overall, this study found differences in respiratory infections, length of hospital stay, and all-cause mortality in neonates receiving cefepime compared to those receiving ceftazidime. Interpretation of these results is complicated by the increased ventilator and central line days, and overall antibiotic exposure in neonates receiving cefepime. Further research is needed to evaluate neonatal outcomes between ceftazidime and cefepime in a larger group setting.

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