Comparative Use of Vancomycin versus Ampicillin for Blood Stream Infections Caused by Ampicillin-susceptible *Enterococcus faecalis*

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Practice Site: Atrium Health's acute care facilities in the Charlotte, North Carolina region including Carolinas Medical Center, Mercy, Pineville, Union, Cleveland, Kings Mountain, Anson, Cabarrus, University, Lincoln, and Stanly.

Background: *Enterococcus* blood stream infections (BSI) are associated with a mortality of 33.9% and inappropriate antimicrobial therapy has been found to be an independent risk factor. However, the association between the choice of antimicrobial agent and mortality in *Enterococcus* BSI has not been well established. Available studies assessing the efficacy of beta-lactam antibiotics compared to glycopeptides in the treatment of Enterococcal BSI have varying results and have not assessed the impact of rapid diagnostic testing. The delay to definitive beta-lactam therapy may obscure the potential difference in mortality between beta-lactams and glycopeptides.

Objective: The primary objective of this study was to compare 30-day all-cause mortality in patients with ampicillin-susceptible and vancomycin-susceptible *Enterococcus faecalis* BSI treated with ampicillin or vancomycin therapy where rapid diagnostic testing is available through multiplex polymerase chain reaction (PCR) blood culture identification (BCID).

Methods: A multisite, retrospective evaluation of adults with *E. faecalis* BSI at Atrium Health acute care facilities from January 2017 to October 2021 was performed. Patients who received at least four days of ampicillin or vancomycin as definitive therapy were analyzed; only initial episodes were included. All positive blood cultures underwent multiplex PCR BCID. Patients with polymicrobial BSI were excluded, or if they received ≥ 50% concomitant use of ampicillin and vancomycin. Secondary objectives included 90-day all-cause mortality, hospital length of stay, incidence of treatment failure, persistent BSI, change from initial definitive therapy, and adverse drug reactions (ADRs). Other microbiology endpoints included time to active treatment, BCID, beta-lactam coverage, definitive therapy, and culture clearance. A sample size of 208 patients was estimated to provide a 15% mortality difference with 80% power. The Mann-Whitney U and t-test was conducted for continuous variables. The Chi-square or Fisher exact test was performed for categorical variables.

Results: In total, 123 patients with *E. faecalis* BSI were analyzed (ampicillin, n = 92; vancomycin, n = 31). Baseline characteristics were similar among the treatment groups except gender and baseline penicillin allergy ($p < 0.001$). All-cause 30-day mortality was not significantly different between patients treated with ampicillin and vancomycin (10.8% vs. 22.6%, $p = 0.130$). No difference was found in secondary objectives except time to definitive therapy was longer for the ampicillin treatment arm (56.7 hours vs. 15.8 hours, $p < 0.001$). The incidence of ADRs were similar between the two groups.

Conclusions: No difference in mortality was observed in the treatment with ampicillin or vancomycin for patients with *E. faecalis* BSI, but the study was not sufficiently powered. Despite the use of rapid diagnostic testing, earlier initiation of ampicillin was not observed. Ampicillin or vancomycin may be reasonable options for treatment of *E. faecalis* BSI, but further research is warranted.