Ceftriaxone versus cefazolin for methicillin-susceptible \textit{Staphylococcus aureus} (MSSA) infections complicated by bacteremia

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Purpose/Background: Methicillin-susceptible \textit{Staphylococcus aureus} (MSSA) bacteremia is the causative bacteria in up to 20\% of all bloodstream infections (BSI), with a mortality rate approaching 25\%. These infections have historically been treated with penicillinase-resistant penicillins after studies showed decreased rates of treatment failure, mortality, and persistent bacteremia when compared to vancomycin. Cefazolin, a first-generation cephalosporin, gained popularity as a treatment option for MSSA BSI as it is administered only three times per day and has excellent in vitro MSSA activity, with reported non-inferiority to penicillinase-resistant penicillins. Ceftriaxone, a third-generation cephalosporin, has in vitro MSSA activity, and the convenience of once-daily dosing. The ease of administration has led some clinicians to use ceftriaxone for MSSA BSI despite an overall lack of high-quality evidence supporting this practice.

Objective: To compare outcomes utilizing cefazolin versus ceftriaxone for the treatment of MSSA infections complicated by bacteremia.

Methods: This study was a retrospective observational cohort study comparing cefazolin versus ceftriaxone for the treatment of MSSA infections complicated by bacteremia. The study population consisted of adult patients admitted to the health system between 2013 and 2017 with at least one positive blood culture for MSSA. Patients were included if they were treated with either cefazolin or ceftriaxone for at least 50\% of the treatment duration. Patients were excluded if they left against medical advice or died within 4 days of index culture, were diagnosed with a polymicrobial infection, were discharged prior to index culture results, were hemodialysis dependent, or were not treated at the discretion of the primary provider. The primary outcome of the study was a composite “unfavorable outcome” defined as 30-day all-cause mortality, treatment failure, or recurrence of \textit{S. aureus} BSI. Secondary outcomes included 30-day readmission, 90-day all-cause mortality, hospital length of stay (LOS), and infection LOS.

Results: 129 patients were included in the study, with 73 receiving cefazolin and 56 receiving ceftriaxone. There was no difference in the composite primary outcome between treatment groups (cefazolin 21\% vs ceftriaxone 16\%; \( p = 0.52 \)). The mean infection LOS was significantly shorter in the ceftriaxone group (cefazolin 14.2 days vs ceftriaxone 11.6 days, \( p = 0.008 \)). Mean hospital LOS, readmission at 30 days, and all-cause 90-day mortality were similar between the cefazolin and ceftriaxone groups.

Conclusions: Ceftriaxone is a reasonable treatment option for patients with MSSA infections complicated by bacteremia with similar outcomes to cefazolin. Treatment with ceftriaxone may decrease the time to discharge after positive blood culture detection, but further studies are needed to confirm this finding.