

P2035 **Benzylpenicillin versus flucloxacillin for penicillin-susceptible *Staphylococcus aureus*: is there evidence to support superiority?**

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Background: In clinical practice, differing opinion exists as to the preferred therapy for patients with penicillin susceptible *Staphylococcus aureus* (PSSA) bloodstream infections (BSIs). However, there is currently insufficient evidence in the literature to adequately compare benzylpenicillin versus other anti-staphylococcal penicillins. Some clinicians argue that benzylpenicillin offers significant advantage due to a lower MIC distribution and ability to obtain higher free drug concentrations. The aim of this study was to compare 30-day mortality of patients treated with benzylpenicillin or flucloxacillin.

Materials/methods: The ANZCOSS study, a large prospective data set from multiple sites within Australia and New Zealand, was used to compare patients treated with flucloxacillin or benzylpenicillin for PSSA BSIs. A logistic regression model was performed to compare 30-day outcome. A propensity score treatment adjusted comparison was then performed using inverse probability of treatment weighting (IPTW).

Results: 915 patients were included in the analysis with an overall mortality rate of 12.9% (benzylpenicillin 10.5%, 33/315 and flucloxacillin 14.2%, 85/600). In the multivariate analysis, a non-significant increased mortality trend was associated with flucloxacillin compared to benzylpenicillin (OR 1.6, 95% CI 0.99 – 2.5, $p = 0.06$). In the boosted regression model, endocarditis and skin and soft tissue infection had strong associations with choice of treatment (Kolmogorov-Smirnov p value <0.001 and 0.011 respectively). In the IPTW model, after balancing was performed, the 30-day mortality OR remained higher with flucloxacillin treatment but was not significantly different from benzylpenicillin (1.02, 95%CI 0.98 – 1.08).

Conclusions: A non-significant increase in mortality was associated with flucloxacillin use compared to benzylpenicillin in the multivariate model. When covariates were balanced using the propensity score model, no significant difference in 30-day mortality outcome was observed. This is the largest reported study in the medical literature to compare benzylpenicillin versus other anti-staphylococcal penicillin. Further studies are required to address the optimal therapy choice for PSSA BSIs.