Beta-lactam (BL) antibiotics promote an IL-1β response in patients with Staphylococcus aureus bacteremia (SaB)

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ABSTRACT

Background: Beta-lactam (BL) therapy has been associated with reduced S. aureus bacteremia (SaB) duration compared to non-BL therapy. It has been recently shown that patients with SaB who had BL therapy had increased IL-1β production compared to non-BL patients. Furthermore, it has been shown that patients with SaB who received BL therapy had increased IL-1β production compared to non-BL patients. Given that a lack of inflammasome mediated IL-1β release has been shown to enhance IL-1β release, this study aims to show that BL therapy results in a more robust IL-1β host response compared to non-BL therapy. A therapeutic regimen of vancomycin or daptomycin (n=35) may have its basis on enhancing IL-1β release. This study aims to show that BL therapy results in a more robust IL-1β host response compared to non-BL therapy to explain, in part, more rapid bacteremia clearance.

Methods: Fifty-nine patients (47 MRSA and 12 MSSA) with diverse SaB sources, including endovascular, extravascular (eg, pneumonia), and catheter-related infections were included. In the first 48 hours, patients were treated with either BL, including oxacillin, ceftaroline, or cefazolin (n=24), versus non-BL vancomycin or daptomycin (n=35). The clinical outcome was SaB bacteremia (median 6.1 pg/mL vs. non-BL 2.8 pg/mL, P=0.0895) when compared to non-BL-treated patients. BL therapy resulted in 23% and 105% increase in IL-1β concentrations on day 1 of bacteremia (median BL 6.1 pg/mL vs. non-BL 2.8 pg/mL, P=0.0895) when compared to non-BL-treated patients. BL therapy resulted in 32% and 44% reduction in IL-1β. The median duration of SaB between BL- and non-BL-treated patients (2.5 days vs 2.0 days respectively).

Conclusions: Given that a lack of inflammasome mediated IL-1β production is associated with prolonged SaB, the significant increases in IL-1β levels in patients treated with BL has important therapeutic implications. This study aims to show that BL therapy results in a more robust IL-1β host response compared to non-BL therapy to explain, in part, more rapid bacteremia clearance.

RESULTS

Patients in BL and non-BL groups had similar IL-1β concentrations on day 1 of bacteremia (median BL 6.1 pg/mL vs. non-BL 2.8 pg/mL, P=0.0895; Figure 2). BL-treated patients had significantly higher IL-1β serum concentrations on day 3 (median BL 7.0 pg/mL vs. 1.9 pg/mL, P<0.007) and on day 7 (12.5 pg/mL vs. 1.56 pg/mL, P=0.016; Figures 3 & 4) when compared to non-BL-treated patients. BL therapy resulted in 23% and 105% increase in IL-1β at days 3 and 7, respectively. IL-1β levels in BL and non-BL treated patients were similar on day 1 of bacteremia.

• Patients in BL and non-BL groups had similar IL-1β concentrations on day 1 of bacteremia (median BL 6.1 pg/mL vs. non-BL 2.8 pg/mL, P=0.0895; Figure 2).

• BL-treated patients had significantly higher IL-1β serum concentrations on day 3 (median BL 7.0 pg/mL vs. 1.9 pg/mL, P<0.007) and on day 7 (12.5 pg/mL vs. 1.56 pg/mL, P=0.016; Figures 3 & 4) when compared to non-BL-treated patients.

• BL therapy resulted in 23% and 105% increase in IL-1β at days 3 and 7, respectively, while non-BL treatment resulted in 32% and 44% reduction in IL-1β (Figure 5).

• The median duration of SaB was similar between BL and non-BL treated patients (2.5 days vs 2.0 days respectively).

CONCLUSIONS

• Given that a lack of inflammasome mediated IL-1β production is associated with prolonged SaB, the significant increases in IL-1β levels in patients treated with BL has important therapeutic implications.

• Previously observed reduced duration of MRSA bacteremia with the addition of BL to vancomycin may have its basis on enhancing IL-1β release. A therapeutic regimen of vancomycin or daptomycin (n=35) may have its basis on enhancing IL-1β release. A therapeutic regimen of vancomycin or daptomycin in combination with BL to treat MRSA bacteremia and use of BL therapy in MSSA bacteremia is strongly advised to improve outcomes based on these results.

REFERENCES


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