Beta-Lactam Infusion in Severe Sepsis (BLISS): a prospective, two-centre, open-labelled randomised controlled trial of continuous versus intermittent beta-lactam infusion in critically ill patients with severe sepsis

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Abstract

This study aims to determine if continuous infusion (CI) is associated with better clinical and pharmacokinetic/pharmacodynamic (PK/PD) outcomes compared to intermittent bolus (IB) dosing in critically ill patients with severe sepsis.

This was a two-centre randomised controlled trial of CI versus IB dosing of beta-lactam antibiotics, which enrolled critically ill participants with severe sepsis who were not on renal replacement therapy (RRT). The primary outcome was clinical cure at 14 days after antibiotic cessation. Secondary outcomes were PK/PD target attainment, ICU-free days and ventilator-free days at day 28 post-randomisation, 14- and 30-day survival, and time to white cell count normalisation.

A total of 140 participants were enrolled with 70 participants each allocated to CI and IB dosing. CI participants had higher clinical cure rates (56 versus 34 %, p = 0.011) and higher median ventilator-free days (22 versus 14 days, p < 0.043) than IB participants. PK/PD target attainment rates were higher in the CI arm at 100 % fT (> MIC) than the IB arm on day 1 (97 versus 70 %, p < 0.001) and day 3 (97 versus 68 %, p < 0.001) post-randomisation. There was no difference in 14-day or 30-day survival between the treatment arms.

In critically ill patients with severe sepsis not receiving RRT, CI demonstrated higher clinical cure rates and had better PK/PD target attainment compared to IB dosing of beta-lactam antibiotics. Continuous beta-lactam infusion may be mostly advantageous for critically ill patients with high levels of illness severity and not receiving RRT.

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Keywords

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