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Continuous vs Intermittent β-lactam Antibiotics in Sepsis

A new study aimed to determine if continuous infusion of a β-lactam antibiotic (piperacillin-tazobactam or meropenem) reduces all-cause mortality at 90 days compared to intermittent infusion in critically ill patients with sepsis.

The BLING III randomised clinical trial was conducted across 104 ICUs in Australia, Belgium, France, Malaysia, New Zealand, Sweden, and the United Kingdom. The recruitment period spanned from March 26, 2018, to January 11, 2023, with follow-up concluding on April 12, 2023.

The study involved critically ill adults (aged 18 and above) who were being treated with piperacillin-tazobactam or meropenem for sepsis. Eligible patients were randomised to receive an equivalent 24-hour dose of a β-lactam antibiotic by continuous infusion (n = 3498) or intermittent infusion (n = 3533). The treatment was administered for a duration determined by the clinician or until the patient was discharged from the ICU, whichever came first.

The study's primary outcome was all-cause mortality within 90 days after randomisation. Secondary outcomes included clinical cure up to 14 days after randomisation, new acquisition, colonisation, or a multiresistant organism/*Clostridioides difficile* infection up to 14 days after randomisation, ICU mortality and in-hospital mortality.

Among 7202 randomised participants, 7031 patients were included in the primary analysis. Within 90 days, 864 of 3474 patients (24.9%) receiving continuous infusion had died compared to 939 of 3507 (26.8%) receiving intermittent infusion. Clinical cure rates were higher in the continuous infusion group (55.7%) compared to the intermittent infusion group (50.0%). No statistically significant differences were observed for other secondary outcomes.

The difference in 90-day mortality between continuous and intermittent infusions of β-lactam antibiotics was not statistically significant in the primary analysis. However, findings suggest that the results could range from no significant effect to a clinically important benefit for continuous infusions in this group of patients.

Study authors believe the BLING III trial provides important evidence to guide antibiotic management and improve outcomes for patients with sepsis. The trial involved over 7,000 patients with sepsis and compared continuous and short intermittent infusions for two common beta-lactam antibiotics. Mortality at 90 days was 2% lower, and clinical cure was 6% higher in patients receiving continuous infusions.

While the difference in survival was not statistically significant, study researchers conclude that these findings represent a likely clinically important benefit of continuous infusions in adult patients treated for sepsis in the intensive care unit with piperacillin-tazobactam or meropenem.

Source: JAMA

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Published on : Sun, 23 Jun 2024