Avoid piperacillin-tazobactam when treating BSI cause by ceftriaxone-resistant pathogens

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The antibiotic combination treatment piperacillin-tazobactam was significantly less effective than meropenem when treating potentially fatal bloodstream infections (BSI) caused by ceftriaxone-resistant *Escherichia coli* and *Klebsiella pneumoniae* and should be avoided when treating these organisms, according to research presented at the 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID).

Researchers from the Centre of Clinical Research at the University of Queensland determined whether piperacillin-tazobactam, a penicillin-based combination therapy, was as effective for treating BSI as the commonly used antibiotic meropenem. Their hypothesis was that definitive therapy with piperacillin-tazobactam was non-inferior to meropenem.

While there was no difference between the two groups regarding subsequent infections of drug-resistant bacteria or *C. difficile*, the difference in mortality rate was significant. Twenty-three patients, or 12.3%, treated with piperacillin-tazobactam died by the 30-day mark compared with seven patients, or 3.7%, who had been treated with meropenem.

"The use of piperacillin-tatobactam as definitive therapy for bloodstream infections caused by *E. coli* or *K. pneumoniae* with non-susceptibility to third-generation cephalosporins was inferior to meropenem and should be avoided in this context," presenting author Dr Patrick Harris

concluded in his presentation.

During the last 10 years the rate of carbapenem resistance has been increasing exponentially worldwide. Researchers urgently need reliable data from well-designed trials to guide clinicians in the treatment of antibiotic resistant Gram-negative infections. Physicians face a situation where meropenem, which is commonly used for bloodstream infection, is suspected of driving resistance to carbapenem, a highly effective antibiotic agent that is usually reserved for known or suspected difficult-to-treat multidrug-resistant (MDR) bacterial infections.

Bloodstream infections carry a high risk for morbidity and mortality. Such infections are common in the hospital setting and they often are difficult to treat because *K. pneumoniae* and *E. coli*, the leading cause of BSIs, have developed resistance to cephalosporins, a class of antibiotics originally made from fungi.

The team enrolled adult patients from 32 sites in nine countries - most patients were recruited in Singapore, Australia and Turkey. The study included 378 patients between February 2014 and July 2017. Healthcare-associated infections were the most common, accounting for more than half of the infections in the study group. Most infections, 60.9%, originated in the urinary tract before spreading to the bloodstream. And 86.5% of the cases were caused by the *E. coli* bacteria.

Harris's team examined the primary outcome for these patients, which was mortality at 30 days after the randomisation. Randomisation occurred within 72 hours of the initial blood culture.

The team also noted secondary outcomes, those consisted of the number of days for each patient to reach the resolution of the infection, the clinical and microbiological success at day four, any relapse of the bloodstream infection or a secondary infection with an organism that

was resistant to the trial drugs or *Clostridium difficile*, which is another type of bacteria that may lead to life-threatening symptoms and is sometimes a side effect of antibiotic treatment.

More information: Abstract no: O1121, The MERINO Trial: piperacillin-tazobactam versus meropenem for the definitive treatment of bloodstream infections caused by third-generation cephalosporin non-susceptible Escherichia coli or Klebsiella spp.: an international multi-centre open-label non-inferiority randomised controlled trial; session Late breaker: Clinical trials, 16:00 - 18:00, Sunday, 22 April 2018, Hall Q

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