ICU antibiotics may be safe for kidneys, says clinical trial

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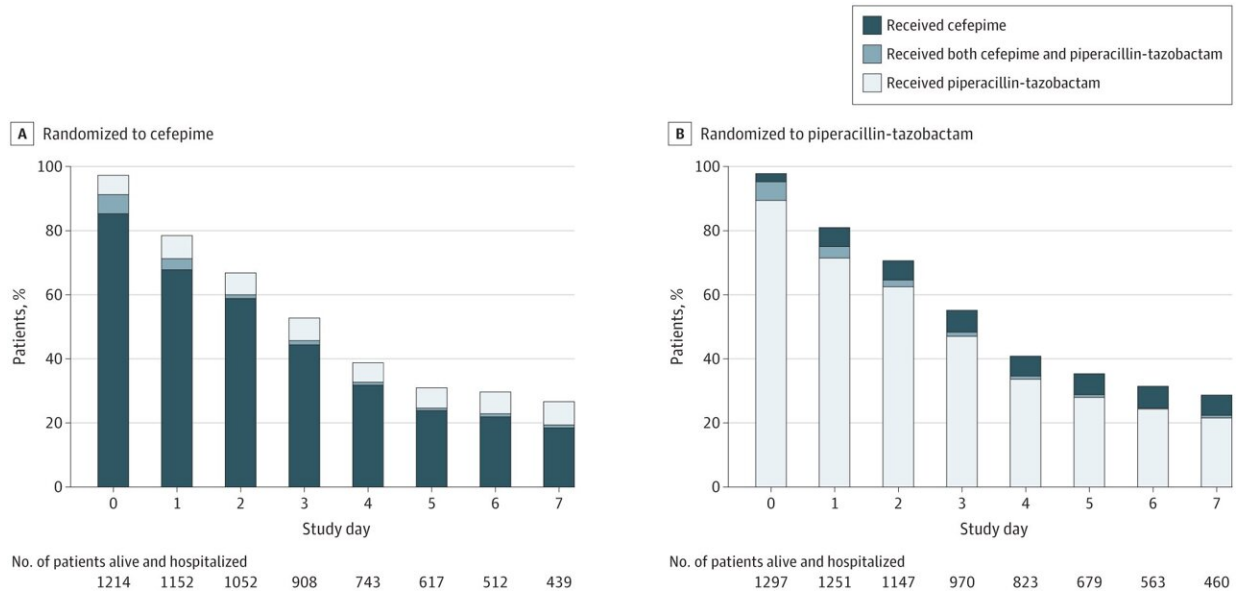

Patients may have received both cefepime and piperacillin-tazobactam on a study day when switching from one antibiotic to the other; 32 patients (1.3%) received both antibiotics on more than 1 consecutive study day. Credit: *JAMA* (2023). DOI: 10.1001/jama.2023.20583

Two "big gun" antibiotics thought to cause kidney failure in ICU patients with a severe bacterial infection, especially when combined with another antibiotic, may be safer for the kidneys than previously reported, following a randomized trial led by Vanderbilt University Medical Center (VUMC).

The findings on cefepime vs. piperacillin/tazobactam were released simultaneously in JAMA and during a presentation from VUMC first author Eddie Qian, MD, assistant professor of Medicine in the Division of Pulmonary and Critical Care Medicine, at ID Week 2023 in Boston.

"These are the two most common antibiotics that we use for treating hospitalized patients, so removing some of the concerns that there are kidney side effects from one of them is really important as far as increasing the treatment options," Qian said.

"I think the big take home point here is, when you're looking at piperacillin/tazobactam and renal dysfunction, our study didn't find a big difference there, and so you should feel comfortable in using that for your patients when they come to the hospital for infection," he said.

The Antibiotic Choice on Renal Outcomes (ACORN) randomized clinical trial compared cefepime vs. piperacillin/tazobactam in adults prescribed one of these antibiotics within 12 hours of presenting to the emergency department or medical intensive care unit at an academic medical center in the U.S. between Nov. 10, 2021 and Oct. 7, 2022.

There were 2,511 patients included in the final analysis with a median age of 58 years. The primary outcome of highest stage of acute kidney injury or death by day 14 was not significantly different between the cefepime group and the piperacillin-tazobactam group.

"There are some observational studies that say piperacillin/tazobactam causes renal failure, especially in combination with another antibiotic called vancomycin," said co-senior author Todd Rice, MD, professor of Medicine and director of the Medical Intensive Care Unit at VUMC. "We didn't find that in our randomized trial."

As a secondary outcome, authors reported that treatment with cefepime

resulted in more neurological dysfunction, with patients in that group experiencing fewer days alive and free of delirium and coma within 14 days in the piperacillin/tazobactam group.

"We really need to dig in deep with cefepime and find out what that really means for our patients and what the risk factors might be," Rice said. "We had some data that cefepime may cause some neurotoxicity—we found a signal for some neurotoxicity, although we are not entirely sure what it means clinically so that needs more study."

The study results could help inform current FDA warnings about renal failure in critically ill patients from piperacillin/tazobactam and neurotoxicity for cefepime, the authors said.

"I suspect, in every single hospital in the US, somebody is getting one or both of these antibiotics every day, so trying to understand their effects in a comparative way is really important to how we can best treat patients and how we can give them the best antibiotic for them, their condition and their infection," Rice said.

More information: Edward T. Qian et al, Cefepime vs Piperacillin-Tazobactam in Adults Hospitalized With Acute Infection, *JAMA* (2023). DOI: 10.1001/jama.2023.20583

Steven Y. C. Tong et al, Acute Kidney Injury With Empirical Antibiotics for Sepsis, *JAMA* (2023). DOI: 10.1001/jama.2023.18591 , jamanetwork.com/journals/jama/fullarticle/2810593

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