

**The objective of this systematic review and meta-analysis was to assess acute kidney injury with combination therapy of vancomycin plus piperacillin-tazobactam, in general, adult patients and in critically ill adults. Rates of acute kidney injury, time to acute kidney injury, and odds of acute kidney injury were compared with vancomycin monotherapy, vancomycin plus cefepime or carbapenem, or piperacillin-tazobactam monotherapy” Luther et al (2018).**

Abstract:

Objectives: The objective of this systematic review and meta-analysis was to assess acute kidney injury with combination therapy of vancomycin plus piperacillin-tazobactam, in general, adult patients and in critically ill adults. Rates of acute kidney injury, time to acute kidney injury, and odds of acute kidney injury were compared with vancomycin monotherapy, vancomycin plus cefepime or carbapenem, or piperacillin-tazobactam monotherapy.

Data Sources: Studies were identified by searching Pubmed, Embase, Web of Science, and Cochrane from inception to April 2017. Abstracts from selected conference proceedings were manually searched.

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Study Selection: Articles not in English, pediatric studies, and case reports were excluded.

Data Extraction: Two authors independently extracted data on study methods, rates of acute kidney injury, and time to acute kidney injury. Effect estimates and 95% CIs were calculated using the random effects model in RevMan 5.3.

Data Synthesis: Literature search identified 15 published studies and 17 conference abstracts with at least 24,799 patients. The overall occurrence rate of acute kidney injury was 16.7%, with 22.2% for vancomycin plus piperacillin-tazobactam and 12.9% for comparators. This yielded an overall number needed to harm of 11. Time to acute kidney injury was faster for vancomycin plus piperacillin-tazobactam than vancomycin plus cefepime or carbapenem, but not significantly (mean difference, -1.30; 95% CI, -3.00 to 0.41 d). The odds of acute kidney injury with vancomycin plus piperacillin-tazobactam were increased versus vancomycin monotherapy (odds ratio, 3.40; 95% CI, 2.57-4.50), versus vancomycin plus cefepime or carbapenem (odds ratio, 2.68; 95% CI, 1.83-3.91), and versus piperacillin-tazobactam monotherapy (odds ratio, 2.70; 95% CI, 1.97-3.69). In a small subanalysis of 968 critically ill patients, the odds of acute kidney injury were increased versus vancomycin monotherapy (odds ratio, 9.62; 95% CI, 4.48-20.68), but not significantly different for vancomycin plus cefepime or carbapenem (odds ratio, 1.43; 95% CI, 0.83-2.47) or piperacillin-tazobactam monotherapy (odds ratio, 1.35; 95% CI, 0.86-2.11).

Conclusions: The combination of vancomycin plus piperacillin-tazobactam increased the odds of acute kidney injury over vancomycin monotherapy, vancomycin plus cefepime or carbapenem, and piperacillin-tazobactam monotherapy. Limited data in critically ill patients suggest the odds of acute kidney injury are increased versus vancomycin monotherapy, and mitigated versus the other comparators. Further research in the critically ill population is needed.

#### Reference:

Luther, M.K., Timbrook, T.T., Caffrey, A.R., Dosa, D., Lodise, T.P. and LaPlante, K.L. (2018) Vancomycin Plus Piperacillin-Tazobactam and Acute Kidney Injury in Adults: A Systematic Review and Meta-Analysis. *Critical Care Medicine*. 46(1), p.12-20.

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