Vancomycin plus Piperacillin/Tazobactam and Acute Kidney Injury in Adults: A Systematic Review and Meta-analysis

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ABSTRACT

BACKGROUND: Recent literature has demonstrated an increased incidence of acute kidney injury with combinations of vancomycin and piperacillin/tazobactam. The objective of this meta-analysis was to assess acute kidney injury with this combination therapy.

METHODS: We performed a systematic literature review and meta-analysis using keywords of vancomycin, piperacillin, and kidney-related terms. Relevant studies in English were identified by searching PubMed/Embase, Web, Science, and Cochran from inception to August 2016, and manual searches of reference lists. Abstracts from conference proceedings were included. Case reports, pediatric studies, and articles not in English were excluded. Odds ratios (OR) and 95% confidence intervals (CI) were calculated using the random effects model in RevMan 5.3.

RESULTS: We identified 10 studies and 12 abstracts with a total of 15,910 patients to be included in the meta-analysis. Fifteen studies compared vancomycin plus piperacillin/tazobactam to vancomycin monotherapy, while seven studies compared vancomycin plus ceftazidime or meropenem and ten compared piperacillin/tazobactam monotherapy. The overall incidence of acute kidney injury was 17.9% (2845/15910); 25.8% (1928/7465) for vancomycin plus piperacillin-tazobactam and 10.8% (917/8445) for comparator. Overall odds ratio was 3.04 (95% CI 2.47-3.73, p<0.0001; F=58%, p<0.0001) versus any comparator. Odds ratios versus vancomycin monotherapy or vancomycin plus ceftazidime or meropenem were similar at OR 3.33 (95%CI 2.37-4.68, p<0.0001; F=60%, p=0.002) and OR 3.35 (95%CI 1.98-5.66, p<0.0001; F=38%, p=0.14), respectively.

CONCLUSION: Available data suggest that the combination of vancomycin plus piperacillin/tazobactam increases the odds of acute kidney injury (AKI) over vancomycin monotherapy and vancomycin plus cepfazidime or meropenem. Confounding by indication and publication bias remain issues with these observational studies. Future comparative safety studies may help to clarify any association.

BACKGROUND

• Acute kidney injury is a well known adverse effect of vancomycin.
• Empiric therapy often includes combination therapy with vancomycin and piperacillin/tazobactam.
• Recent literature has demonstrated an increase in acute kidney injury with this combination.

METHODS

- We searched Pubmed, Embase, Web of Science, and Cochran from inception to August 2016.
- Search terms included vancomycin, piperacillin, nephrotoxicity, kidney, renal, adrenal, and safety.
- Case reports/series, pediatric studies, and articles not in English were excluded.
- Abstracts from conferences (IDWeek, Interscience Conference on Antimicrobial Agents and Chemotherapy [ICAAC], American College of Clinical Pharmacy [ACCP], Society of Critical Care Medicine [SCCM], and American Society of Health-System Pharmacy [ASHP]) midyear meeting were searched separately.
- We compared the odds of AKI for the combination of vancomycin plus piperacillin/tazobactam to vancomycin monotherapy, vancomycin plus cepfazidime or meropenem, and piperacillin/tazobactam monotherapy.
- Adjusted odds ratios were used whenever possible.
- Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated using the random effects model in RevMan 5.3 and the log-transformed inverse variance for individual studies.

RESULTS

- Literature search identified 10 published observational studies and 12 conference abstracts for inclusion.

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REFERENCES

• Vancomycin and piperacillin/tazobactam increases the odds of AKI.
• The relationship between AKI and this common combination therapy could be clarified with comparative safety studies.

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