A case of acute kidney injury with vancomycin and piperacillin/tazobactam

Abstract

Background: Acute kidney injury can be attributed to several causes, including drug-induced nephrotoxicity. A dramatic and acute increase in serum creatinine has been observed in a patient receiving vancomycin and piperacillin/tazobactam therapy. Documentation of potential kidney injury during concomitant therapy with these two agents is found in current literature.

Objective: To describe a patient case in which the concomitant use of vancomycin and piperacillin/tazobactam resulted in acute kidney injury.

Design: Case Report

Setting: A 522-bed community hospital.

Patient: A Hispanic female with normal renal function presents with osteomyelitis in both feet. During therapy with vancomycin and piperacillin/tazobactam administrations, acute and significant increases in serum creatinine were observed.

Intervention: Discontinuation of vancomycin and administration of acetylcysteine.

Measurements: Serum creatinine levels and timing of offending agents as well as the doses (vancomycin, piperacillin/tazobactam) were all documented.

Results: Serum creatinine levels of the patient increased from 1.0mg/dL up to 5.1mg/dL over the three days with three total doses of vancomycin and 2 to 3 doses of piperacillin/tazobactam each day. The increase in serum creatinine correlated with the concomitant administration of these two agents.

Conclusion: Patients receiving both vancomycin and piperacillin/tazobactam require close monitoring for signs of acute kidney injury. While some risk factors have been proposed in literature, further research is needed to further define these risk factors and time to acute kidney injury with these medications.

Keywords: vancomycin, piperacillin/tazobactam, nephrotoxicity

Background

Acute kidney injury can result from a multitude of factors, including drug-induced causes. Medications like vancomycin and piperacillin/tazobactam have shown to be correlated with deterioration of the kidneys when used in excess or concomitantly with other potential offending agents. While these agents have been both been associated with potential nephrotoxicity there is limited data on the exact mechanisms and roles in potential kidney injury. Further, no patient case reports describing kidney injury with concomitant use of vancomycin and piperacillin/tazobactam is found in current literature that describes the series of events leading to acute kidney injury.

Although there is no known mechanism in which vancomycin may induce kidney injury, current animal data suggests that it has oxidative effects on cells of the proximal renal tubule. The primary mechanism thus appears to be necrosis due to renal tubular ischemia secondary to oxidative effects of vancomycin. In addition to oxidative stress and resultant mitochondrial damage, contributions from the complement pathway and inflammation have been postulated. Evidence of tissue repair have also been detected in addition to necrosis in animal studies. The most common risk factor for vancomycin-associated nephrotoxicity is an increased serum trough concentrations. Various studies have found an increased risk of nephrotoxicity as trough concentrations increase, with trough concentration greater than 15milligrams/liter (mg/L) showing a moderate to high risk, while a trough concentration greater than 20mg/liter showed a much greater risk. This vancomycin-associated nephrotoxicity may be reversible in some patients with studies revealing that renal function may return to baseline or below predefined toxicity thresholds within a week or less following discontinuation of vancomycin.

Piperacillin/tazobactam, the other offending agent of concern, may induce kidney injury by causing interstitial nephritis (AIN). Drug-induced AIN (DIAIN) is a known cause of impaired renal function and deterioration especially with antibiotics such as piperacillin/tazobactam and non-steroidal anti-inflammatory drugs (NSAIDs). AIN is defined as an increased levels of inflammatory infiltrates such as lymphocytes (mostly T cells), macrophages, eosinophils, and plasma cells as well as edema within the renal tubules and interstitium which is usually associated with renal dysfunction. The pathogenesis of DIAIN is believed to be on an immunologic basis such as drug components interacting with endogenous antigens of tubular basement membrane (TBM), as evidenced by the common appearance of extrarenal hypersensitivity reactions. It is suggested that piperacillin/tazobactam can bind to normal components of TBM or can mimic the actions of the normal antigen present in TBM.
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A 40-year-old, 60 in, 70.7kg, Hispanic female was transferred from an outside hospital for a higher level of care for an initial complaint of a left foot infection. She had a long-standing history of type-1 diabetes mellitus, hypertension and diabetic peripheral neuropathy. Her home medication regimen prior to admission included amitriptyline 25mg PO daily, lisinopril/hydrochlorothiazide 20/12.5mg PO daily and Novolin® 70/30: 50units PO twice daily and as needed medication use included oxycodone PO twice daily and as needed. Specifically for the infection, the patient was started on daptomycin 6mg/kg IV every 24hours, while vancomycin and contrast dye are known to potentially cause nephrotoxicity. Although there is some data on mechanisms of nephrotoxicity for each of agents above, there is limited data of the synergistic nephrotoxicity caused by the combination of the two antibiotics. One study comparing the use of vancomycin with piperacillin/tazobactam and vancomycin with cefepime found higher incidence of acute renal failure in patients given both vancomycin and piperacillin/tazobactam than with cefepime; however, no statistical significance was demonstrated.1 Because both antibiotics are eliminated through renal excretion and show nephrotoxicity individually, it is predicted that the concomitant use of vancomycin and piperacillin/tazobactam can cause a higher incident of nephrotoxicity than when used monotherapy.1,2,8

Nephrotoxicity can be defined as patients who developed acute renal failure. Acute renal failure can be defined as serum creatinine (SCr) increase by 0.5mg/dL or increase by 50% from baseline.9 In a person without any kidney disease, serum creatinine is constant with very small variability. However, serum creatinine tends to increase in compromised kidneys and glomerulus filtration rate declines.9 Although there are many medications that have been shown to be directly correlated with nephrotoxicity, there has yet to be sufficient reports of piperacillin/tazobactam, when used concomitantly with vancomycin, to augment the effects of nephrotoxicity.

Case report

A 40-year-old, 60 in, 70.7kg, Hispanic female was transferred from an outside hospital for a higher level of care for an initial complaint of a left foot infection. She had a long-standing history of type-1 diabetes mellitus, hypertension and diabetic peripheral neuropathy. Her home medication regimen prior to admission included amitriptyline 25mg PO daily, lisinopril/hydrochlorothiazide 20/12.5mg PO daily and Novolin® 70/30: 50units PO twice daily and as needed. Specifically for the infection, the patient was started on daptomycin 6mg/kg IV every 24hours, while vancomycin and contrast dye are known to potentially cause nephrotoxicity. Although there is some data on mechanisms of nephrotoxicity for each of agents above, there is limited data of the synergistic nephrotoxicity caused by the combination of the two antibiotics. One study comparing the use of vancomycin with piperacillin/tazobactam and vancomycin with cefepime found higher incidence of acute renal failure in patients given both vancomycin and piperacillin/tazobactam than with cefepime; however, no statistical significance was demonstrated.1 Because both antibiotics are eliminated through renal excretion and show nephrotoxicity individually, it is predicted that the concomitant use of vancomycin and piperacillin/tazobactam can cause a higher incident of nephrotoxicity than when used monotherapy.1,2,8

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Conclusion

This case report shows that there may be additive nephrotoxic effects of piperacillin/tazobactam when it is added to vancomycin. While the large jump in creatinine may be also attributed to IV contrast dye, the timeline lends itself to the conclusion that this combination should at least lead to increased monitoring of renal function in patients in which it is initiated.

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Conflict of interest

The author declares no conflict of interest.

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