CAN THE COMBINATION OF VANCOMYCIN AND PIPERACILLIN/TAZOBACTAM (ZOSYN®) INCREASE THE RISK OF RENAL FAILURE?

Vancomycin (VAN) is known to cause nephrotoxicity (acute tubular necrosis). Prior to purification, the rate of nephrotoxicity was as high as 50%, but recent rates are felt to be closer to 5%. Penicillins such as piperacillin-tazobactam (PTZ) may rarely cause nephrotoxicity by causing interstitial nephritis. Three recent studies suggest the combination of these two antibiotics may be associated with a higher risk of nephrotoxicity than either agent alone. The studies are summarized in Table 1.

Because they are all small retrospective trials with several limitations including various dosing regimens used, all of the authors of these trials conclude that large scale prospective randomized trials are needed to draw firm conclusions. However, given the large OR of 2.48 to 5.36, and the consistent results of these three trials, some caution in utilizing the combination of VAN and PTZ may be warranted.

Utilizing Negative MRSA Screen and Blood Cultures to Guide De-escalation:

Methicillin Resistant Staphylococcus aureus (MRSA) continues to be a significant pathogen in health care associated infections. Initiation of empiric anti-MRSA therapy is often appropriate, but clinicians may have difficulty determining eligibility for de-escalation from empiric therapy. Dangerfield BS, et al. reviewed the utility of nasal PCR testing in predicting MRSA as a causative organism in pneumonia patients. In their retrospective review, nasal swabs were positive for MRSA in 62 of 435 (14.3%) of patients whereas 25 (5.7%) have a positive MRSA culture (23 respiratory, 2 blood). Patients with confirmed pneumonia who had both a nasal MRSA screen and blood culture or respiratory specimen were included. In the presence of culture-positive MRSA infection, a positive nasal PCR had 88% sensitivity, 90.1% specificity, 35.4% positive predictive value, and 99.2% negative predictive value (NPV). Another study by Robicsek A, et al. had similar findings – 99% and 98% NPV for bloodstream and respiratory tract infections, respectively. Boyce JM and colleagues analyzed a convenience sample of 91 patients diagnosed with HCAP in the absence of a respiratory culture. Empiric vancomycin or linezolid was discontinued in patients who had a negative nasal culture for MRSA. In-hospital mortality was only 7.7% in these patients, and they did not have any evidence of MRSA infection at time of death.

Conclusion:

In conclusion, some preliminary data suggests that the combination of VAN and PTZ may increase the risk of nephrotoxicity. Prospective, randomized trials are needed. However, it would seem prudent to try to limit the duration of the use of this combination. Antibiotics should always be de-escalated when culture results are available. If a patient
has a negative MRSA swab in conjunction with negative cultures, studies suggest that vancomycin can safely be discontinued. The Antimicrobial Stewardship Team or Infectious Disease is available if assistance with antibiotic therapy is needed.

Table 1: Vancomycin and Piperacillin-Tazobactam Nephrotoxicity

<table>
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<th>Reference</th>
<th>Patients</th>
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<th>Results</th>
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<td>Burgess LD, et al. Comparison of the incidence of VAN-induced nephrotoxicity in hospitalized patients with and without concomitant PTZ. Pharmacotherapy 2014;34:670</td>
<td>191 adult patients with normal baseline renal fx who received at least 48 hours of VAN. Of these, 92 received PTZ.</td>
<td>Single center retrospective cohort study utilizing a univariate analysis to determine risk factors for nephrotoxicity and a multivariate analysis to compare groups.</td>
<td>Nephrotoxicity was observed in 8.08% and 16.3% of patients on VAN and combination group respectively (p=0.041). The addition of PTZ to VAN resulted in an adjusted OR for nephrotoxicity of 2.48 (p=0.032).</td>
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<td>Meaney CJ, et al. VAN-associated nephrotoxicity in adult medicine patients: incidence, outcomes and risk factors. Pharmacotherapy 2014;34:653</td>
<td>125 adult internal medicine patients receiving VAN treatment for a minimum of 72 hours. Had to have serum creatinine of less than 1.4 for women and 1.5 for men.</td>
<td>Retrospective cohort study utilizing a multivariate analysis to determine risk factors for nephrotoxicity</td>
<td>Concomitant PTZ occurred in 13 (76.5%) patients in nephrotoxicity group compared to 45 (41.7%) in no nephrotoxicity group. PTZ was associated with an OR of 5.36 for nephrotoxicity (95% CI 1.41-20.5)</td>
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<td>Gomes DM, et al. Comparison of acute kidney injury (AKI) during treatment with VAN in combination with PTZ or cefepime. Pharmacotherapy 2014;34:662</td>
<td>224 adult patients without pre-existing renal dysfunction receiving either PTZ and VAN or cefepime and VAN for more than 72 hours.</td>
<td>Retrospective matched cohort study. Data analyzed through propensity matched pairs and conditional logistic regression.</td>
<td>The incidence of AKI was 34.8% in the VAN PTZ group as compared to 12.5% in the VAN cefepime group (p&lt;0.0001). After adjusting for sources of bias, PTZ and VAN combination found to be independent predictor of AKI</td>
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References:


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