Vancomycin and Piperacillin-Tazobactam Combination Therapy – Evaluating the risk of Acute Kidney Injury (Sub-analysis VancMan Study)

McLaren E, Banakh I, Loh G, Cam SL, Meanger D, Wanniarachchi L.

Corresponding author: EMcLaren@phcn.vic.gov.au

Peninsula Health Pharmacy Department

Introduction

- Piperacillin-tazobactam (PTZ), a β-lactam penicillin-β-lactamase inhibitor, is often combined with vancomycin (VAN) to treat severe infections including: osteomyelitis, sepsis and hospital acquired pneumonia.
- Acute kidney injury (AKI) is a common occurrence in hospitalised patients and is a known side effect of VAN based treatment.
- Rates of AKI with PTZ monotherapy are relatively low, however, there are increasing reports in current literature that suggest the combination of VAN and PTZ increase the risk of AKI.
- VancMan study explored the prescribing and therapeutic drug monitoring practices of vancomycin at Frankston Hospital in Victoria.
- The secondary aim of the VancMan study was to determine if the combination of VAN and PTZ increases the risk of AKI in patients treated at Frankston Hospital and the significance of the interaction.

Method

- The VancMan study was a retrospective cohort study conducted at Frankston Hospital between 14 April 2014 and 19 April 2015.
- All patients initiated and treated with VAN more than 1 dose during the specified period at the study site were included in the study.
- Data was collected from electronic health records and therapeutic drug monitoring (TDM) forms completed by pharmacists.
- Data collected included: patient demographics, comorbidities, types of infections treated, nephrotoxic drug therapies, inotrope use and Intensive Care Unit (ICU) admission status during hospitalisation.
- AKI was defined as increase in baseline serum creatinine (SeCr) level by >1.5 times.
- Pre-specified secondary analysis:
  - Rate of AKI in patients treated with combination of VAN and PTZ therapy compared to VAN therapy alone.
- AKI incidence was analysed using Chi squared and logistic regression.
- Due to the retrospective nature of the study, it received an exemption from the Human Research Ethic Committee.

Results

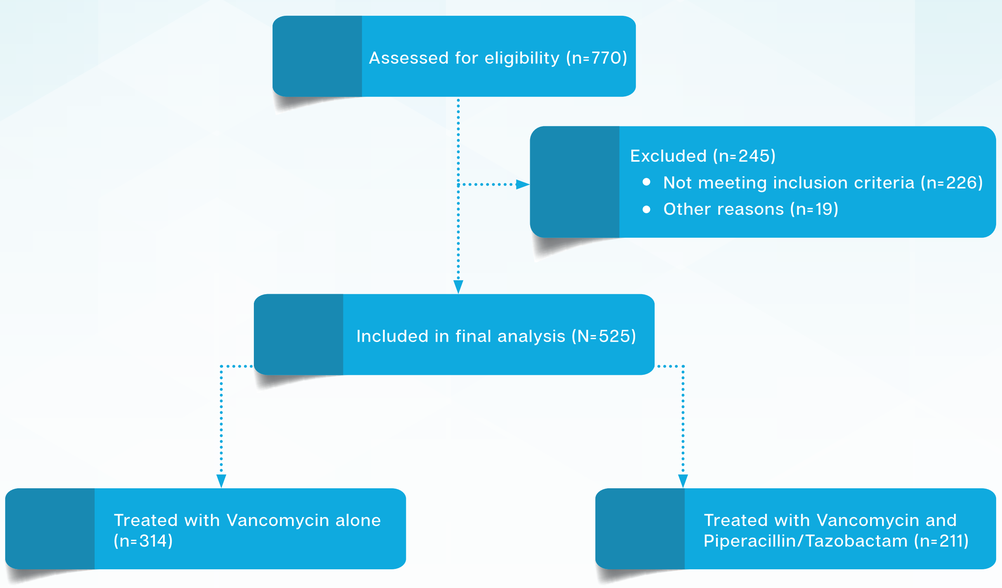

Figure 1: Patient Selection

Results (continued)

- The most common indications for VAN-PTZ combination therapy were sepsis or skin infections.

Table 1: Patient Demographics	Number (525)
Gender	
Females	220 (41.9%)
Males	305 (58.1%)
Age (years; mean)	63.6 (95%CI 62.0-65.2)
Weight (kg; mean) (n=328)	81.9 (95%CI 79.2-84.7)
Mean duration of PTZ (days)	4 (1-17)
VAN-PTZ combination therapy	211 (40.2%)
Initial SeCr (µmol/L)	117.0 (26-795)
Peak SeCr PTZ + VAN (µmol/L)	138 (36-795)
Intensive Care Unit Admission	159 (30.3%)
Nephrotoxins	
Aminoglycosides	44 (8.4%)
Amphotericin	1 (0.2%)
ACEI/ARBs*	130 (24.8%)
Diuretics	168 (32.0%)
Vasopressor	68 (13.0%)
Other nephrotoxins	77 (14.7%)

*ACEI = angiotensin converting enzyme inhibitor / ARB = angiotensin receptor blocker

- VAN-PTZ combination therapy was associated with higher risk of AKI with HR of 1.7 (95% CI 1.01-2.96, p=0.046) and earlier emergence of AKI when compared to VAN alone (3.8 days vs 5.2 days, p=0.014).
- Chronic kidney disease (28.1% vs 11.3% p=0.001) and ICU admission (21.5% vs 9.9%, p=0.001) were associated with increased AKI rates.

Table 2: Rates of AKI when VAN is Prescribed with Nephrotoxins versus VAN Alone		
	AKI Rate	P-Value
PTZ (n=211)	17.5% vs 10.5%	0.020
Aminoglycosides (n=44)	22.7% vs 12.5%	0.064
Diuretics (n=168)	20.2% vs 10.1%	0.001
Vasopressors (n=68)	29.4% vs 10.9%	<0.001

Discussion

- The results of this study confirm findings from previous research indicating that there is a significant interaction between VAN-PTZ to increase the risk of AKI compared to VAN therapy alone.
- The results confirm previous findings of an earlier onset of AKI with the combination of these antibiotics by approximately 1.5 days compared to VAN therapy alone.
- Patients started empirically on the VAN-PTZ combination should have therapy reviewed as early as possible and deescalated when culture results are available to potentially reduce the risk of AKI.
- The literature reports a 58% increase in length of stay as well as increased morbidity if AKI occurred while on VAN-PTZ combination therapy.
- Care should be taken when VAN is combined with other nephrotoxins such as diuretics and vasopressors as there is an increased rate of AKI.
- While this was a single centre, retrospective study, the size of the included population and the similarity of the results to the previous research suggest that the results may be applied to clinical practice.
- Future guidelines and antibiotic stewardship practices will need to be adjusted based on these results.