Use of oral vitamin C for prevention of vancomycin-induced nephrotoxicity

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Background

- Vancomycin is a glycopeptide antibiotic which is frequently used to treat resistant Gram-positive infections, including methicillin-resistant *Staphylococcus aureus* (MRSA).
- One of the most frequent adverse effects associated with vancomycin is nephrotoxicity, occurring in up to 40% of patients who receive vancomycin therapy.[1]
- Preclinical studies suggest that the mechanism of vancomycin-induced nephrotoxicity may be due to oxidative stress, mitochondrial damage, and inflammatory responses.[1,2,3]

Risk Factors for Vancomycin-Induced Nephrotoxicity (VIN)

- Effectiveness and toxicity are generally thought to be based on the ratio of area under the curve to minimum inhibitory concentration (AUC/MIC). AUC of greater than 600 mg*h/L is associated with increased risk of toxicity.[4]
- Higher vancomycin trough levels, especially levels greater than 20 mg/L, have been associated with an increased risk of toxicity[1,4,5]
- Certain medications, including ACE inhibitors or ARBs[5], NSAIDs[5], diuretics[5], radiologic contrast, aminoglycosides, and piperacillin/tazobactam[6,7,8] have been associated with an increased risk of nephrotoxicity when used along with vancomycin

Previous Studies of Antioxidants for VIN

- Ocak et al.[9] in 2015 found that antioxidants including vitamin E and vitamin C reduced the nephrotoxic effect of vancomycin in rats.
- Akundi et al.[10] in 2015 found a non-statistically significant reduction in rates of VIN in patients receiving vitamin C.

Study Objective

- Determine whether vitamin C administered orally at a dose of 500 mg twice daily reduces the incidence of acute kidney injury in patients receiving vancomycin therapy.

Study Design and Methods

- Retrospective, single-center, medical chart review study approved by TTUHSC IRB
- Study Site: Hendrick Medical Center, a 564-bed community hospital in Abilene, Texas
- Study subjects identified if they received vancomycin along with vitamin C (experimental group), or if they received vancomycin alone (control group)
- Patient selection criteria:

Inclusion Criteria	Exclusion Criteria
• Age between 18-89 years • Admitted to Hendrick Medical Center after January 1, 2012 • Tolerating oral diet/medications • Received IV vancomycin for at least 48 hours	• Underlying kidney impairment or pre-existing AKI • Received vitamin C at a dose other than 500 mg twice daily • History of kidney stones • Pregnancy • Prisoners

Study Outcomes

- **Primary**: Incidence of VIN in patients on vancomycin and given vitamin C compared with patients not given vitamin C. VIN is defined based on RIFLE crtieria[11] as an increase in serum creatinine of either 0.5 mg/dL or 50% over baseline following initiation of vancomycin.

Statistical Analysis

- **Continuous data**: Analyzed using Student's t-test
- **Categorical data** (including primary outcome)**:** Analyzed using Chi-square or Fisher's exact tests

A p-value of less than 0.05 considered significant

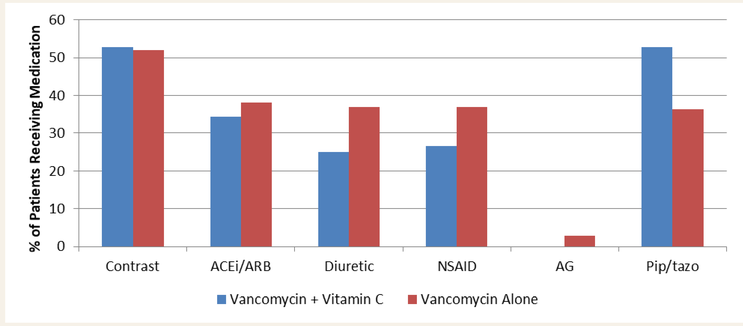
Results

- 1824 patient charts were evaluated for inclusion in the study, and 345 met inclusion criteria
- The most frequent reasons for exclusion were duration of therapy less than 48 hours (496 patients), pre-existing renal impairment (418 patients), and alternate vitamin C dosing (396 patients)
- Of the included patients, 172 received vitamin C, and 173 did not

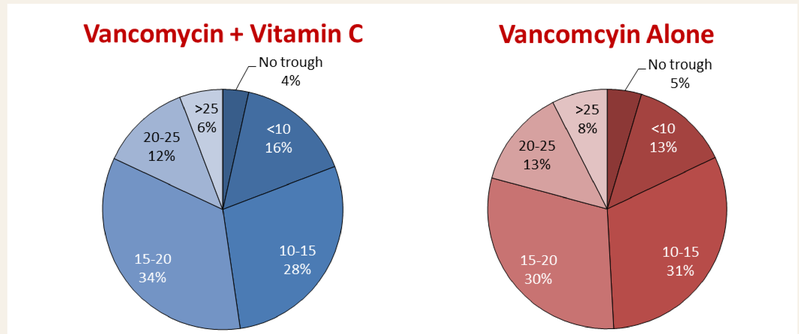
Patient Characteristics

	Vancomycin + Vitamin C (n=172)	Vancomycin Alone (n=173)
Age	57.6 ± 16.7	57.0 ± 16.5
Female sex	80 (47%)	79 (46%)
Weight (kg)	88.9 ± 34.2	89.7 ± 33.2
Baseline CrCl (mL/min)	95 ± 35	105 ± 41
Comorbid conditions		
Cardiovascular disease	60 (35%)	80 (46%)
Diabetes mellitus	75 (44%)	65 (38%)
Lung disease	55 (32%)	44 (25%)
Cancer	21 (12%)	29 (17%)
Critical care setting	19 (11%)	21 (12%)
Length of stay (days)	6 (2-50)	7 (2-44)
Vancomycin duration (days)	4 (2-36)	4 (2-32)
Vancomycin doses	8 (2-59)	8 (2-68)
Vancomycin daily dose (mg)	2404 ± 846	2471 ± 868
Vancomycin average dose (mg)	1244 ± 277	1262 ± 282
Vitamin C duration (days)	5 (1-36)	--

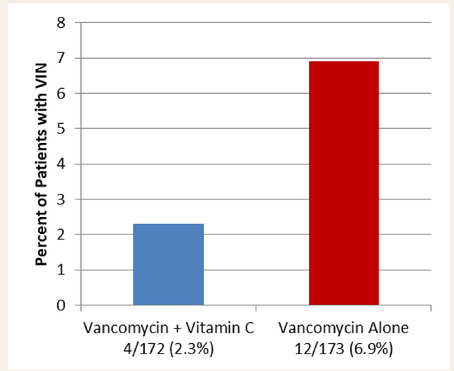
Concomitant Nephrotoxic Medications



Vancomycin Trough Levels



Study Outcome (Incidence of VIN*)



*p=0.042 for difference between groups

Discussion

- Vitamin C administered orally at a dose of 500 mg twice daily appears to be associated with a reduced rate of vancomycin-induced nephrotoxicity
- The number needed to treat is approximately 22, meaning that we would need to treat 22 patients receiving vancomycin with vitamin C in order to prevent one case of VIN
- Strengths of this study: Statistically significant benefit found, information was collected on other factors that may influence occurrence of VIN
- Limitations of this study: Retrospective, observational study, cannot determine causality, and confounding factors may exist

Conclusion

- Vitamin C administered orally at a dose of 500 mg twice may be beneficial in preventing vancomycin-induced nephrotoxicity, but additional research is needed to confirm this finding

References

https://docs.google.com/document/d/1AllNR3EoeJO83QcRUhK8x6I7jkO3mbKMsq9IxkXRKpw/edit?usp=sharing