Elevated Vancomycin levels and Renal Injury Occur Commonly with Empiric and Non-Indicated Vancomycin Use

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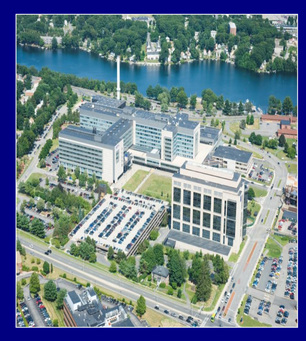


Abstract

Background and Objective:
Vancomycin is commonly used to treat infections with resistant gram positive organisms, esp. Methicillin resistant *Staphylococcus aureus* (MRSA). In 2009, new guidelines advised higher vancomycin trough levels (15-20 mcg/ml) when treating serious infections due to MRSA. High trough levels (> 20mcg/ml) have been associated with nephrotoxicity. Guidelines from professional societies advocate using vancomycin for empiric treatment of health care associated pneumonia (HCAP) pending culture results. Despite evidence and guidelines to the contrary, vancomycin is often administered for simple cellulitis. Empiric use of vancomycin has increased, and high trough levels often develop. The purpose of our investigation was to ascertain what percent of elevated vancomycin troughs were due to non-indicated vancomycin use, or due to empiric use, for which lower trough levels are recommended We hypothesized that renal injury in this circumstance was not rare.

Methods:
Retrospective chart review at UMass Memorial Medical Center (UMMC) in Worcester, Massachusetts. One hundred adult patients were randomly selected who had a vancomycin trough > 20 or < 40 mcg/mL between August 2013 and February 2014. Patients on dialysis, those with a baseline creatinine $\geq$ 2 mg/dL and patients in the intensive care unit were excluded. Patients could only be included in the data once per hospital admission.

R***esults***:
79% of elevated trough levels were in patients receiving vancomycin empirically. The average elevated trough was 24.6 mcg/ml. 16% of patients had clinical specimens that grew MRSA. One third of empiric vancomycin use was for treatment of pneumonia, 22% of empiric use was for treatment of cellulitis. 15% of empiric use was for diabetic foot infection or osteomyelitis. 28% of patients treated empirically, who did not have culture proven infections necessitating vancomycin, suffered nephrotoxicity with an increase in serum creatinine of more than 1.5 times baseline during therapy

Conclusions:
High vancomycin troughs with empiric therapy are common. Renal injury is often seen concurrently. It is possible that much of this renal injury could be avoided by more judicious use of vancomycin. A minority of patients had culture positive infections with Gram positive organisms requiring vancomycin. We suggest that overuse is occurring, and is due in part to guidelines for HCAP that prompt overuse, and in part to mis-interpretation regarding indications for high trough levels.

Background

Guidelines from the American Society of Health-System Pharmacists, the Infectious Disease Society of America and the Society of Infectious Disease Pharmacists, published in 2009, advise targeting higher trough levels of vancomycin when treating MRSA infections than were routinely used in the past. Multiple studies have demonstrated the importance of choosing initial appropriate antimicrobial therapy when treating patients with severe sepsis and septic shock. Professional guidelines for treatment of hospital acquired pneumonia and HCAP advocate that empiric antibiotic therapy include an agent active vs. MRSA such as vancomycin. It is likely that these guidelines have influenced health care providers to overuse vancomycin, and to use larger doses. Nephrotoxicity is a side effect of high vancomycin levels . Patients with HCAP are heterogeneous and do not all have an equivalent risk of infection with multi-drug resistant organisms, including MRSA. Recent studies suggest that guideline concordant therapy of HCAP may be associated with worse patient outcomes including a greater likelihood of readmission and more superinfection., among others.

Results

Table 1: Patients with high Vancomycin troughs (20-40 mcg/ml)

Patient Characteristics		
Sex		
	M	51%
	F	49%
Age (years)		
	mean	65.12
	range	25-96
Vanco trough level (ug/ml)		
	mean	24.636
	range	20-36.1
Day of therapy for initial elevated trough	mean	4.9
	range	2-14
Culture positive for MRSA		16%

Table 2: Additional risk factors for renal injury

Risk Factor	% positive
Concomitant Aminoglycoside	2%
NSAIDS	9%
Intravenous contrast administration	27%
Diuretic usage	35%
Diabetes mellitus	41%
Hypertension	63%

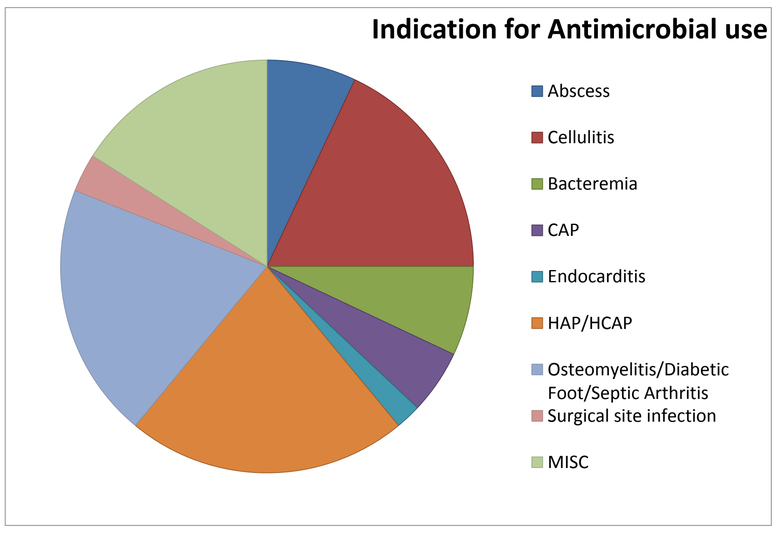


Figure 1:

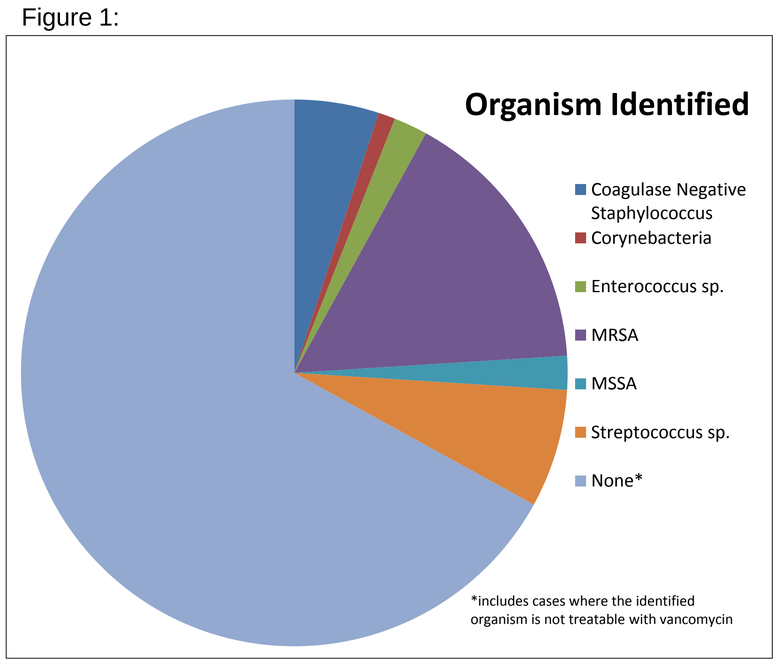
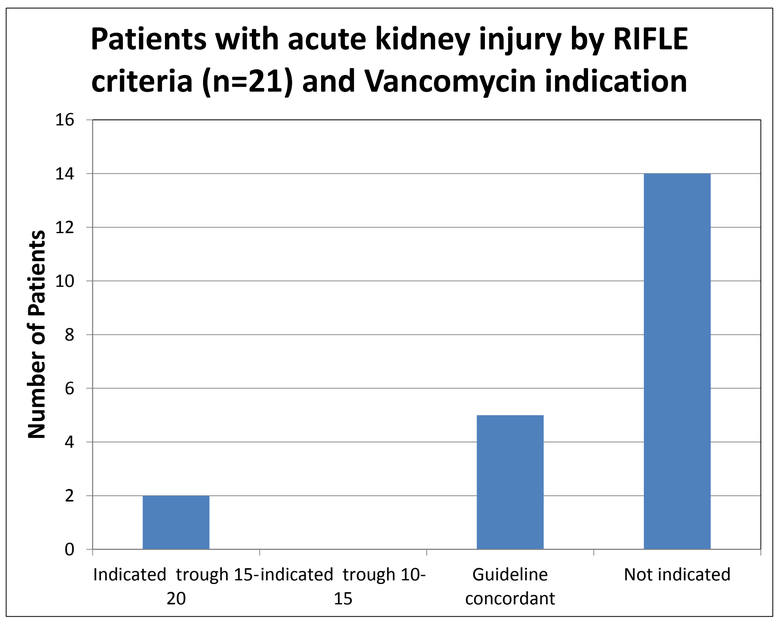


Figure 2:



Indicated trough 15-20: positive culture for MRSA and infection other than skin and soft tissue infection
Indicated trough 10-15: positive culture for MRSA and skin/soft tissue infection
Guideline concordant: use of vancomycin for an indication suggested by published guidelines, not supported by culture data
Not indicated: Vancomycin use not recommended for clinical illness (e.g.. Diffuse cellulitis)

Conclusions

The majority of patients in our hospital with elevated vancomycin trough levels (between 20-40 mcg/ml) are receiving empiric therapy that is not directed by positive cultures. The initial high vancomycin trough occurred after an average of five days of therapy. There is a potential to de-escalate therapy if there is not a positive culture for MRSA; this could potentially avert nephrotoxicity. 22% of patients with high troughs were administered vancomycin for non-purulent cellulitis, despite the fact that current literature and guidelines recommend using beta lactam antibiotics for this indication. In our institution patients with HCAP usually receive empiric vancomycin in concordence with published guidelines. There is a growing body of literature that patients with HCAP may have better outcomes with antibiotic therapy concordant with community acquired pneumonia guidelines. More judicious use of vancomycin will likely avoid unnecessary toxicity and lead to improved outcomes.

References

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