Effectiveness of a pharmacist managed vancomycin dosing protocol in achieving therapeutic levels in a Community Medical Center

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Abstract

Background: Vancomycin is commonly used for severe gram-positive infections. Previous studies have shown that subtherapeutic dosing of vancomycin is common. The objective of this study was to evaluate whether the implementation of a pharmacist-managed protocol increased the attainment of therapeutic levels without compromising patient safety.

Methods: The hospital database was used to identify inpatients that received vancomycin through standard care (STA) versus protocol (PRO). Patients in the PRO group received an initial dose based on the institutional nomogram with subsequent dose adjustments based on patient specific pharmacokinetic parameters. Patients were included if they were 18 years of age or older, had a creatinine clearance greater than 40 mL/min at baseline, and had a vancomycin trough level drawn near steady state. Patients with one-time orders, on hemodialysis, pregnant, or on surgical prophylaxis were excluded. The primary outcome was achievement of therapeutic trough levels, defined as 10-20 µg/mL. Secondary outcomes included acute renal failure (ARF, defined as an increase in sCr of 0.5 mg/dL or more on two consecutive days) and thrombocytopenia. Data were analyzed using descriptive and inferential statistics.

Results: A total of 465 patients (164 STA and 301 PRO) were included in the analysis. Baseline characteristics were similar. The source of infection and distribution of bacteria cultured was similar between groups. Therapeutic trough levels were more likely to be reached in the PRO group (71% vs. 34%, P < 0.0001) with a mean initial trough concentration of 9.44 +/- 4.2 µg/mL in the STA group and 15.58 +/- 6.5 µg/mL in PRO group (P < 0.0001). The incidence of ARF was similar in both groups (3.7% STA and 4.0% PRO; p=0.86) as was the development of thrombocytopenia (7.9% STA and 10.6% PRO; p=0.33).

Conclusion: A pharmacist-managed vancomycin protocol increases the likelihood of attaining therapeutic vancomycin levels without compromising patient safety. Additional analyses are required to evaluate the impact of protocol dosing on patient outcomes.

Background

- Studies have shown that subtherapeutic dosing of vancomycin is common, leading to an unlikely probability of achieving therapeutic trough levels of 10-20 µg/mL and possibly leading to treatment failure.[1]
- Recently, higher doses of vancomycin have been necessary to account for increasingly resistant strains of MRSA.[2] Also, complicated infections such as meningitis, bacteremia, osteomyelitis, pneumonia, and endocarditis require higher doses to achieve higher therapeutic trough levels of 15-20 µg/mL .[2]
- To avoid the development of resistance, a trough level greater than 10 µg/mL is recommended.[3]
- Previous data has shown that the use of nomogram-based protocols improved the attainment of therapeutic trough levels.[4]

Objective

- To evaluate whether the implementation of a pharmacist-managed protocol increased the attainment of therapeutic levels without compromising patient safety.

Methods

- Retrospective review of 465 adult patients who received vancomycin dosing based on standard care (STA) versus protocol (PRO).
- Inclusion criteria: 18 years of age or older, baseline creatinine clearance (Cockcroft-Gault) of ≥40 mL/minute.
- Exclusion criteria: one time doses, hemodialysis, surgical prophylaxis, pregnant patients, pediatric patients.
- Primary outcome: achievement of therapeutic trough levels, defined as 10-20 µg/mL at the time of first trough draw.
- Secondary outcomes: acute renal failure (ARF, defined as an increase in sCr of 0.5 mg/dL or more on two consecutive days) and thrombocytopenia.

Results

Table 1: Patient demographics and culture results

Variable	STA (n=164)	PRO (n=301)
Age ± SD (years)**	59.0 ± 17.0	55.2 ± 16.8
Female (%)	29.9	33.6
CrCl ± SD (mL/min)**	73.94 ± 28.79	81.35 ± 35.59
BMI ± SD (kg/m²)**	28.26 ± 8.77	30.18 ± 10.05
Location at initiation (n, %)**		
General Medicine	154 (93.9)	220 (73.1)
Intensive Care Unit	10 (6.1)	61 (20.3)
Emergency Department	0	20 (6.6)
Indication (n, %)		
Bacteremia	20 (12.2)	14 (4.7)
CNS	4 (2.4)	6 (2.0)
Osteomyelitis	4 (2.4)	12 (4.0)
Respiratory infection	30 (18.3)	52 (17.3)
Sepsis	20 (12.2)	33 (11.0)
SSTI	53 (32.3)	126 (41.9)
Empiric	23 (14.0)	36 (12.0)
Other	10 (6.1)	22 (7.3)
Organism (n, %)		
MRSA	51 (31.1)	68 (22.6)
MSSA	26 (15.9)	47 (15.6)
S. epidermidis	14 (8.5)	28 (9.3)
Other Staphylococcus	2 (1.2)	8 (2.7)
Alpha-hemolytic Streptococcus	2 (1.2)	4 (1.3)
Beta-hemolytic Streptococcus	3 (1.8)	15 (5.0)
Gamma-hemolytic Streptococcus	6 (3.7)	9 (3.0)
Other	6 (3.7)	16 (5.3)
Unidentified	54 (32.9)	107 (35.5)

**=p<0.05

Table 2: Initial trough level distribution

Trough Levels	STA (n=164)	PRO (n=301)
Initial mean (µg/mL) ± SD**	9.44 ± 4.23	15.58 ± 6.52
Trough range (10 – 15 µg/mL) (n, %)	47 (28.7)	111 (36.9)
Trough range (15 – 20 µg/mL) (n, %)**	8 (4.9)	103 (34.2)
Trough range (10 – 20 µg/mL) (n, %)**	55 (33.6)	214 (71.1)
Trough ≥ 10 µg/mL (n, %)**	60 (36.6)	262 (87.0)

**=p<0.05

Figure 1: Initial Vancomycin Dosages

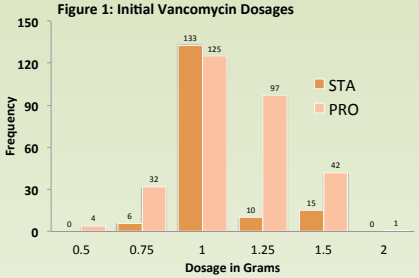


Figure 2: Initial Administration Frequency

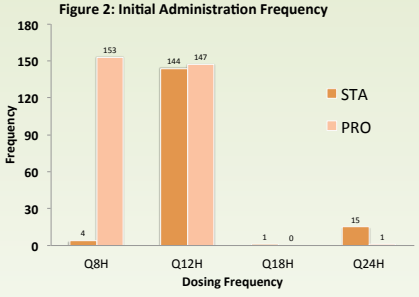
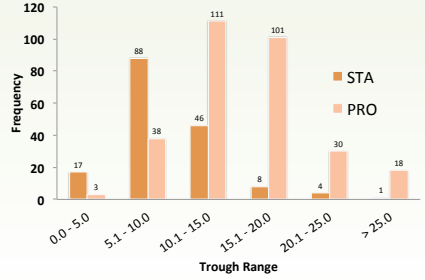


Figure 3: Distribution of Initial Trough Levels



Results

Table 3: Adverse Events

Event	STA (n=164)	PRO (n=301)
Acute Renal Failure	6 (3.7)	12 (4.0)
Thrombocytopenia	13 (7.9)	32 (10.6)
P=NS for all events		

Discussion

- Dose and frequency were significantly increased in the PRO group.
- Therapeutic trough levels (10-20 µg/mL) were more likely to be reached in the PRO group than in the STA group (71% vs. 34%; P<0.0001).
- Trough levels of 15-20 µg/mL were more likely to be achieved by PRO patients (34% vs. 5%; P<0.0001).
- Trough levels of ≥10 µg/mL were achieved in a greater number of PRO patients (87% vs. 37%; P<0.0001).
- Mean initial trough level was therapeutic in the PRO group (15.58 ± 6.5 µg/mL) and subtherapeutic in the STA group (9.44 ± 4.2 µg/mL); P<0.0001.
- Incidence of ARF or thrombocytopenia was similar in both groups.

Conclusions

- The likelihood of attaining therapeutic vancomycin levels at the time of initial trough draw is increased with a pharmacist-managed protocol.

Future Work

- Analyze variables influencing therapeutic trough levels.
- Influence of patient variables on the incidence of nephrotoxicity.
- Identification of which renal function estimates correlate best with trough levels.
- Clinical outcomes with the use of protocol dosing.

Disclosure

- All affiliations and persons represented on this presentation have no conflicts of interest or financial interest with data presented.

References

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