



BON SECOURS RICHMOND
PHARMACY & THERAPEUTICS COMMITTEE
VANCOMYCIN DOSING & THERAPEUTIC LEVELS
9/99

Recommendations:

- Revise the trough goal of the Bon Secours Pharmacy Pharmacokinetic Dosing Services to 10 mcg/ml, and up to 15 mcg/ml for life threatening infections.
- Delete peak vancomycin levels from the laboratory listing. Discourage the ordering of peak as efficacy is related to the trough. A timed random level may be ordered for physicians requiring a peak.
- Bon Secours Pharmacy Pharmacokinetic Dosing Services will no longer order peak levels as pharmacokinetic data analysis may be performed using troughs. Troughs will be monitored twice weekly on initiation of therapy and then once to twice weekly thereafter depending on the patient's condition.
- A dosing nomogram is recommended to simplify dosing.

Findings:

- Vancomycin serum levels meet most of the criteria for therapeutic drug monitoring: no clinical clearly observable therapeutic endpoint, unpredictable dose/serum level relationship, toxicity and/or lack of effectiveness is dangerous, correlation between serum drug levels and efficacy and/or toxicity, and serum levels must be readily available and inexpensive, and narrow therapeutic window.
- Nephrotoxicity due to vancomycin occurs in 5-7% of patients and in 35-35% when combined with an aminoglycoside. Nephrotoxicity occurs more frequently when troughs exceed 10 mcg/ml. Levels higher than 10 mcg/ml should be reserved for patients with life threatening infections.
- Most Pharmacokinetic Dosing Services are no longer ordering peak vancomycin levels.
- Nationally, timing of peak levels is inconsistent, with recommendations for peaks to be drawn from immediate post infusion to 2 hours post infusion.
- Vancomycin exhibits 2-3 compartment pharmacokinetics; measured peak levels are very sensitive to both the infusion period and the time the level is drawn post dose. Peak therapeutic ranges must reflect both the infusion period and the time post dose the level is drawn. Timing of post-dose levels is easily compromised on busy units limiting their value.

Infusion Period Range	Time level Drawn	Common Therapeutic Peak Ranges	Trough
1 hour	2 hours	18-30 mcg/ml	5-10 mcg/ml
1 hours	2 hours	18-26 mcg/ml	5-10 mcg/ml
1 hour	1 hour	30-40 mcg/ml	5-10 mcg/ml
2 hours	2 hours	20-30 mcg/ml	5-10 mcg/ml

- Time-dependent antibacterials, including vancomycin, exhibit saturable relationship between the kill rate and antibacterial concentration. Exceeding the MIC in excess of 4-5 times does not result in further killing activity. The MIC 90% for most organisms is ≤ 2 mcg/ml. Vancomycin is protein bound approximately 30-55%, therefore obtaining a trough of 10 mcg/ml would be optimal for most infections and 15 mcg/ml for life threatening infections.

- Vancomycin exhibits a post antibiotic effect of 2-3 hours against staphylococcus aureus, maintaining concentrations well below the MIC doubles the post antibiotic effect (sub MIC effect).
- The time vancomycin concentrations are above the MIC is best related to outcome. Trough levels of 10 mcg/ml will be above the MIC 100% of the dosage interval.
- High initial concentrations offer no advantage in bacterial killing or mortality in animal models and large initial loading doses are not advised.
- Cost saving will be realized to the patient and Bon Secours System by not using peak levels. A conservative estimate of saving is \$2,500, which includes only lab cost.
- Patient comfort will be increased by fewer lab draws.
- There is inconsistency in the timing of peak vancomycin levels locally (see chart below).

Cost Analysis

Analysis of Peak Levels Drawn										
	1999 Jan-Jun					1998				
	SMH	MRMC	RCH	SCH	Yearly Total Estimate	SMH	MRMC	RCH	SCH	Yearly Total
Tobramycin	58	8	23	16	210			6		10
Gentamicin	116	4	6	8	268	426	44	69	44	582
Vancomycin	120	7	22	9	316	244	73	59	73	390
Total	294	19	51	33		670	61	134	117	
	1999 Lab Cost for Peaks (estimated)					1998 Lab Cost for Peaks				
Tobramycin	\$4.10 per level				\$861					\$41
Gentamicin	\$9.25 per level				\$2,479					\$5,383.5
Vancomycin	\$7.75 per level				\$2,449					\$3,022.5

Infusion Period and Timing of Levels				
	Aminoglycosides		Vancomycin	
	Infusion Period (Hours)	Peak: Hours Post Infusion	Infusion Period (Hours)	Peak: Hours Post Infusion
SMH	1	0.5	2	2
MRMC	0.5	0.5	1.5	1
RCH	0.5	0.5	1	2.5
SCH	0.5	0.5	2	2

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