Vancomycin
Dosing & Monitoring

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Outline

• List the therapeutic uses of vancomycin

• Discuss the side effects associated with vancomycin

• Discuss the rational for using vancomycin drug concentrations

• Discuss the dosing strategy for vancomycin, based on PK and PD properties.
Vancomycin-Therapeutic Uses

- Tricyclic glycopeptide antibiotic.
- Active against many gram positive organisms.
- Used mainly for the treatment of severe or resistant staphylococcal (MRSA) and enterococcal infections.
- Used as first line therapy in patients allergic to first line antibiotics.
Vancomycin-Side Effects

- Red Man Syndrome
- Nephrotoxicity
- Ototoxicity
PK & PD of Antibiotics

Why do we need to know?

Maximum BENEFIT

Minimal SIDE EFFECTS
Vancomycin-Side Effects

- Red Man Syndrome
- Nephrotoxicity
- Ototoxicity
Vancomycin-Side Effects

**Red Man Syndrome**

- Characterized by a histamine-like reaction during or immediately following vancomycin infusion.

- Causes flushing, tingling, pruritis, tachycardia, erythematous macular rash of the face, neck, upper trunk, back and arms

- Hypotension may occur

- Can be avoided by reducing the rate of infusion to 15 mg/min
Vancomycin-Side Effects

• Red Man Syndrome
• Nephrotoxicity
• Ototoxicity
Vancomycin-Side Effects

Nephrotoxicity & Ototoxicity

- Vancomycin nephrotoxicity is not fully understood.
- Early preparations were associated with nephrotoxicity.
- Large doses and high trough levels have been correlated with nephrotoxicity.
- Combination with aminoglycosides increases the risk of acute renal failure.
- Ototoxicity has been described in a few cases but not fully established.
- Ototoxicity appears to be associated with high vancomycin levels.
Is Reducing the Dose the Solution..?
Vancomycin Pharmcodynamics-Efficacy

- Vancomycin has a concentration independent activity.
- Increasing the concentration does not increase the kill curve.
- Time above MIC (>50%) is the indicator of efficacy.
- There is a relationship between serum concentrations and treatment success/failure.
Pharmacokinetic/Pharmacodynamic Predictors of Efficacy

PK/PD parameters
- T > MIC
- Peak/MIC
- 24-h AUC/MIC

AUC = "how much abx is required to inhibit growth in a test tube"

MIC = "amount of drug"

Concentration vs. Time (hours)

C_max (Peak)

Time > MIC
Vancomycin Dosing Guidelines
2009

Dosage:

- Larger vancomycin doses to achieve higher troughs are recommended.

- Initial vancomycin dosages should be calculated on the basis of actual body weight, including for obese patients.

- Subsequent dosage adjustments should be based on actual serum concentrations, to achieve targeted therapeutic concentrations.
Case 1

• 60 yo male patient presented to the Emergency Department (ED) with severe respiratory distress, hypotension and fever. The patient was admitted to the ICU and started on: Norepinephrine, vancomycin, and piperacillin/ticarcillin.

• Weight: ABW 70 kg, IBW 60 kg

• Renal function: SCr 1.5, estimated ClCr = 55 ml/min

• Liver function: normal
Case 1

Vancomycin Dosing

Dose is based on pt’s body weight (70 kg)
Dose of 15-20 mg/kg is recommended
Round to the closest 250 mg.
Vancomycin has poor oral absorption.

Vancomycin 1000 mg IV
Vancomycin Nomogram Dosing

Usual dose: 15-20 mg/kg

Vancomycin is mainly cleared renally

Dosing frequency depends on the renal function

The following nomogram can be used to initiate vancomycin dosing. **This nomogram should NOT be used for patients on hemodialysis or peritoneal dialysis.** Determine dose from weight and interval according to the estimated creatinine clearance. Vancomycin dosing is based on actual body weight.

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>25-41 kg</th>
<th>42-57 kg</th>
<th>58-75 kg</th>
<th>79-89 kg</th>
<th>90-110 kg</th>
<th>&gt;110 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mg)</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
<td>1500 mg</td>
<td>1750 mg</td>
<td>2000 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CLcr (ml/min)</th>
<th>&gt; 100</th>
<th>80-99</th>
<th>60-79</th>
<th>40-59</th>
<th>25-39</th>
<th>&lt;25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Interval</td>
<td>12 hours</td>
<td>18 hours</td>
<td>24 hours</td>
<td>36 hours</td>
<td>48 hours</td>
<td>Per Levels</td>
</tr>
</tbody>
</table>
Case 1

Vancomycin Dosing

Vancomycin 1000 mg IV Q24h

Check trough level before the 4th dose

Target trough: >10 mg/L
15-20 mg/L (severe infections)
Vancomycin Dosing Guidelines
2009

Vancomycin serum concentrations:

• It is recommended that the vancomycin trough levels always be maintained at >10 mg/L.

• To improve penetration, to increase the probability of optimal target serum concentrations, and to increase optimal serum concentrations, a vancomycin trough of 15-20 mg/L is recommended.

• Available evidence does not support monitoring of peak serum concentration.

• The vancomycin dosing interval is adjusted, based on the steady state trough concentration.
Assess the patient’s clinical condition
Vancomycin Hemodialysis Dosing

• Negligible elimination with conventional dialysis filters; elimination is increased with high-flux filters.

• Give usual dose of 15-20 mg/kg

• Re-dose with 15-20 mg/kg when concentration is <15 or <20 mg/L for serious infections.
Summary

• Vancomycin is commonly used for the treatment of resistant or severe gram positive organisms.

• The main side effects: red man syndrome, nephrotoxicity, ototoxicity.

• Red man syndrome may be reduced by slowing the infusion rate.

• Nephtotoxicity and ototoxicity appear to be associated with high dose.
Summary

• Vancomycin dose (15-20 mg/kg) is based on the patient’s actual weight.

• Vancomycin dosing frequency depends on the patient’s renal function.

• Trough levels are recommended to assess the dose.

• Vancomycin has a concentration-independent pharmacodynamic profile, and therefore, the peak value is not recommended.
Thank You

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