The Management of Vancomycin and the Aminoglycosides

Presented by:
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Infusion Educator

Objectives

- Identify the common diagnosis
- Recognize the appropriate doses
- Review the correct timing and procedure for blood level monitoring
- Identify the process in adjusting the dose and/or interval
- Describe the prevention, assessment and management of adverse reactions

Vancomycin
**Common Diagnosis**

- Vancomycin
  - Empiric Therapy
  - Nosocomial pneumonia
  - Endocarditis
  - Bacteremia
  - Osteomyelitis
  - Bacterial meningitis
  - C-diff (PO)
  - Cellulitis
  - Meningitis

- Synergy
  - Gentamicin
    - Penicillin-Resistant Pneumococci
    - MRSA
  - β-Lactam
    - Methicillin-resistant staphylococci (Staphylococcus aureus, Staphylococcus epidermidis, and Staphylococcus haemolyticus)
    - This includes penicillin derivatives (penams), cephalosporins (cephems), monobactams, and carbapenems.

**Dosing**

<table>
<thead>
<tr>
<th>VANCOMYCIN DOSES</th>
<th>INFUSION RATE BASED ON DOSE (approx. 15 mg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT (kg)</td>
<td>Dose (mg)</td>
</tr>
<tr>
<td>≥ 93</td>
<td>1500</td>
</tr>
<tr>
<td>75-91</td>
<td>1250</td>
</tr>
<tr>
<td>59-74</td>
<td>1000</td>
</tr>
<tr>
<td>42-58</td>
<td>750</td>
</tr>
<tr>
<td>33-41</td>
<td>500</td>
</tr>
</tbody>
</table>

*Guideline for Antimicrobial Usage 2012-2013 Cleveland Clinic*
Dosing

• **Determine Patient’s Ideal Body Weight**
  - Men: IBW = 50kg + 2.3(inches over 5 ft)
  - Women: IBW = 45.5kg + 2.3(inches over 5 ft)
  - IBW = _____________

Dosing

• **Calculate Creatinine Clearance (CrCL)**
  - Note: Certain disease states or other factors may alter the relationship between Scr and CrCL resulting in overestimation or underestimation of CrCL
  - If patient is > 60 years old and Scr <1, use 1 for Scr.
  - If Total Body Weight is < the Ideal Body Weight, use Total Body Weight to calculate CrCL.
  - Male = (140-age) (IBW kg) = ____ ml/min [x 0.85 if female] = ____ ml/min
  - [Formula: 72 x SCR]

http://www.globalrph.com/multiple_crl.htm

Dosing

• **Vancomycin – Interval**

<table>
<thead>
<tr>
<th>VANCOMYCIN DOSE INTERVAL BASED ON ESTIMATED CRCL</th>
<th>Dosing interval (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCL (ml/min)</td>
<td></td>
</tr>
<tr>
<td>≥ 80</td>
<td>q12h</td>
</tr>
<tr>
<td>40-79</td>
<td>q24h</td>
</tr>
<tr>
<td>25-39</td>
<td>q48h</td>
</tr>
<tr>
<td>&lt;25</td>
<td>One dose, then check a random vancomycin level in 24-48h; reduce when level &lt;15-20mcg/ml</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>250-750mg after each hemodialysis session</td>
</tr>
</tbody>
</table>

*Guidelines for Antimicrobial Usage 2012-2013 Cleveland Clinic*
### Dosing

| Weight | CrCl [mL/min] | <60 | 30-59 | 15-29 | <15 or dialysis, JHD, CRRT | 10-19 | 10-29 | 10-25 | 10-20 | 10-15 | 10-10 | 7-10 | 7-5 | 5-4 | 5-2 | 2-1 | 1-0.5 |
|--------|--------------|-----|-------|-------|---------------------------|-------|-------|-------|-------|-------|-------|------|-----|-----|-----|-----|-----|-----|
| 40-49  | 750 mg       | 710 mg | 700 mg | 740 mg | 1000 mg, then re-dose by level | 1000 mg | 1000 mg | 1000 mg | 1000 mg | 1000 mg, then re-dose by level | 1500 mg | 1500 mg | 1500 mg | 1500 mg | 1500 mg, then re-dose by level | 2000 mg |
| 10-59  | 1000 mg      | 1000 mg | 1000 mg | 1000 mg | 1000 mg, then re-dose by level | 1000 mg | 1000 mg | 1000 mg | 1000 mg | 1000 mg, then re-dose by level | 1500 mg | 1500 mg | 1500 mg | 1500 mg | 1500 mg, then re-dose by level | 2000 mg |
| 50-75  | 1000 mg      | 1000 mg | 1000 mg | 1000 mg | 1000 mg, then re-dose by level | 1000 mg | 1000 mg | 1000 mg | 1000 mg | 1000 mg, then re-dose by level | 1500 mg | 1500 mg | 1500 mg | 1500 mg | 1500 mg, then re-dose by level | 2000 mg |

**Monitoring**

- Vancomycin

<table>
<thead>
<tr>
<th>Recommended Trough Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td>Device Infection</td>
</tr>
<tr>
<td>Endocarditis</td>
</tr>
<tr>
<td>Meningitis</td>
</tr>
<tr>
<td>Osteomyelitis</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>Pyelonephritis</td>
</tr>
<tr>
<td>Sepsis/Bacteremia</td>
</tr>
<tr>
<td>Soft tissue</td>
</tr>
<tr>
<td>Synergy</td>
</tr>
<tr>
<td>Wound Infections</td>
</tr>
</tbody>
</table>

### Dose & Interval Adjustment

- Vancomycin

<table>
<thead>
<tr>
<th>Dosage Interval Adjustments Following Each Trough Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trough Result (mcg/ml)</strong></td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>&gt;5</td>
</tr>
<tr>
<td>5-10</td>
</tr>
<tr>
<td>10-15</td>
</tr>
<tr>
<td>15-20</td>
</tr>
<tr>
<td>20-25</td>
</tr>
<tr>
<td>&gt;25</td>
</tr>
</tbody>
</table>

Cleveland Clinic Guidelines 2012-2013

Antimicrobial Stewardship Program Guidelines 2014-2015 by The Johns Hopkins Hospital
Aminoglycosides

Common Diagnosis
- Aminoglycosides
  - Empiric
    - Gentamicin, Tobramycin, Amikacin, Streptomycin
      - Pneumonia
      - Sepsis
      - UTI
      - Endocarditis
  - Synergy
    - Vancomycin
      - Penicillin-Resistant Pneumococci
      - MRSA

Dosing
- Gentamicin/Tobramycin/Amikacin – Actual body weight unless patient obese then adjusted body weight (ABW).
  - Dose (mg/kg) – Round dose to nearest 20mg

<table>
<thead>
<tr>
<th>Dosing Interval</th>
<th>Tobramycin/ Gentamicin</th>
<th>Amikacin</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>q8h</td>
<td>1.5mg</td>
<td>5mg</td>
<td>Peak and trough with third dose</td>
</tr>
<tr>
<td>q12h</td>
<td>2mg</td>
<td>7mg</td>
<td>Peak and trough with third dose</td>
</tr>
<tr>
<td>q24h</td>
<td>2.5mg</td>
<td>9mg</td>
<td>Peak and trough with third dose</td>
</tr>
<tr>
<td>Once a day</td>
<td>3mg</td>
<td>11mg</td>
<td>Peak and 24-hour random level; redose when random level is &lt;2mcg/mL (tobramycin/gentamicin) or &lt;8 mcg/mL amikacin)</td>
</tr>
</tbody>
</table>
Dosing

- **Determine Aminoglycoside dosing weight (kg)**
  - For non-obese patients, use the patient’s Actual Body Weight
  - If the patient is obese (actual body weight > 25% over IBW), use adjusted body weight (ABW):
    - ABW = IBW + 0.4 (Total Body Weight – IBW)
  - [http://www.manuelsweb.com/nrs_calculators.htm](http://www.manuelsweb.com/nrs_calculators.htm)

Gentamicin/Tobramycin/Amikacin – Interval

<table>
<thead>
<tr>
<th>Serum Creatinine</th>
<th>0.8</th>
<th>1.0</th>
<th>1.2</th>
<th>1.5</th>
<th>2.0</th>
<th>&gt;2.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
</tr>
<tr>
<td>80</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
</tr>
<tr>
<td>70</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
<td>q24h</td>
</tr>
<tr>
<td>60</td>
<td>q12h</td>
<td>q12h</td>
<td>q12h</td>
<td>q12h</td>
<td>q12h</td>
<td>q12h</td>
</tr>
<tr>
<td>50</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
</tr>
<tr>
<td>40</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
</tr>
<tr>
<td>30</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
<td>q8h</td>
</tr>
</tbody>
</table>

Monitoring

- **Aminoglycosides**
  - With every 3rd dose

<table>
<thead>
<tr>
<th>Indication/Site of Infection</th>
<th>Desired Concentrations (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTI</td>
<td>Gentamicin/Tobramycin/Amikacin</td>
</tr>
<tr>
<td>- Synergy in gram (+) infections</td>
<td>Peak</td>
</tr>
<tr>
<td>4 mcg/mL</td>
<td>&lt;2 mcg/mL</td>
</tr>
<tr>
<td>intra-abdominal</td>
<td>8-10 mcg/mL</td>
</tr>
<tr>
<td>Sepsis</td>
<td>8-10 mcg/mL</td>
</tr>
</tbody>
</table>

Guidelines for Antimicrobial Usage 2012-2013 Cleveland Clinic
Dose & Interval Adjustment

- **Aminoglycosides**
  - Adjust the dose by 20mg
  - Adjust the interval by 8 hours
  - Trough > 2 mcg/mL hold dose and draw random trough 8-12 hours later

Adverse Reactions

- **Vancomycin**
  - **Hypersensitivity**
    - RED MAN Syndrome
  - **Symptoms**
    - Pruritus – a rash usually involving the head, neck and torso
    - Complaints of itching, burning and general discomfort
    - Severe reactions can include hypotension, angioedema, headache, chills, fever, chest pain and dyspnea.
Adverse Reactions

- Vancomycin
  - Hypersensitivity
    - RED MAN Syndrome
      - Mechanism
        - Large release of histamine
        - Idiopathic

Adverse Reactions

- Vancomycin
  - Hypersensitivity
    - RED MAN Syndrome
      - Treatment
        - Slow the rate
        - Antihistamine
        - 50mg IV or PO

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Resistance
Adverse Reactions

- Vancomycin and Aminoglycoside
  - Resistance
  - Causes
    - Low trough
    - Extended therapies
    - Repeated therapies

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Nephrotoxicity

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Nephrotoxicity
    - Mechanism
      - Renal cleared
      - Can accumulate
      - Acute renal failure
Adverse Reactions

- Vancomycin and Aminoglycoside
  - Nephrotoxicity
    - Prevention
      - Once daily dosing
      - Frequent serum creatinine levels
      - Accurate trough levels
      - Hydration
      - Accurate I & O's

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Nephrotoxicity
    - Treatment
      - Discontinue therapy or if unable reduce dose and/or frequency
      - Hydration

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Ototoxicity
Adverse Reactions

- Vancomycin and Aminoglycoside
  - Ototoxicity
    - Mechanism
      - Damage to the balance portion of the inner ear
      - Usually caused by
        - Dose
        - Potentiating medications
        - Genetics

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Ototoxicity
    - Prevention
      - Frequent and accurate blood levels
      - Once daily dosing
      - Educating the patient of the risks and symptoms

Adverse Reactions

- Vancomycin and Aminoglycoside
  - Ototoxicity
    - Treatment
      - Stop therapy immediately
      - No actual treatment
      - Educate patient about safety issues.
      - Will improve with time but never entirely resolves
Alternatives

- Daptomycin (Cubicin) & Linezolid (Zyvox) have been proven effective in MRSA infections.
  - Duration of therapy
  - Labs
  - Cost
  - Interactions and side effects (zyvox)

Conclusion

- Tried and True – these medications have been used for 50+ years. They can be used alone or synergistically.
- Resistance has emerged due to misuse/overuse.
- Accurate and timely blood serums are needed to manage effectively

Questions

"Mom is a nurse. I’m not sure why she wears pajamas to work, but it’s probably because she always needs a nap."
References

- Guidelines for Antimicrobial Usage 2012-2013
  Cleveland Clinic
- Stanford Hospital and Clinics Antibiotic Dosing Reference Guide 2011
- RQHR Aminoglycosides & Vancomycin Protocol – Pharmacy Practice revised May/09
- PRMCE Anti-infective Selection Guidelines for Adults – Last Revision March 2010
- Schilling, Neuner & Rehm: Vancomycin: A 50-something-year-old antibiotic we still don’t understand.
  Cleveland Clinic Journal of Medicine Volume 78
  *Number 7 July 2011

References

- 2014 by The Johns Hopkins Hospital Antimicrobial Treatment Recommendations For Adult Inpatients; Stewardship Program.
- Pharmacokinetics Training Packet for Pharmacists – The Nebraska Medical Center, Clarkson and University Hospital – revised 1/09, 6/12
- University of Pennsylvania Medical Center Guidelines for Antimicrobial Therapy updated 5/2/2012