

Pharmacy 407 Case Studies
Vancomycin / EID Aminoglycoside Monitoring
December 9, 2011

The following cases will be discussed on December 9, 2009 9-11 am. There will be a short quiz at the beginning of the class. Please bring your i-clickers.

Learning Goals and Objectives

Goals

To learn about the recent guidelines for the therapeutic drug monitoring of vancomycin and the application of these guidelines in patients receiving vancomycin therapy.

To learn to apply the dosing and monitoring guidelines for Extended Interval Dosing (EID) with the aminoglycoside antibiotics.

References:

1. *Therapeutic Monitoring of Vancomycin in Adults – Summary of consensus Recommendations from the American Society of Health-System Pharmacist, the Infectious diseases Society of America, and the Society of Infectious Diseases Pharmacists. Pharmacotherapy 2009; 29(11): 1275-1279*
2. *Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health –System Pharmacists, the Infectious Disease Society of America and the Society of Infectious Diseases Pharmacists. Am J Health – Syst Pharm – Vol 66 Jan 1, 2009*
3. *Vancomycin Serum Concentrations Monitoring and Dosing Guideline Revised Version – Alberta Health Services Laboratory Bulletin February 2009 Vol 14 No.3 (Attached) Note; These guidelines replace the 2006 Bugs and Drugs Guidelines.*

Vancomycin Monitoring

Background

The approach to monitoring vancomycin levels has changed dramatically over the last decade. Before this time, peak and trough concentrations were routinely measured and vancomycin dosing adjusted based on those levels.

The concept of vancomycin monitoring was re-evaluated in the 1990's. By this time, it was felt that measuring peak concentrations was of little value since it was unlikely that toxicity or efficacy correlated well with the peak concentration. Routine monitoring of vancomycin was not felt necessary in many patients. However, some patients, who are severely ill, or who have rapidly changing renal function etc. do benefit from monitoring of serum vancomycin levels, but trough levels are all that are required.

Dosing adjustments are often made by adjusting the dosing interval, however in some patients it may be appropriate to adjust the dose. The standard dosing interval has been q12h or q8h in those with adequate renal function. In adjusting a dose when the serum trough concentration is below the level required for adequate treatment of the disease state, a change in dosing interval from q12h to q8h is frequently made for those initially receiving q12h dosing. An increase in dose based on the percentage increase in trough required (assuming linear pharmacokinetics of trough levels), may be chosen for patients requiring a smaller incremental adjustment of trough levels. Following the dose change, resulting serum levels checked before the 4th dose. Occasionally an adjustment of the dosing interval to q6h is required. However, in patients with meningitis, the recommended initial dosing interval is q6h. In this case, if the serum trough levels are not in the therapeutic range (15 – 20 mg/L), the dose is usually increased rather than adjusting the dosing interval to less than q6h. (Fortunately, in most cases of meningitis, vancomycin can be discontinued after the culture and sensitivity results of the infecting pathogen are known).

Case #1

TB is a 27 year old female transferred from Saskatoon on April 27th for treatment on the Burn Unit. She suffered 2nd and 3rd degree burns to 65% of her body following a house fire.

Patient data as of April 28th:
Electrolytes:

Na	137	mmol/L
K	3.9	mmol/L
Cl	105	mmol/L
Scr	55	μmol/L
BUN	3.9	mmol/L

Admission wt: 60kg
Height: 165cm
Medications prior to admission: Effexor
Allergies: penicillin, peanuts

TB is scheduled for surgery for debridement and grafting on May 1st. As part of her initial admission work up, cultures are sent (blood, urine, sputum, swabs of burns, MRSA screen).

April 27th Swabs from burns on abdomen: Enterococcus sp isolated

April 28th blood cultures: Enterococcus faecalis in 2/2 vials

Ampicillin	S
Vancomycin	S

The plastic surgery resident on call is paged with the blood culture results and requests your help in treating the patient.

What initial dosing regimen of vancomycin would be appropriate for this patient?

1g over 60 min q12h

Why? 15mg/kg (60X15 = 900 --> round to 1g).

Q12H because good renal function or even Q8H b/c burn pt & rapid CL

20-25mg/kg as a loading dose

b/c she's high risk -- lesions in skin

When should vancomycin serum levels be monitored in this case?

Check before the 4th dose

Burn patients --> high Vd & higher clearance
Therefore in this case, a load is not wrong

May even do before 4th dose to see where she's at as her CL is so high --> want to avoid underdosing

Pneumo patients
and other serious
infections --> 20 is
normal

Target trough --> 10-15 or even 10-20 (in the notes because people may change it if it comes back as 16)

For exam: 10-15

Case # 2

WJ is a 68 year old man who was admitted to the surgery ward for hemicolectomy for colon cancer. Five days after surgery he spikes a temperature of 39.1 degrees, he becomes hypotensive and disorientated. On examination, his abdomen is tender and distended.

Patient data:

Na	135	μmol/L
K	4.2	μmol/L
Cl	102	μmol/L
Scr	140	μmol/L
BUN	9.3	μmol/L
WBC	19.5	x 10 ⁶ /L
Hgb	109	g/L

Current Wt: 80kg Ht: 172cm
Allergies: NKA

WJ is sent for a CT abdomen and is found to have an intra-abdominal fluid collection. It is drained under ultrasound guidance and the fluid is sent for culture. In the meantime, he is started empirically on Vancomycin 1g IV q12h and Piperacillin/Tazobactam 4.5g IV q8h.

Abdominal fluid culture: *S. aureus*

Cloxacillin	R
Cefazolin	R
Clindamycin	R
TMP/SMX	R
Vancomycin	S

right after? or right before 4th?
IS this a peak or a trough?
(in this case --> trough)

May increase interval
or even Q36H based on CrCl
Q48H --> easier to administer
(1.5 days not so good)

The surgical residents ask for you help adjusting WJ's antibiotic regimen. It was suggested that vancomycin levels be done after the 3rd dose. The vancomycin levels came back at 27.3 mg/L. What adjustments would you suggest in his dosing regimen at this point? Target levels 10-15

Intra-abdominal fluid collection --> even though drained --> target a little higher as it may re-collect (use 15)

Use ratio --> 1250/day OR
keep at q12h and drop the dose to 750

Does he need pip/tazo as well? maybe not! Pip/tazo doesn't cover MRSA -- may be some gram (-)'s or anaerobes in there as it is an abdo infection.

Case #3

J.D. is an 18 month old 28 lb. boy who was brought in to the emergency department by his parents in the evening. He has a 24 hour history of fever, poor feeding, and vomiting. He has been quite lethargic since the afternoon.

On questioning, it is found that this boy attends daycare centre 2 days a week and has a 4 year old sister at home who also attends the same daycare.

On physical exam, his temperature was 40.2°C, HR 140 BPM, BP 80/50, RR 50 and a positive Brudzinski sign was elicited. Meningitis was suspected and a lumbar puncture was performed. CSF was sent for a gram stain, cell count, protein and glucose content and culture and sensitivity and blood chemistry.

J.D. was started on Cefotaxime 1 g I.V. q6h and vancomycin 200 mg I.V. q6h.

Results of culture and sensitivity of the CSF were:

S. pneumoniae

Sensitive to
Vancomycin

Resistant to
Penicillin, Ampicillin, Cefotaxime, Ceftriaxone

Routine Blood Chemistry

Na	135	μmol/L
K	3.9	μmol/L
Cl	104	μmol/L
BUN	6	μmol/L
Cr	72	μmol/L

Need length for CrCL

Vancomycin is continued and trough levels are ordered after the third dose. The levels reported are 9 mg/L. What recommendations would you make at this point?

keep interval the same (q4h is too low?) --> double the dose.

Target --> 15-20 b/c CNS infection

May even use ratio here

Even if organism is resistant to cefotaxime --> may keep it because of synergy

Synergy: check audio

Refer to Jamali's lecture

Case 4

Mr. A.S. is a 68 year old gentleman who is 5'7" weighing 80 kg.
He is diagnosed as having pyleonephritis. Tobramycin 80 mg I.V. q8h is prescribed.

Physical Findings

Temperature	39°C
HR	130 BP
BP	130/85 mmHg

Costovertebral pain
Urinary frequency and urgency

Lab Findings

Na	137 mmol/L
K	4.8 mmol/L
Cl	102 mmol/L
Cr.	170 µmol/L
BUN	7 mmol/L

Gram stain of urine showed gram negative rods and many polymorphs with occasional casts.

Questions

What would the calculated $C_{p_{max}}$ and $C_{p_{min}}$ be with the prescribed dose?

peak: 9, trough: 3-4

What are the possible consequences of giving the prescribed dose?

Calculate the dose of tobramycin using EID.

560 --> round to 500 q6h

Cipro IV? Resistance to cipro is 21% --> cut-off is 10%
for empiric dosing .. therefore cipro not an option

Add cefotaxime/ceftriaxone if empiric therapy

If the serum concentration of tobramycin 8 hours following your calculated EID dosing is 9 mg/L, what dosing adjustment would you recommend?

What recommendations would you make in this case?