

Tutorial 1 : Introduction to PK

Improving Patient Outcomes With Personalised Medicine

In this short tutorial, we're going to look at how you can calculate a customised dose of vancomycin for an individual patient. This is a complex case, based on a real patient. Details have been altered to preserve patient privacy. In this tutorial, we're going to focus on vancomycin, although discussion questions may include other drugs.

The style in which these tutorials are written is based on the problem/case-based learning approach commonly used by Australian universities.

Introduction

You are a student on rotation at Ipswich Hospital in Brisbane embedded in a medical team, and you've been asked to provide support for antibiotic dosing decisions. On your first day, your supervisor decides to test your skills, and asks you to look at vancomycin dosing in Amy Smith. You ask for a brief overview of the case, and your supervisor gives you a brief case summary to date (Triggers 1 & 2).

Trigger 1: Presentation

Mrs Smith, a 62 year female (62kg, 167cm) presented at 21:00 with suspected sepsis secondary to a diabetic ulcer. On presentation to the emergency department via ambulance, she had the following vital signs:

- Temperature 39°C
- Pulse 140/min
- BP 70/40
- Confused

In emergency she was treated with:

- Fluid resuscitation with normal saline
- 1 mcg/kg/min norephenephrine IV via central line
- Empiric antibiotic therapy for sepsis

Discussion Questions

What end-organ effects is septic shock likely to cause?

Which are relevant for the pharmacokinetics of antibiotics?

What further tests would you order to determine this? What would you expect them to show from the above vital signs?

Trigger 2: Commencing Antibiotic Therapy

Prior to the commencement of antibiotic therapy for sepsis, three sets of bloods are taken and sent to the lab to determine antibiotic sensitivity. Blood tests are done, and the report is:

Hb	132 g/L	(130 - 180 g/L)
WBC	14.8 x 10 ⁹ /L	(4.0 - 10.5 x 10 ⁹ /L)
Sodium	139 mmol/L	(135 – 145 mmol/L)
Potassium	4.1 mmol/L	(3.5 – 4.5 mmol/L)
Chloride	107 mmol/L	(95 – 110 mmol/L)
Creatinine	150 umol/L	(50 – 110 micromol/L)
Urea	8 mmol/L	(3 – 8 mmol/L)

Without waiting for results, the emergency team start empiric antibiotic therapy:

- Piperacillin / Tazobactam 4.5g QID @ 22:00
- Vancomycin 500mg @ 2200

ACTIONS

1. **Log into DoseMe - you should already have an account - if not, go to <https://dosing.com.au/tutorial1/> and follow the link on the right.**
2. **Add Mrs Smith as a patient, and add a course of vancomycin.**
3. **Before recording any doses of vancomycin to Mrs Smith, generate a dose report for the following target:**

Note: While an infusion length of 0.5 hours is likely to be too short for the calculated dose, DoseMe will automatically increase the infusion length for vancomycin so that the infusion rate does not exceed 10mg/min.

4. **Add a laboratory result for Mrs Smith, recording serum creatinine only, 150 µmol/L @ 8:30am.**
5. **Generate a new dose report for the target on the right.**

Calculate Dose

Simulate Dose(s)
Peak/trough
Trough only
AUC (Exposure)

Target Trough mg/L

Infusion Length hours

Dosing Period hours

Number of Doses doses

Generate historical / retrospective dose recommendation

Calculate Next Dose

Discussion Questions

Why are both piperacillin / tazobactam and vancomycin both given for empiric therapy of sepsis? What is the coverage of each?

What's the standard initial dose of vancomycin for a 62kg patient (hint: look at the dosing report)? Why has Mrs Smith been given less, and can you relate this to her presenting complaint, vital signs, and lab results?

Why does the second dose report differ from the first? What does this suggest about the clearance route of vancomycin?

What dose does the standard vancomycin guidelines suggest be given in this case? - Refer to: <https://metrosouth.health.qld.gov.au/sites/default/files/msh-vancomycin-guidelines.pdf>

Trigger 3: Ongoing Antibiotic Treatment

Your supervisor continues to explain the course of treatment for the patient. The following three doses were given:

Dose Time	Amount	Infusion Length
Two days ago, 2200	500 mg	1 hour
Yesterday, 0900	500 mg	1 hour
Yesterday, 2200	500 mg	1 hour

Unfortunately, only one lab was ordered, today at 1000:

Creatinine 152 umol/L (50 – 110 micromol/L)
 Vancomycin 17.3 mg/L

ACTIONS

1. Record the above doses and laboratory results in DoseMe.

Discussion Questions

Given the concentration-time plot, is the patient at steady-state, and would you change the dose? Raise it? Lower it?

ACTIONS

2. Calculate a dose for the following target:

Calculate Dose

Simulate Dose(s)
 Peak/trough
 Trough only
 AUC (Exposure)

Target Trough 15 mg/L

Infusion Length 0.5 hours

Dosing Period 12 hours

Number of Doses 6 doses

Generate historical / retrospective dose recommendation

3. Use the dose simulator to compare what the outcome of the guidelines-based dose would be (refer to: <https://metrosouth.health.qld.gov.au/sites/default/files/msh-vancomycin-guidelines.pdf>).

Discussion Questions

What dose would you given in clinical practice to this patient? Justify why.

Extension Discussion Questions

What does the red line correspond to? See the paper used for how the population clearance is calculated: <http://www.ncbi.nlm.nih.gov/pubmed/16304155> - refer to table 3, row 4.

If the red line (population average model with individual data) contains this additional information, is it effectively the same as the nomogram linked above? Is it similar?

Given that the population / average patient line differs significantly from what we've seen in this particular patient, what does this suggest about the variability in response to a given dose of drug across the population? Can you find the overall variability of clearance in this population?

Looking at the patient group used in this study, how does it compare to your local hospital patients? Bayesian fitting will correct for this, do you understand how?