Vancomycin administered by continuous infusion should be dosed according to clearance and not based on the patient's body weight

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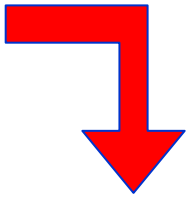
The problem

- Continuous infusion (CI) of vancomcyin is gaining increasing popularity because of facilitated therapeutic drug monitoring and nursing [1].

1. Van Herendael *et al*. Ann Intensive Care. 2012; 2:22

- In a literature survey, we observed that several authors mention the dosage of vancomycin in "*mg per kg of body weight*" during the infusion [see e.g. 2,3], which seems to be widely used by clinicians [4].

2. Wisocki *et al.* Antimicrob Agents Chemother. 2001; 45:2460-7.
3. Roberts *et al.* Antimicrob Agents Chemother. 2011; 55:2704-9
4. Buyle *et al*. Eur. J. Clin. Microb. Inf. Dis. 2013. 32:763-8



Patients assigned to the CIV group received vancomycin at 15 mg/kg infused over 60 min, followed by a continuous infusion of 30 mg/kg. Except for the first 15 mg/kg, which was adjusted according to the baseline serum creatinine concentration, the same initial dosage was given to everyone. The treatment was

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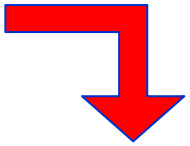
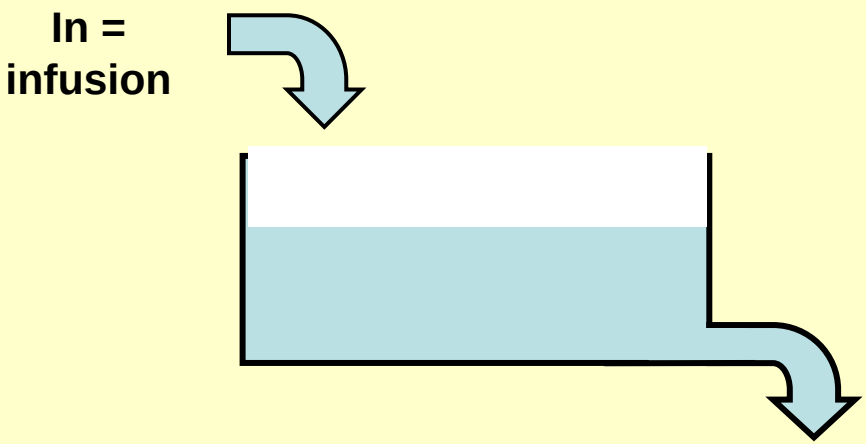


In this study, the choice of antibiotic regimen was at the discretion of the clinician; published recommendations (15-mg/kg loading dose followed by 30-mg/kg daily dose calculated on the total body weight [TBW]) (33),

The concept of continuous infusion

- The aim of continuous infusion is to maintain its serum level at a fixed value (after the loading dose) which is like maintaining the level of water in bath constant.



Once a bath is at the desired level (i.e. after the loading dose), <u>maintaining</u> its level constant does not depend upon its volume but of the ratio of tap and drain flows (which must be equal: in = out…)

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Where is the error ? (1)

The concentration at steady state is given by

$$C_{ss} = K_o/CL \quad \text{(eqn.1)}$$

where - K_o is the rate if infusion (in mg/h)
- CL is the clearance (in L/h)

The creatinine clearance is the calculated one (Cockroft-Gautl)

$$CC_rCL = ((140\text{-age}) \times \mathbf{weight} / (Pl.creat. \times 72)) \times F$$

where Pl.creat is the plasma creatinine
F is a factor related to sex (1 for male)

and this formula **includes the weight** !

Where is the error ? (2)

If you now divide K_o (rate of infusion) by the weight, you count **two times** the weight, which leads to incorrect serum levels

$$C_{ss} = (K_o/\mathbf{weight}) / ((140\text{-age}) \times \mathbf{weight} / (\text{Pl.creat.} \times 72)) \times F$$

The poster show also simulation demonstrating that

- wile the creatinine clearance is linearly related to the weigh in the Cockroft & Gault's formula
- serum the levels calculated by equation #1 are not linearly related to the weight used in Cocktroft & Gault's formula to calculate the clearance

Incorrect levels if dividing the daily dose by the weight: example for patients with **the same renal function** but **increasing weights**

Patient's CC_rL (ml/min)	Patient's weight (kg)	daily dose as mg/kg [1]	total daily dose in 24h (mg)	C_{ss} [2] (mg/L)
100	**50**	30	**1500**	**16.03**
100	**60**	30	**1800**	**19.23**
100	**70**	30	**2100**	**22.44**
100	**80**	30	**2400**	**25.64**

[1] as most often but erroneously recommended in the literature (e.g., refs 2-3) for daily dose during the continuous infusion

[2] calculated according to equation 1 and using a correction factor of 0.65 (commonly accepted ratio of vancomycin to creatinine clearance [5])

5. Moellering et al. Ann Intern Med 1981; 94:343-346

Conclusions and recommendations

- Dosing vancomycin by weight (mg/kg) during continuous infusion is a mistake as it leads to incorrect values if patients deviate from ideal body weight.

- Clinicians wishing to use vancomycin (or any other drug) by continuous infusion should administer first a **loading dose** calculated on the basis of body weight (typically, for vancomycin, 20 mg/kg over 1h for a patient with normal V_d [0.75 l/kg]);

- then **start the infusion** and **adjust their dose on the basis of clearance only** (typically, for vancomycin, 11 mg/h for CC**r**Cl of 0.1L/h with linear increment or decrement for each variation of 10 %)

- Practical recommendations are available from ref. [6] and from our web site (***http://www.facm.ucl.ac.be/vancomycin***)

6. Ampe et al. Int J Antimicrob Agents 2013 May;41(5):439-46