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 vancomycin is gaining increasing popularity because of facilitated therapeutic drug monitoring and nursing [1].


- 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].


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), maintaining its level constant does not depend upon its volume but of the ratio of tap and drain flows (which must be equal: in = out...)

In = infusion

Out = clearance
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 a bath at the desired level (i.e. after the loading dose). Maintaining its level constant does not depend upon its volume but on the ratio of tap and drain flows (which must be equal: in = out...).
Where is the error? (1)

The concentration at steady state is given by

\[ C_{ss} = \frac{K_o}{CL} \]  (eqn.1)

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

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

\[ CC_{rCL} = \frac{((140-\text{age}) \times \text{weight})}{(\text{Pl.creat.} \times 72)} \times F \]

where \( \text{Pl.creat} \) 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 $K_0$ (rate of infusion) by the weight, you count \textbf{two times} the weight, which leads to incorrect serum levels

$$C_{ss} = \frac{K_0}{\text{weight}} \div \left( \frac{(140-\text{age}) \times \text{weight}}{(\text{Pl.creat.} \times 72)} \right) \times F$$

The poster shows also simulation demonstrating that

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

<table>
<thead>
<tr>
<th>Patient's CC(_{r,l}) (ml/min)</th>
<th>Patient's weight (kg)</th>
<th>daily dose as mg/kg (^1)</th>
<th>total daily dose in 24h (mg)</th>
<th>(C_{ss}) (^2) (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>50</td>
<td>30</td>
<td>1500</td>
<td>16.03</td>
</tr>
<tr>
<td>100</td>
<td>60</td>
<td>30</td>
<td>1800</td>
<td>19.23</td>
</tr>
<tr>
<td>100</td>
<td>70</td>
<td>30</td>
<td>2100</td>
<td>22.44</td>
</tr>
<tr>
<td>100</td>
<td>80</td>
<td>30</td>
<td>2400</td>
<td>25.64</td>
</tr>
</tbody>
</table>

\(^1\) 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])

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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 CCrCl 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)