Vancomycin pharmacokinetics in alcohol and intravenous drug abusers

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Purpose
To characterize vancomycin pharmacokinetic parameters in:

• non-cirrhotic alcoholics
• patients with alcohol-induced cirrhosis
• intravenous drug abusers (IVDA).

Background

• Elimination of vancomycin is primarily by glomerular filtration (80-90%), but the liver may also be involved to a small extent.
• Chronic consume of ethanol induces hepatic enzymes and can lead to hepatic damage. Both factors could affect vancomycin elimination.
• Moreover, the use of drugs of abuse could also affect vancomycin clearance.

Methods

• Retrospective study in the aforementioned patients treated with vancomycin and therapeutic drug monitoring (TDM), between 2009-2012, in a Tertiary Hospital University.
• Clinical and pharmacokinetic reports from TDM (PKS Abbot*) were reviewed to obtain demographic characteristics, hepatic/renal surrogates, initial/recommended dosage, steady state (SS) distribution volume (Vd), clearance (CL), Cmax and Cmin.
• Control values were obtained from patients with normal renal function from an in-house internal database.
• Therapeutic target was: 7-12 mg/L for Cmin.
• Patients with renal failure (creatinine clearance: CLcr < 60 mL/min) were excluded.
• Results are shown as mean ± SD (T-test for comparisons to controls).

Results

Sixty-five patients were included. Demographic data were similar between groups (table 1).

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Control</th>
<th>Non-cirrhotic alcoholics</th>
<th>Cirrhotic</th>
<th>IVDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>20</td>
<td>18</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>59.45 ± 13.2</td>
<td>52.67 ± 11.4</td>
<td>58.5 ± 10.5</td>
<td>42.8 ± 9.48</td>
</tr>
<tr>
<td>Weight(kg)</td>
<td>75</td>
<td>100</td>
<td>88.8</td>
<td>88.8</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>32.55 ± 3.09</td>
<td>27.73 ± 6.49</td>
<td>25.3 ± 5.85</td>
<td>29 ± 3.65</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1.126 ± 1.05</td>
<td>0.80 ± 0.82</td>
<td>4.90 ± 5.85</td>
<td>1.24 ± 1.34</td>
</tr>
<tr>
<td>Cmax/Crofoot-Gault (mg/min)</td>
<td>96 ± 20.69</td>
<td>134.72 ± 39.98</td>
<td>111.6 ± 24.27</td>
<td>135.6 ± 28.54</td>
</tr>
</tbody>
</table>

However, there are some differences between groups:
• IVDA patients were significantly younger than patients in other groups.
• Non-cirrhotic alcoholics were heavier than the rest of groups.
• Albumin values were lower in alcoholic patients. Cirrhotic patients were also characterized by higher bilirubin values.
• It is also remarkable that the majority of patients were men.

Pharmacokinetic results are shown in table 2.

<table>
<thead>
<tr>
<th>CL (L/h)</th>
<th>Control</th>
<th>Non-cirrhotic alcoholics</th>
<th>Cirrhotic</th>
<th>IVDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.27 ± 1.47</td>
<td>6.40 ± 2.16</td>
<td>4.27 ± 1.38*</td>
<td>6.53 ± 1.91</td>
<td></td>
</tr>
<tr>
<td>Vd (L/Kg)</td>
<td>0.75 ± 0.33</td>
<td>0.64 ± 0.16</td>
<td>0.68 ± 0.10</td>
<td>0.59 ± 0.09</td>
</tr>
<tr>
<td>Initial dosage (mg/kg/day)</td>
<td>29.23 ± 5.75</td>
<td>26.55 ± 7.35</td>
<td>27.28 ± 9.01</td>
<td>28.05 ± 6.12</td>
</tr>
<tr>
<td>Cmax (mg/L)</td>
<td>9.76 ± 5.49</td>
<td>7.91 ± 4.26</td>
<td>10.37 ± 4.51</td>
<td>5.30 ± 3.04*</td>
</tr>
<tr>
<td>Cmin (mg/L)</td>
<td>22.65 ± 8.45</td>
<td>16.65 ± 5.09*</td>
<td>23.37 ± 6.94</td>
<td>16.21 ± 4.29*</td>
</tr>
</tbody>
</table>

| Table 2. Pharmacokinetic data. *p<0.05 |

• As regards to pharmacokinetic parameters (CL, Vd), significant differences were only observed in CL in cirrhotic patients (p= 0.02).
• A tendency to higher CL values in non-cirrhotic alcoholic patients and IVDA is present in these data, as well.
• Although initial dosages were similar to control group, Cmax and Cmin values were significantly lower in IVDA.

Conclusions

• Vancomycin CL is significantly decreased in cirrhotic patients, probably due to hepatorenal syndrome. An initial reduced dosage might be considered.
• Vancomycin CL tends to be higher in alcoholics and in IVDA patients but results are not significant. Higher doses could be needed to obtain therapeutic concentrations.
• Therefore, vancomycin TDM is highly advisable in all these groups of patients.

References

Authors have no conflict of interest in this study.

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