PHC-029

Vancomycin pharmacokinetics in alcohol and intravenous drug abusers

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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.

Purpose

To characterize vancomycin pharmacokinetic parameters in:

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

Methods

• Retrospective study in the aforementioned patients treated with vancomycin and therapeutic drug monitoring (TDM), between 2009-2012, in a Tertiary University Hospital.
• 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^{SS}), clearance (CL), C^{SS}_{min} and C^{SS}_{max}.
• Control values were obtained from patients with normal renal function from an in-house internal database.
• Therapeutic target was 7-12 mg/L for C^{SS}_{min}.
• 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).

	Control	Non-cirrhotic alcoholics	Cirrhotic	IVDA
Number of patients	20	18	18	9
Age(years)	59.45 ± 13.20	52.67 ± 11.4	58.5 ± 10.53	42.8 ± 9.48
Sex (%male)	75	100	88.8	88.8
Weight(kg)	69.6 ± 9.84	84.11 ± 25.30	73.44 ± 15.63	74.7 ± 17.78
Albumin (g/L)	32.55 ± 3.09	27.73 ± 6.49	25.3 ± 5.85	29 ± 3.65
Bilirrubin (mg/dL)	1.126 ± 1.05	0.80 ± 0.82	4.90 ± 5.85	1.24 ± 1.34
ClCr Crockoft-Gault (mL/min)	96 ± 20.69	134.72 ± 39.98	111.6 ± 24.27	135.6 ± 28.54

Table 1.Demographic data

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

Pharmacokinetic results are shown in table2.

	Control	Non-cirrhotic alcoholics	Cirrhosis	IVDA
CL (L/h)	5.27 ± 1.47	6.40 ± 2.16	4.27 ± 1.18*	6.53 ± 1.91
Vd^{SS} (L/Kg)	0.75 ± 0.33	0.64 ± 0.16	0.68 ± 0.10	0.59 ± 0.09
Initial dosage (mg/kg/day)	29.23 ± 5.75	26.55 ± 7.35	27.28 ± 9.01	28.05 ± 6.12
C^{SS}_{min} (mg/L)	9.76 ± 3.49	7.91 ± 4.26	10.37 ± 4.51	5.30 ± 3.04*
C^{SS}_{max} (mg/L)	22.65 ± 8.45	16.65 ± 5.09*	23.37 ± 6.94	16.21 ± 4.29*

Table 2. Pharmacokinetic data. *p<0.05

• As regards to pharmacokinetic parameters (CL, Vd^{SS}), 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, C^{SS}_{min} and C^{SS}_{max} 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

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Authors have no conflict of interest in this study.
18th EAHP Congress, Paris, France.