

Materials and Methods A retrospective study was conducted from February to April 2012. All patients treated with VPA were included and grouped depending on whether VPA was part of their home treatment or not.

Variables collected were: dose, indication, total VPA serum concentration (C), drug interactions classified as $\geq C$ by Lexi-Comp, glomerular filtration rate (GFR), Child-Pugh score, albumin and bilirubin.

Results 30 patients were treated with VPA, 24 of whom were on VPA before admission (15 epilepsy, 9 psychiatric disorders and 1 unknown reason).

Reasons for admission were: 5 convulsions, 12 psychiatric disorders and 13 causes unrelated to VPA. At discharge 27 patients continued on VPA with a mean dose similar to the dose at admission.

C was determined in 14 patients: 5 were within the reference range (50–100 mg/L); 2 above, achieving therapeutic levels before discharge and 7 below. In these latter cases, 3 had an albumin < 4.2 g/dL, but none reached $C > 50$ mg/L after correcting it with the J. Hermida formula which is a theoretical method for normalising C in hypoalbumenic patients. GFR, Child-Pugh score and bilirubin were normal. Mean time between changes in dose and C determinations was 1.5 days (0–5 days).

21 drug interactions were detected in 15 patients, involving a total of 10 drugs. Only 2 interactions were reported: VPA meropenem and VPA lamotrigine.

Conclusions Changes in free fraction of VPA, due to hypoalbuminaemia, liver or kidney disease and hyperbilirubinaemia, must be detected.

C should be measured once a steady state has been achieved (3–5 days).

Drug interactions affecting VPA should be added to the pharmacy service's interaction notification programme.

No conflict of interest.

PHC-028 THERAPEUTIC DRUG MONITORING OF DARUNAVIR IN TWO DIFFERENT TREATMENT MODALITIES

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Background Darunavir (DRV) is a protease inhibitor (PI) that when boosted with ritonavir is effective against both wild-type and PI-resistant HIV. It's relatively long half-life supports once-daily dosing (QD) in treatment-naïve patients. To treat treatment-experienced patients twice-daily dosing (BID) is preferred.

Purpose To analyse the need for therapeutic drug monitoring (TDM)-guided interventions for darunavir and their results in patients receiving darunavir/ritonavir both in BID and QD modalities.

Materials and Methods A prospective study that included 38 patients was performed: 21 (55.3%) in the BID group and 17 (44.7%) in the QD group. Plasma darunavir levels were determined using an HPLC method and viral loads (VL) were measured. Assessments were performed at inclusion and whenever VL was detectable. Patients with detectable VL load were subjected to intervention (change in dose and/or adherence reinforcement) and another plasma drug determination was scheduled. Interventions were considered successful if VL became undetectable.

Results Abnormal plasma drug levels (outside a 1000–8000 ng/ml range) were found in 13/38 (15.6%) determinations which correspond to 9 patients and in all cases detectable VL were also found. Among measures yielding normal levels the proportion of cases

with detectable VL was 49/83 (59%). TDM-guided interventions were performed in 22/38 (58%) patients and were successful in 11 of them (7 BID and 4 QD).

Mean plasma levels in the BID group were greater than in the QD group: 3715 ng/ml (SD: ± 1679) and 2830 ng/ml (SD: ± 1030) respectively ($p < 0.02$). In the BID group cases with undetectable VL had mean plasma levels superior to those of cases with detectable VL: 4524 ng/ml (SD: ± 1679) versus 3375 (SD: ± 1679), $p < 0.05$.

Conclusions TDM-guided interventions could be useful in patients receiving darunavir/ritonavir and experiencing viral failure, especially if the BID dosing modality is used.

No conflict of interest.

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 consumption 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 characterise vancomycin pharmacokinetic parameters in non-cirrhotic alcoholics, patients with alcohol-induced cirrhosis and intravenous drug abusers (IVDAs).

Materials and Methods Retrospective study in the aforementioned patients treated with vancomycin in whom therapeutic drug monitoring (TDM) was performed, 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 (V_{dSS}), clearance (CL), CSS-min and CSS-max. The therapeutic target was 7–12 mg/L for CSS-min. Patients with renal failure ($CL_{Cr} < 60$ mL/min) were excluded. Results are shown as a mean \pm SD (T-test for comparisons with controls).

Results Sixty-five patients were included. Demographic data were similar between the groups. 87.7% were men. Pharmacokinetic data is shown in table 1. As regards pharmacokinetic parameters, significant differences were only observed in CL in cirrhotic patients ($\#p = 0.02$).

Conclusions Vancomycin CL is significantly decreased in cirrhotic patients, probably due to hepatorenal syndrome. Initial dose reduction might be considered. Vancomycin CL tends to be higher in alcoholics and IVDAs. Higher doses could be needed to obtain therapeutic concentrations. Therefore, vancomycin TDM is highly advisable in all these groups of patients.

Abstract PHC-029 Table 1

	Control	Non-cirrhotic alcoholics	Cirrhosis	IVDA
Number of patients	20	18	18	9
CL (L/h)	5.27 \pm 1.47 [#]	6.40 \pm 2.16	4.27 \pm 1.18 [#]	6.53 \pm 1.91
V_{dSS} (L/Kg)	0.75 \pm 0.33	0.64 \pm 0.16	0.68 \pm 0.10	0.59 \pm 0.09
Initial dosage (mg/kg/day)	29.23 \pm 5.75*	26.55 \pm 7.35*	27.28 \pm 9.01*	28.05 \pm 6.12*
CSS _{min} (mg/L)	9.76 \pm 3.49	7.91 \pm 4.26	10.37 \pm 4.51	5.30 \pm 3.04

* $p > 0.05$; $\#p = 0.02$

No conflict of interest.