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The pharmacist's role in improving valproic acid prescriptions

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Background:

Valproic acid (VPA) is 90-95% protein bound to albumin; this binding is saturable so other parameters that can modify the free fraction of VPA should be taken into account.

Porpouse:

To identify improvement areas for VPA usage and monitorization in a tertiary hospital where Pharmacy Service does not routinely send pharmacokinetic dose adjustment recommendations.

Materials and methods:

A retrospective study was conducted from February to April 2012. All patients treated with VPA were included.

Variables collected were: dosage, indication, total VPA serum concentration (C), drug-interactions classified as ≥C by Lexi-Comp®, glomerular filtration rate (GFR), analytical Child-Pugh, albumin and bilirubin

Results:

30 patients on VPA treatment

- 6 patients initiated treatment during hospitalization
- 24 were on VPA before admission
  - 15 epilepsy
  - 9 psychiatric disorders
  - 1 unknown reason

At discharge → 27 patients on VPA → mean dose similar to admission dose

Admission reasons → 5 convulsions, 12 psychiatric disorders, 13 causes unrelated to VPA

- C was determined in 14 patients:

5 patients: C = 50-100mg/L

7 patients: C < 50mg/L
- 4 patients had albumin > 4,2g/dL
- 3 patients had albumin < 4,2g/dL

2 patients: C > 100mg/L, achieving therapeutic levels before discharge

J. Hermida et al formula [1]

Theoretical method for normalizing C in hypoalbumenic patients:

$$C_N = \alpha_H C_H / 6.5$$

α_H = free fraction of VPA corresponding to patient's albuminemia
C_H = total concentration of VPA
C_N = total normalized concentration of VPA

None reached C>50mg/L after correcting it.

- GFR, analytical Child-Pugh and **bilirubin** were normal.

- Mean time between changes in dosage and C determinations was 1,5 days (0-5days).

-21 drug-interactions: in 15 patients, 10 drugs involved, 2 interactions reported: VPA-meropenem and VPA-lamotrigine.

Conclusion:

Changes in free fraction of VPA, due to hypoalbuminemia, liver or kidney disease and hyperbilirubinemia, must be detected.
C should be measured once steady state has been achieved (3-5days).
Drug-interactions affecting VPA should be added to Pharmacy Service's interaction notification program.

1- Hermida J, Tutor JC. A Theoretical Method for Normalizing Total Serum Valproic Acid Concentration in Hypoalbuminemic Patients. J Pharmacol Sci 97, 489 – 493 (2005)