Hepatic adverse effects of valproic acid: Management strategies

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Abstract:

INTRODUCTION: Valproic acid (VPA) is a widely prescribed first-generation antiepileptic drug. It can induce different liver adverse effects (AEs) which range from mild to severe.

MATERIALS AND METHODS: A retrospective study was conducted by collecting 9-year reports (from January 2015 to June 2023) of VPA-associated hepatic AEs. It was collected in the Regional Center of Pharmacovigilance of Sfax (Tunisia). Causality was evaluated with the French Bégaud *et al.* imputability method. Plasma VPA concentrations were measured using an automated enzyme immunoassay (INDIKO).

RESULTS: We collected the eight cases of hepatic cytolysis with varying severity: Six had mild elevations of liver enzymes, one presented with moderately severe cytolysis and one case was fatal. There management strategies were guided by both transaminase levels and VPA concentrations. For those with alanine aminotransferase levels ≥5 times the upper limit of normal (ULN), we conducted the drug discontinuation. However, for patients with lower levels of transaminases, plasma VPA level measurement was recommended. The concentrations were within or near the ULN. Management consisted of either withdrawal or dose reduction, depending on associated clinical symptoms. Additional investigations to rule out nondrug-related causes performed in five cases were negatives. Most patients recovered favorable outcome after discontinuation or VPA dose reduction.

CONCLUSION: Management of VPA-induced hepatic cytolysis requires integrating the severity of liver enzyme elevations, plasma drug level measurements, and the results of etiological investigation to guide the clinical decisions.

Keywords:

Hepatic adverse effects, imputability, management strategies, severity, valproic acid