

RGH Pharmacy E-Bulletin

Volume 31 (1): July 28, 2008

A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH
© Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia 5041

Sodium valproate in bipolar disorder – dosage and monitoring

Bipolar disorder is estimated to occur in about 1% to 2% of the population. It is a recurrent, debilitating illness characterised by episodes of mania or hypomania, depression, and possibly ‘mixed episodes’ with both manic and depressive features.

Sodium valproate (often referred to as a ‘mood stabiliser’) is one of the pharmacological options for the management of acute mania and also for prophylaxis against recurrent episodes. Though not fully established, its mode of action in bipolar disorder is attributed to increased brain levels of gamma-aminobutyric acid (GABA).

Recommendations regarding the clinical benefit, or lack thereof, of measuring plasma concentrations of sodium valproate vary between sources. The half-life of sodium valproate is reported as 8 to 12 hours and steady state concentrations are reached after 3 to 5 days. If levels are taken they should therefore be pre-dose trough levels measured after steady state has been reached.

The Australian Therapeutic Guidelines: Psychotropic (2003) state that therapeutic serum/plasma concentration ranges for acute mania are reasonably well established and suggest that a concentration of 43mg/L or greater is needed in acute mania, while toxicity is likely at concentrations greater than or equal to 122mg/L. Within this range, dose should be determined by clinical response.

The initial recommended dosage of sodium valproate is 400 mg to 800 mg orally per day, in two divided doses with the dosage increased every two to three days by increments of 200 mg to 500 mg per day and concentrations measured after the recommended three to five days. Alternatively, a loading dose strategy may be used to produce a more rapid response, with an initial oral dose of 20 mg/kg. Most patients will require a dose of 1000 mg to 2000 mg per day, though some may need 3000 mg or higher.

There is no established therapeutic range in prophylactic treatment though it is suggested that the range developed for its use in epilepsy is used as a guideline (50 to 100 mg/L). The recommended initial dosage is as for acute mania; however the dose can be increased more slowly, usually in weekly increments. Most patients require a daily dose of 1500 to 3000 mg to obtain therapeutic plasma concentrations.

It has been suggested that plasma concentrations should be interpreted with caution and not relied on solely as a guide to dosage due to a lack of a clear-cut relationship between concentration and effect, with high inter-individual variability; wide diurnal fluctuations in serum levels; and occurrence of dose dependent plasma protein binding.

The primary reasons for measuring serum valproate levels in bipolar disorder are to monitor patient compliance with treatment, and to help avoid toxicity. Compliance can be an important issue, particularly at the onset of a manic episode, as patients often lose insight into their illness and their need for medication.

Acknowledgment – This E-Bulletin is based on work by Anita Marwood, Senior Clinical Pharmacist, RGH

FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
Information in this E-Bulletin is derived from critical analysis of available evidence – individual clinical circumstances should be considered when making treatment decisions. You are welcome to forward this E-bulletin by email to others you might feel would be interested, or to print the E-Bulletin for wider distribution. Reproduction of this material is permissible for purposes of individual study or research.