

Re: Sodium Valproate-Induced Myopathy in a Child

رد: الاعتلال العضلي الذي يسببه دواء صوديوم فالبرويت في طفل

Sir,

I read with interest the letter to the editor by Ahmed published in the SQUMJ February 2015 issue.¹ The patient, after a diagnosis of childhood-onset epilepsy with absence seizures, was started on 250 mg of sodium valproate in two divided doses (20 mg/kg). As response to treatment was inadequate, the dose of the drug was gradually increased over the following weeks to the maximum permissible dose of 500 mg twice daily.¹ Six months later, slowly developing myopathy was observed. Based on the clinical picture, a myopathic needle electromyography pattern and low serum carnitine levels, the author attributed the myopathy to carnitine deficiency secondary to valproate therapy.¹

Nakajima *et al.* reported that the long-term treatment of paediatric patients with sodium valproate could have an impact on specific acylcarnitines and proposed that this effect is augmented by simultaneous use of other anticonvulsants.² However, they also noted that valproylcarnitine formation through the use of therapeutic sodium valproate seems insufficient for the development of severe carnitine deficiency.² Hence, such biochemical changes in acylcarnitines in children are not clinically significant.^{2,3} I presume that the development of myopathy in the patient described by Ahmed cannot be solely attributed to valproate therapy, as the drug was prescribed at permissible doses.¹

The myopathy in the studied patient may be due to a carnitine palmitoyltransferase (CPT) II deficiency. This condition leads to a disorder of long-chain fatty-acid oxidation.⁴ There are several clinical presentations of CPT II deficiency, including the myopathic form, which is usually mild and can manifest from infancy to adulthood. Myopathic CPT II deficiency can be associated with myoglobinuria and manifest as exercise-induced muscle pain and weakness.⁴ There is evidence that valproate is among the factors that trigger myopathy in CPT II-deficient patients.⁴ Tandem mass spectrometry are used to measure serum and plasma acylcarnitines.³ Reduced CPT enzyme activity indicate a definitive diagnosis. However, new advances in molecular genetic testing have provided an improved non-invasive diagnostic method with the presence of the *carnitine palmitoyltransferase 2* gene (the only gene associated with CPT II deficiency).⁴

Although, to the best of my knowledge, no studies yet exist which investigate CPT II deficiency in Saudi Arabia, the high prevalence of consanguinity in this region might be a strong indicator of its potential existence.⁵ Consanguinity is significantly associated with various patterns of inborn errors of the metabolism.⁶ A myopathic form of CPT II deficiency ought to be seriously considered for this reported patient and suitable laboratory tests employed.¹ However, the patient reported by Ahmed could still be included among the paediatric valproate-associated myopathy cases reported in the literature.¹

Valproate is a broad-spectrum antiepileptic drug. In high-risk patients, carnitine supplementation with combined antiepileptic drug therapy, carnitine-free enteral tube feeding and the maintenance of a healthy body weight have been recently recommended to prevent epilepsy-related complications.⁷ However, controlled, randomised and multicentre studies are needed to investigate the therapeutic and prophylactic roles and the optimal administration of carnitine supplementation during valproate therapy.

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