≈ ORAL PRESENTATIONS ≈

OP 027

The Use of Multi-Dose Activated Charcoal in Phenytoin Toxicity secondary to Genetic Polymorphism

Chan BSH, Sellors K., Chiew A. [1, 2], Buckley N.[1, 2]

Clinical Toxicology Unit, Prince of Wales Hospital, Sydney, Australia,

New South Wales Poisons Information Centre, Sydney, Australia

Abstract

We present 3 patients with chronic phenytoin toxicity secondary to reduced cytochrome enzyme function. MDAC was used in two patients with a resultant reduction in the half-life of phenytoin. One patient with chronic phenytoin toxicity did not have MDAC and is used for comparison.

Results: A 75 year-old lady was commenced on phenytoin 300mg daily for seizure prophylaxis following a neurosurgical procedure. Over the following fortnight she gradually declined with confusion, slurred speech, nystagmus and ataxia. A phenytoin level performed after two weeks of receiving phenytoin was 156 µmol/L (40-80 µmol/L). Phenytoin was ceased but she remained unwell and her levels remained persistently elevated over the next 10 days with no apparent elimination. She was commenced on MDAC, 25 g x 12 doses with dramatic drop of the phenytoin levels and improvement of her neurological function with a calculated half-life of 44 hours during the administration of MDAC. Formal genetic testing revealed she was a 'poor metaboliser with respect to CYP2C9 (3*/3*) enzyme activity.

A 65 year old lady presented with a dislocated left prosthetic hip following a fall whilst intoxicated. She had a history of alcohol-related seizures for which she took phenytoin 100mg daily. Her phenytoin level was noted to be elevated on admission at 150 µmol/L. The phenytoin level remained elevated over the next 24 hours. She was commenced on MDAC (50 gm followed by 25 gm x 3 doses every 4 hours). Her phenytoin level fell with a calculated half-life of 27 hours during the administration of MDAC. Genetic testing showed she was a 'poor metaboliser with respect to being a heterozygous carrier of CYP2C9*3 and heterozygous carrier of 2C19*2 alleles.

A 58 year-old man with a background history of myotonic dystrophy presented with a 2 day history of vertigo, lethargy and altered level of consciousness. He was normally on 500 mg phenytoin for tongue mytonia. His initial phenytoin level was 196 µmol/L. Phenytoin was

ceased and his condition improved by day 4. The calculated phenytoin half-life was 178 hrs. Genetic testing showed he was a 'poor metaboliser' with respect to being a heterozygous carrier of CYP2C9*3 allele.

Conclusions: These three cases were patients prone to phenytoin toxicity secondary to a genetic polymorphism with reduced cytochrome 2C9 enzyme function. MDAC was shown to work in two cases with a very large reduction in phenytoin half-lives when compared with a third case who did not receive MDAC.