Charcoal Hemoperfusion for Phenytoin Intoxication

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Accidental ingestion of phenytoin can lead to severe neurological sequelae. Charcoal hemoperfusion decreases phenytoin levels but has never been reported before in children. We present a child with accidental ingestion of phenytoin who responded to charcoal hemoperfusion.

Key words: *Charcoal, Hemoperfusion, Phenytoin, Poisoning*.

Phenytoin is a commonly prescribed antiepileptic drug. However, it has a narrow therapeutic range, and a total serum level >20 mcg/mL is associated with clinically relevant toxicity [1]. Deaths have been reported at levels of 50-70 mg/L. However, treatment recommendations beyond supportive care are unclear, and effectiveness of extracorporeal elimination techniques is still under debate [2]. From the clinical point of view, urgent lowering of phenytoin concentration may reduce the risk of dysrhythmia, shorten length of stay in the intensive care, possibly reduce the risk of nosocomial infection, presumably reduce costs, and may therefore be favorable [3]. We present a case of accidental ingestion of phenytoin that was treated successfully with four sessions of charcoal hemoperfusion, resulting in both clinical improvement and normalization of serum phenytoin concentration.

CASE REPORT

A 4 year old child was referred from a district hospital for sudden onset of altered sensorium and involuntary head nodding movements of 12 hours duration. There was no history of fever, trauma and the parents denied any intoxication. There was no significant family history except epilepsy in father, who was receiving phenytoin. On examination, she had nystagmus and head nodding movements and was in altered sensorium with a Glasgow coma scale of 10/15. Pupils were normal size and reacting to light, deep tendon reflexes were slightly depressed, Babinski sign was positive, and fundal examination was normal. A differential diagnosis of posterior fossa mass lesion or drug intoxication was entertained.

Airway, breathing and circulation were attended to and stabilized. CT scan of the brain and cerebrospinal fluid analysis were normal. The child was started on supportive measures and phenytoin intoxication was suspected in view of nystagmus, altered sensorium and father being on phenytoin. Serum phenytoin levels were elevated and in the toxic range 88 mcg/mL (therapeutic levels: 10-20 mcg/mL). She was started on supportive measures and nasogastric feeds. Oral activated charcoal at that stage was not thought of as it was already 42 hours after ingestion [4].

The sensorium continued to be the same, and the levels, repeated a week later, were still elevated (94 mcg/mL). Parents were counseled about the other options available including hemodialysis and hemoperfusion. Parents consented for charcoal hemoperfusion. Charcoal hemoperfusion was done with a cellulose-coated activated charcoal hemoperfusion column. Charcoal hemoperfusion cartridge (Hofpal, Sweden) adult size was used since pediatric cartridge was not available. The only complication noted was mild thrombocytopenia (platelet count of 90-100,000/mm) in the first session that recovered back to the reference range on the 3rd day. Four sessions of charcoal perfusion was performed and the child recovered subsequently without any sequelae. The serum phenytoin levels 24-hour after each hemoperfusion cycle were 56 µg/mL, 26 µg/mL, 23 µg/mL and 12 µg/mL, respectively.

DISCUSSION

The narrow therapeutic index, the wide inter-individual variability in the rate of phenytoin metabolism and clearance, and the saturation (zero-order) pharmacokinetics of phenytoin are responsible for the observed dose-related toxicity [5]. The plasma half-life of phenytoin has been shown to be dose dependent in humans. In other words, the time required for the plasma level to halve itself increases as the concentration of the drug increases. An explanation for the non exponential decline of phenytoin is that the biotransformation mechanism approaches saturation at higher plasma levels [6] and in the absence of displacing agents, is bound tightly to plasma proteins (87% to 93%) [7]. Therefore,

disappearance of phenytoin is not a simple exponential process and doesn't follow apparent first order kinetics, the elimination follows a zero order kinetics. This would explain the persistence of symptoms for several days at high plasma concentrations of the drug [6]. The increase in the concentration levels from 89 to 94 mcg/mL can be attributed to the absorption from the gut [6, 8]. The half life of phenytoin after the first hemoperfusion was 64 hours and was 43 hours after the 2nd hemoperfusion. The half life of phenytoin decreases as the levels decrease, as seen in our child as the various metabolic pathways are no longer saturated, and is in accordance with other reports [6, 9].

There have been a lot of controversy with regard to management of phenytoin overdose [1,8,10]. Benefit from charcoal hemoperfusion [10] and usage of molecular adsorbent recirculating system [1] have been reported. The role of charcoal can be explained by the fact that bound phenytoin has been found to dissociate from albumin in the presence of activated charcoal and subsequently becomes adsorbed to the activated charcoal [10].

There have been few reports of charcoal hemoperfusion being not effective in oral intoxication as it was attributed to absorption from the gut continuously and the levels coming back to the pre-hemoperfusion state. There has been only one report to the best of our knowledge of overdosage in a child who was treated conservatively [9]. There have been no pediatric reports of usage of any of these modalities in treatment of phenytoin overdose. Charcoal hemoperfusion was planned in view of evidence indicating severe neurological disabilities with phenytoin overdose [8]. The absolute indications for hemoperfusion in children in phenytoin toxicity are not described as reports of this condition in literature are very few. We suggest that elimination techniques may be considered in children with prolonged toxic concentrations of phenytoin.

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