

Case Report

Tandem plasmapheresis with hemodialysis in phenytoin intoxication: a case report

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ABSTRACT

A 4 year old girl presented with accidental Phenytoin poisoning in comatose state with bilateral spontaneous intermittent choreoathetoid movements. Serum Phenytoin levels at admission were highly elevated 74 µg/ml. Ideal intervention so far in such situation is probably Molecular Absorbent Recirculating System (MARS) followed by charcoal hemoperfusion especially if serum phenytoin levels are very high or persistently elevated. As the child did not improve with supportive management, tandem plasmapheresis with hemodialysis was started. Three such sessions were carried out. Patient made full recovery after third session. This is the first case of tandem plasmapheresis and hemodialysis in phenytoin toxicity in a child. After 2 days, she developed acute visual, tactile hallucinations and psychomotor agitation. Tactile hallucinations were insects crawling over body parts (cocaine bugs). Serum phenytoin level at this point of time was found 19 µg/ml i.e. in therapeutic range but much lower than the initial stage (74 µg/ml). Her symptoms improved with administration of short course of haloperidol for 2 days. To our knowledge, this is the first case of tactile hallucination in the form of cocaine bug, in pediatric patients with acute phenytoin toxicity. Under adverse situations, where treatment modalities like MARS or charcoal hemoperfusion are not feasible, tandem plasmapheresis with hemodialysis can be used with similar success. Phenytoin toxicity also leads to tactile hallucination in the form of cocaine bug. As these child injuries are predictable and preventable, parents should be best educated regularly about such injury risks and effective measures to prevent such injuries.

Keywords: Tandem plasmapheresis with hemodialysis, Phenytoin, Toxicity, Children

INTRODUCTION

Phenytoin is one of the oldest anti-epileptics drugs which continue to be prescribed even today. The plasma half-life at therapeutic levels is 12-24 hours. It carries a special risk of dose-related toxicity.¹ Toxicity from acute ingestion consists of triad of ataxia, nystagmus and drowsiness, while the severe toxicity may result in death² or permanent neurological disability.³ Treatment guidelines for removing excess drug from circulation in

severe toxicity, especially in comatose children are not well defined. The modality of choice for removal of bound phenytoin has been albumin dialysis (MARS i.e. molecular absorbent recirculating system).^{4,5} However, it is expensive and not easily available. Alternatively, charcoal hemoperfusion, hemodialysis and plasmapheresis have been used with variable success.³ Hereby, we report a case of accidental severe phenytoin poisoning in a 4 year old girl who was treated with tandem sessions of plasmapheresis (PP) and hemodialysis

(HD) and resulted in prompt recovery. To best of our knowledge, this is the first application of sequential plasmapheresis (PP) and hemodialysis (HD) in management of phenytoin toxicity in a child.

CASE REPORT

Four year old girl presented to the hospital emergency in altered sensorium. Child had ingested uncounted number of Eptoin tablets (100 mg) 5 days back. Her mother, a known case of seizure disorder was on oral phenytoin tablets 100 mg thrice a day. There was no history of fever, trauma or any seizures. She was at primary health care facility for initial 5 days, where supportive treatment was given. On day 6, she came to our hospital. The patient was comatose, her GCS was 7/15 (E2 M3 V2). Her examination revealed: PR 122/min, RR 22/min with shallow breathing, BP 110/70 mmHg, and temp was 99.1°F. She had also intermittent choreoathetoid movements. Both pupils were normal size and sluggishly reacting to light. Horizontal nystagmus was present bilaterally. Fundus was normal. Deep tendon reflexes were suppressed and plantar reflexes were extensor. With this background and clinical spectrum, diagnosis of severe acute accidental phenytoin intoxication was made. Serum phenytoin level was 74 µg/ml. Complete blood count, liver and renal function tests, and serum electrolytes levels including CSF analysis, were normal. Serum albumin was slightly low (2.6 g/dl). She was continued with supportive management and orogastric feeds, in a hope for spontaneous recovery. As there was no improvement in sensorium after 7 days of drug ingestion, consent for extra corporeal elimination of drug was obtained. Tandem sessions of plasmapheresis (PP) and hemodialysis (HD) were started as there was no facility for MARS and charcoal hemoperfusion. Each plasmapheresis session consisted of one plasma exchange with replacement fluid being 5 % albumin. Immediately after each PP session, 3 hours of HD was done using high flux hemodialyzer. A total of 3 such sessions were done. There was dramatic improvement in her condition after initiation of extra corporeal removal. Her GCS improved to 10/15, 12/15 after first two sessions. At the end of 3rd cycle, she became fully conscious. So, we stopped PP and HD at this stage. Serum phenytoin levels were measured 24 hours after each session and were 63 µg/ml, 41 µg/ml, and 25 µg/ml, respectively. No complications occurred throughout intervention period. The child made full recovery. After 2 days of last dialysis, child developed tactile hallucinations with psychomotor agitation. Tactile hallucinations were insects crawling over body parts (cocaine bugs) and child used to pick up and throw imaginative insects. Serum phenytoin level at this stage was 19 µg/ml. Other biochemical parameters including electrolyte, blood sugar were normal. Haloperidol was started. Hallucination and abnormal behavior subsided over next 2 days. Haloperidol was discontinued and patient discharged. During follow ups, child has been behaving normally.

DISCUSSION

Though phenytoin is a widely prescribed antiepileptic, its narrow therapeutic index with wide inter-individual variability in clearance results in wide spectrum of adverse effects ranging from minor to severe and at times life threatening. Following massive ingestion of phenytoin, cytochrome p450 enzyme system becomes saturated, leading to zero-order kinetics in which only a fixed amount of phenytoin is eliminated over a period. This results in too prolonged half-life (24 to 230 hours in overdose) and rapid rise in serum concentrations.⁶ Only free unbound Phenytoin is biologically active. Blood levels reflect total serum concentration of the drug. Central nervous system tissue phenytoin levels are even higher than the serum.³ Our child was in coma for more than a week. This can be attributed to hypoalbuminemia in the child where free phenytoin was available in the circulation causing prolonged toxicity. Even death has been reported in severe toxicity.⁷

There has been no consensus regarding management of severe phenytoin toxicity. As there is no antidote, treatment is supportive only. MARS is aimed at removing albumin-bound toxic molecules. Although the efficacy of MARS for the removal of phenytoin has been demonstrated, its use is limited by its availability, technical applicability and high costs.⁴ In severe intoxication hemodialysis has been used to accelerate elimination of total body burden of the drug.⁸

This sequential PP and HD as one tandem procedure was first described by Siemi et al.⁹ Our rationale for combined approach is that plasmapheresis removes protein bound drug from circulation. Following that free phenytoin is released from stores into circulation. Subsequently, hemodialysis eliminates remaining phenytoin. The half-life of phenytoin after first and last session was respectively 103 hours and 46 hours. This observation was in concordance with earlier report⁵ i.e. for phenytoin, half-life decreases with declining serum levels. Although psychosis is a manifestation of phenytoin toxicity, tactile hallucinations are less widely recognized.¹⁰ This is the first report of tactile hallucination (cocaine bugs) in pediatric patient of phenytoin intoxication.

Message: Acute phenytoin intoxication with accidental oral ingestion of phenytoin tablets is common in toddlers. Hypoalbuminemia can lead to prolonged toxic effects even at moderately high serum phenytoin levels especially in children. In severe toxicity, extracorporeal means of elimination like MARS, charcoal hemoperfusion are preferred lines of treatments. However, under adverse circumstances, tandem plasmapheresis with hemodialysis may be considered. Phenytoin poisoning also leads to acute psychosis and tactile (cocaine bugs) hallucinations. As these injuries are predictable and preventable, parent best educated regularly about risks and effective measures to prevent them.

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REFERENCES

1. Hwang WJ, Tsai JJ. Acute phenytoin intoxication: causes, symptoms, misdiagnosis and outcomes. *Kaohsiung J Med Sci*. 2004;20:580-5.
2. Bhawna S, Rahul H, Swayam P, Kdam N, Pankaj G. Phenytoin toxicity presenting as encephalopathy with fatal outcome: a case report. *J Neurol Res*. 2013;3(6):184-6.
3. Craig S. Phenytoin poisoning. *Neurocrit Care*. 2005;3(2):161-70.
4. Anne-Corne Lie J.M. de Pont. Extracorporeal treatment of intoxications. *Curr Opin Crit Care*. 2007;13:668-73.
5. Poddutoor PK, Lokesh L, Mehul AS, Farhan ARS. Charcoal hemoperfusion for phenytoin intoxication. *Indian Pediatr*. 2012;49:152-3.
6. Holcomb R, Lynn R, Harvey B Jr, Sweetman BJ, Gerber N. Intoxication with 5,5-diphenylhydantoin (Dilantin): clinical features, blood levels, urinary metabolites, and metabolic changes in a child. *J Pediatr*. 1972;80:627.
7. Larry B, Mellick J, Alan M, Garya M. Presentations of acute phenytoin overdose. *Am J Emerg Med*. 1989;7(1):61-7.
8. Ghannoum M, Troyanov S, Ayoub P, Lavergne V, Hewlett T. Successful hemodialysis in a phenytoin overdose: case report and review of the literature. *Clin Nephrol*. 2010;74(1):59-64.
9. Guido F, William FC, Shih HSH. Tandem hemodialysis and plasma exchange. *Pediatr Nephrol*. 2014;29(11):77-82.
10. Benatar MG, Sahin M, Davis RG. Antiepileptic drug-induced visual hallucinations in a child. *Pediatr Neurol*. 2000 Nov;2(5):439-41.

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