Successful use of sustained low efficiency dialysis in a case of severe phenobarbital poisoning

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Abstract

A 30-year-old female presented with coma and subsequent cardiac arrest caused by phenobarbital overdosage, requiring ventilatory and vasopressor support. She had also developed severe hypoxia following gastric aspiration. Initial therapy, including activated charcoal and forced alkaline diuresis, failed to significantly lower her drug levels and there was minimal neurological improvement. As she was hemodynamically unstable, and unsuitable for conventional dialysis, she was put on sustained low efficiency dialysis (SLED) to facilitate drug removal. SLED resulted in marked reduction in plasma level of phenobarbital, which eventually led to early extubation, improved cognition and aided full recovery. Thus, we concluded that SLED can be an effective alternative in cases of severe phenobarbital poisoning, where conventional hemodialysis or hemoperfusion cannot be initiated, to hasten drug elimination and facilitate early recovery.

Keywords: Barbiturate, hemodialysis, phenobarbital, poisoning, sustained low efficiency dialysis

Introduction

Phenobarbital is used mainly as an anti-epileptic. Though the newer drugs are preferred over phenobarbital, it is still widely in use, especially in the developing countries and hence frequently causes toxicity in accidental or suicidal overdosage. Until date, the extracorporeal treatment of choice for severe phenobarbital poisoning remains a matter of debate and limited data is available on the same, especially in the presence of hemodynamic instability. We report a successful use of sustained low efficiency dialysis (SLED) in the management of such a case.

Case Report

A 30-year-old female who was a known case of chronic depression aggravated by postpartum status (history of child-birth 6 months back) and on venlafaxine therapy was found unconscious, with grunting and frothing from mouth, 4 h after a suspected overdosage of 54 g of phenobarbital (90 tablets of 60 mg each). Being healthcare personnel, she had access to phenobarbital tablets. She had a cardiac arrest en route and required chest compressions and mouth to mouth breathing for about ½ h until she reached the emergency department.

There she was intubated and ventilated, with a Glasgow coma scale (GCS) score of 3/15 and bilaterally 3 mm reacting pupils. She required vasopressor support with noradrenaline. Toxicology screen came back positive for barbiturate, and she was shifted to the Intensive Care Unit (ICU). In the ICU, she was further resuscitated with fluids. She developed severe hypoxia due to large aspiration of gastric contents, possibly during transport.

We opted for initial treatment in the form of forced alkaline diuresis with sodium bicarbonate, ventilator support (assist control/volume control mode with high positive end-expiratory pressure and low tidal volume) and gastric decontamination with activated charcoal every six hourly for 48 h. Therapeutic hypothermia was not advocated as barbiturates are neuroprotective and can cause hypothermia.¹ Broad-spectrum antibiotic
coverage was given. The first measured phenobarbital level (about 20 h from time of ingestion) was 198 mcg/ml. After 2 days of therapy, the phenobarbital level came down to only 153.8 mcg/ml. Given the lack of progress of her neurological status (GCS E1M4Vt), we opted for a trial of 4 h SLED with dialysate-flow rate 300 ml/min, blood-flow rate 150 ml/min and no fluid removal, since she was hypotensive and requiring noradrenaline support. Following the first dialysis her phenobarbital level dropped from 198 mcg/ml to 153.8 mcg/ml. After 2 days of therapy, the phenobarbital level came down only to 153.8 mcg/ml. Given the lack of progress of her neurological status (GCS E1M4Vt), we opted for a trial of 4 h SLED with dialysate-flow rate 300 ml/min, blood-flow rate 150 ml/min and no fluid removal, since she was hypotensive and requiring noradrenaline support. Following the first dialysis her phenobarbital level dropped from 153.8 mcg/ml to 92.5 mcg/ml, hemodynamics improved and vasopressors were tapered off. Following the next dialysis, the drug level further dropped to 40.7 mcg/ml, patient started having spontaneous eye opening and became restless for which mild sedative in the form of dexmedetomidine in a low dose had to be started. Phenobarbital level continued to fall subsequently and in the next day with a drug level of 27.8 mcg/ml and a remarkably improved GCS, the patient was extubated. Within the following 6 h, she started communicating verbally and started taking oral feeds. A full psychiatric assessment was carried out and she was started on appropriate medication. She was shifted out of the ICU the next day and went on to make a full recovery.

**Discussion**

Phenobarbital is one of the long-acting barbiturates with low lipid solubility. They bind to gamma-aminobutyric acid_\textsubscript{A} (GABA_\textsubscript{A}) receptors and increase GABAergic transmission at the nerve terminal, thus decreasing excitability, especially of the central nervous system.\[2\] They are well absorbed from the gastro-intestinal tract, distributed throughout the body; volume of distribution (V\textsubscript{d}) reported as 0.54-0.9 l/kg.\[3\] They are metabolized by the liver and also excreted through the urine in unchanged form.\[2\]

Therapeutic serum drug level is 10-40 mcg/ml. Toxic dose is in the range of 6-10 g,\[4\] and most toxicity occurs after oral ingestion,\[5\] with lethal effect reported at serum level of 80 mcg/ml.\[6\] (Our patient had taken 54 g of the drug, initial serum level was as high as 198 mcg/ml).

Toxicity manifests as sedation rapidly progressing to coma, respiratory failure, hypotension and hypothermia. Owing to the long half-life, the hospital stay is typically prolonged.\[2\]

Supportive care remains the mainstay of barbiturate intoxication.\[2,7\]

Hemodynamics should be stabilized by initially fluid resuscitation and later vasopressors. Alkalization should be done to facilitate solubility of the long-acting barbiturates (acidic compounds) and hence urinary excretion.

Gastric decontamination should be done by activated charcoal at a dose of 1 g/kg body weight initial dose followed by 20 g at 6 h interval, since prolonged absorption of phenobarbital can happen from gastro-intestinal tract.\[8\] Gastric lavage is helpful only if initiated within 60 min of ingestion.\[9\]

Severe barbiturate toxicity and nonreversal of symptoms warrants the use of hemoperfusion or hemodialysis.\[4,10\]

Our patient still being hypotensive and on vasopressor support was not a candidate for conventional high-flow dialysis. Charcoal hemoperfusion has its cost constraints and availability issues.

This led us to give a trial of SLED, which proved equally efficacious. The fall in phenobarbital level by 40% following first and 56% following second SLED can be considered to be reasonably good clearance [Figure 1].

A few studies have been done to correlate early hemodialysis with decreased morbidity and early recovery.\[3,11\]

Most literature advocate hemoperfusion over hemodialysis.\[9\] (Though high-flow hemodialysis [blood-flow rates 400 ml/min],\[3\] may be equally efficacious).\[5\] Historically, the superiority of hemoperfusion was based on the comparison with low-efficiency dialyzer with low blood-flow rates,\[3\] though debated by some authors.\[9\]
Barbiturates with their high $V_d$ were conventionally thought to be nondialyzable and they can cause rebound phenomenon.\cite{12} However, phenobarbital being a long-acting drug has low lipid solubility, modest $V_d$ and only 20-40% protein binding,\cite{13} satisfying the criteria for being a dialyzable toxin.

Two previous case reports showed similar favorable results in phenobarbital overdosage treated by hemodialysis with a blood-flow rate between 180 ml/min and 200 ml/min and dialysate-flow rate of 500 ml/min.\cite{11,14}

In this case, even SLED with a blood-flow rate of 150 ml/min and dialysate-flow rate of 300 ml/min helped in lowering blood phenobarbital level, which led to improved cognitive functions and hemodynamics, and ultimately complete recovery.

**Conclusion**

Sustained low efficiency dialysis might be taken under consideration as an extracorporeal treatment modality in severe phenobarbital poisoning with hemodynamic instability where conventional hemodialysis may be difficult to initiate.

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**References**


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