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# Effect of Haemodialysis in Phenobarbital Toxicity: A Case Report

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**Abstract:** ***A 18 years old male presented with coma caused by a phenobarbital toxicity, requiring critical care admission. This male has done suicide attempt by consuming multiple tablets of Phenobarbitone of 60mg each around 50 tablets (total 3 gm). Phenobarbital is a long-acting barbiturate, which in an overdose can cause central nervous system depression, respiratory failure and haemodynamic instability; these patients can remain obtunded for many days. After initial supportive therapy, he was dialysed to help in elimination of the drug. Haemodialysis resulted in markedly reduced plasma level of phenobarbital, which decreased the length of stay in critical unit and aided full recovery.***

**Keywords:** coma, phenobarbital toxicity, suicide attempt, overdose, haemodialysis

## 1. Background

Barbiturates bind to the beta-subunit of gama-aminobutyric acid A (GABA-A) receptor, increasing the duration of opening of the chloride ion channel and potentiating the neuroinhibitory effect of GABA. The channel kinetics of GABA-A receptor have been explained by a three-state model with chloride channel open-time constants of 1, 4 and 11ms -opening more frequently and moving from a lower to a greater state as GABA concentration increase. [1] Barbiturates promote the opening of GABA-A receptors in their longer lived state and at a higher frequency. It has been shown that in higher doses, barbiturates directly stimulate GABA-A receptors outside of the presence of GABA itself. [2]

The net effect of barbiturates is neuroinhibition, and as such they have multiple clinical applications, including as anxiolytic, antiepileptic and anaesthetic agents.

Phenobarbital is a long-acting barbiturate, with a narrow therapeutic index and a wide inter-individual variability in the rate of metabolism. This narrow therapeutic range 10-30 mg/L (10-30 mcg/mL) means that level required for relieving anxiety and producing sedative effects are very close to those associated with toxicity. A phenobarbital overdose can cause central nervous system depression, along with respiratory failure and haemodynamic instability. [3] Furthermore, given the reported half life of 5 days, these patients can remain obtunded for some time. [4]

Historical treatment of a barbiturate overdose is based on supportive care, activated charcoal and urinary alkalinisation along with the application of extracorporeal treatments such as haemoperfusion or haemodialysis

## 2. Case Report

A 18 years old male brought by family members to emergency department in unconscious state with alleged history of deliberate self harm with multiple tablets consumption suspected Phenobarbital (60 mg each around 50 tablets- total 3 gm) within 2 hours of consumption.

On presentation to emergency department patient was unconscious with pulse rate 70/ min, BP-110/70mmhg, Resp. Rate-16/min, SpO2 - 94% on Room Air, Blood Sugar level-116 mg%.

No Pallor, Icterus, Edema feet, JVP normal.
Heart sounds was normal.

Respiratory system was normal with no in drawing of intercoastal muscles, not using accessory muscles of respiration.

CNS examination: Patient not responding to deep painful stimuli, bilateral planter reflexes absent, bilateral deeptend on reflexes diminished, bilateral pupils were small sluggishly reacting to light. On examination patients glassgow coma scale (GCS) was **3/15**

Patient was shifted immediately to Intensive care Unit and where gastric lavage with charcoal done and oxygen support provided as requirement.

Patient was in coma, although he remained haemodynamically stable and there was no respiratory paralysis. Patient started with supportive treatment, two cycles of alkalinisation of urine (forced alkaline diuresis) and intravenous fluids given. Patient's urine output was adequate.

On investigating,

Serum Phenobarbital level on day of admission was 107 mg/L (Therapeutic Range is 10-30mg/L) Hb-11.8 gm/dL, WBC-9100/mm3, Platelets-1, 96, 000/mm3, Sr. Sodium-140.8 mmol/L, Sr. Potassium-3.75 mmol/L, Ionic Calcium 1.17 mmol/L, Sr. Magnesium-1.96mg/dL, Sr. calcium-8.96 mg/dL. Ecg was normal, Liver enzymes were normal, kidney function was normal.

Other toxicology screen was negative.

On day 2 instead of all supportive management patients neurological status not improved. All vital parameters were normal

On day 3 after 48 hours of observation and supportive management patient given 1st cycle of haemodialysis of 3 hours duration with zero ultrafiltrate. After one cycle of haemodialysis patient improved and regained consciousness but not fully oriented. And Sr. Phenobarbital level reduced to 54mg/L.

On next day again 2nd cycle of haemodialysis of 2 hours duration with zero ultrafiltrate given. After 2nd dialysis patient was conscious and oriented.

Patients serum phenobarbital level after two haemodialysis estimated was 24 mg/L (24 mcg/mL).

Reduced from 107mg/L to 24mg/L.

The patient was fit for discharge from critical care unit within 24 h and went on to make a full recovery. A complete psychiatric assessment was made before discharge from hospital.

## 3. Discussion

Phenobarbital is one of the sedative-hypnotic agents which belongs to the barbiturates class of drugs. Phenobarbital offers a wide array of clinical uses that commonly include anti-seizure management. [7]

**Pharmacokinetics** [7]

**Absorption:** Rapid and complete absorption occurs after oral or IV administration.

**Time of Peak Plasma Concentration:** 30 minutes to 1 hour for oral formulations; 5 minutes for IV injection

**Distribution:** Rapidly distributed to all tissues and fluids

**Metabolism:** Metabolized primarily via acetylation in the liver (hepatic microsomal enzyme system)

**Excretion:** About 25 to 50% of unchanged drug is excreted in the urine. It is important to remember clearance rates vary with patients and their specific presentations. For instance, terminally ill cancer patients on phenobarbital may need dose adjustments due to reduced clearance of this drug.

Phenobarbital overdose is a healthcare emergency and requires teamwork from the entire healthcare spectrum to help the patient. It is imperative to implement the management of cardiac and respiratory status quickly. [7]

The range of phenobarbital deemed effective without causing issues to an individual is between 10 to 40 mcg/mL. Once blood levels increase above 40 mcg/mL, the patient is in a lethal range and at substantial risk. [7] Haemoperfusion was originally deemed to be superior due to its effectiveness in removing highly protein bound drugs, such as phenobarbital which displays 40-60% protein binding. [3]

Haemodialysis is most effective for drugs with a low molecular weight, high water solubility and small volume of distribution, which is true of phenobarbital, with volumes of distribution reported at 0.54-0.9 L/kg. [3, 4] Haemodialysis has been shown in this case, as well as others reported in the literature, to be an effective treatment in high-dose phenobarbital overdose. Plasma clearance of phenobarbital by high-flux haemodialysis has been shown to be 30 times that of hepatic clearance, and 10 times greater than the rate achieved with activated charcoal. [5] This, combined with the fact that haemodialysis is less expensive and more widely available than haemoperfusion, makes it an appealing choice for this group of patients. [6]

In summary, this case presents a young male with phenobarbital overdose resulting in coma that was treated successfully with two sessions of haemodialysis.

## 4. Conclusions

- Phenobarbital remains an important drug that is open to abuse and overdose with significant potential for morbidity and mortality.
- Haemodialysis is widely available in the critical care setting and increases the elimination of phenobarbital.
- Haemodialysis can significantly reduce the length of critical care stay in patients with overdose.

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