International Journal Dental and Medical Sciences Research
Volume 7, Issue 1, Jan - Feb 2025 pp 22-24 www.ijdmsrjournal.com ISSN: 2582-6018

Hemodialysis saves from Phenobarbital coma

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Submitted: 01-01-2025 Accepted: 10-01-2025

I. INTRODUCTION

Barbiturates are sedative-hypnotic drugs and are derivates of barbituric acid and were introduced clinically in the early 1900s. Over the past years, barbiturates have been used for a lot of indications, including insomnia, psychiatric disorders, anaesthesia, alcohol withdrawal, seizures, and elevated intracranial pressure.These drugs have a narrow therapeutic index, are highly addictive, and carry a high risk for toxicity.Drug overdose constitutes 10% of cases of poisoning in India .Though the usage of phenobarbitone has decreased over years,it is still being prescribed for seizures, alcohol withdrawal and sedation . Differentiating phenobarbitone overdose from other causes of coma is important because phenobarbitone overdose is completely treatable(1,2).

II. CASE STUDY

A 20 year old male,a k/c/o seizure disorder on T.Phenobarbital 60 mg po BD ,T.Brivaracetam 50 mg po BD ,T.Lacosamide 100 mg po BD since 3 years came to ED with complaints of dizziness,imbalance while walking,slurred speech and decreased responsiveness. Attenders found an empty bottle of phenobarbital in his room and brought him to hospital.

The patient's airway was threatened –so was intubated and put on mechanical ventilation.His initial vitals were PR-130/min,reg,BP- 80/60 mmHg,RR- 8/min ,SpO2-67% with RA.GCS- E1V1M1 and pupils – normal in size andnormally reactive,Temp-97.5 F.BP improved with 1 litre IV bolus and maintained at 100/70 mmHg.

VBG showed mild lactic acidosis.No abnormality detected in ECG,Pocus and X-ray. On examination, CNS – had diminished reflexes,hypotonia B/L plantar- mute. Differential diagnosis of posterior circulation stroke,NCSE,Phenobarbital toxicity ,brivaracetam toxicity ,ethanol co-intoxication was suspected.

Patient was started on supportive care, MDAC and urinary alkalinization.MRI STROKE protocol showed – No significant abnormality.Drug screen was negative .Patient's S.Phenobarbitone levels came out to be 80 µg/ml .Serum brivaracetam, lacosamide ,ethanol levels came out to be normal .Because of prolonged coma , the patient was taken up for two session of hemodialysis. The patient's clinical condition gradually improved ,he was extubated and discharged home safely after psychiatric evaluation after 6days .

III. DISCUSSION

Phenobarbitone ,a CNS depressant ,acts by enhancing the inhibitory action of GABA-A receptor. Barbiturates bind to the alpha subunit of GABA receptor increasing the duration of opening of cell membrane chloride channel.The increase in chloride influx leads to hyperpolarization of the postsynaptic neuronal cell membrane causing inhibition of the transmission of epileptic activity.At higher serum concentrations, phenobarbitone also interferes with Na+ and K+ transmembrane transport and conductance. Presynaptically, it also decreases the Ca2+ influx which results in the decreased release of excitatory neurotransmitters such as glutamate and aspartate.

It can be administered by both parenteraland oral routes. It is rapidly absorbed in the small intestine after oral ingestion and has a bioavailability of >95%.The average volume of distribution of phenobarbital ranges between 0.54 and 0.73 L/kg in adults with plasma protein binding of 55% . Newborns and young infants have a larger volume of distribution ranging from 0.8 to 1 L/kg .Protein binding is further decreased in pregnancy and newborns.Phenobarbitone has poor lipid solubility and longer duration of action.At steady state, the CSF concentration is similar in adults and infants ranging between 43% and 60% of plasma concentrations.Phenobarbital readily crosses the placenta and plasma concentrations in neonates are similar to those in the mother. It is also secreted in breast milk in which its concentrations are 40% of those in plasma.(3)
Elimination half-life in adults ranges from 50 to 150 hours (3-5 days) after a single intravenous injection.In the first weeks of life elimination of phenobarbital is much slower resulting in a half-life of 77 to 404 hours, decreasing in older children to

about 60 hours(1.5 days).The half-life of phenobarbitone is prolonged in patients with liver cirrhosis (130 ± 15 h)(4).

It is metabolized by liver to inactive metabolites through cytochrome P450 system mainly CYP2C9 plays a major role in hepatic metabolism with minor contribution from CYP2C19 and CYP2E1 and excreted in urine.Around 20–25% of administered dose of phenobarbitone is renally excreted unchanged in the urine.(4)

The therapeutic range is 10 to 40µg/ml.Concentrations > 80µg/ml are fatal.Barbiturates' effects on the brain include confusion, decreased mental status, ataxia, dysarthria, coma, and loss of brain stem reflexes. Depression of the respiratory medullary centres can cause decreased ventilation and apnoea. Barbiturates affect the cardiovascular system via vasodilation of peripheral blood vessels, depression of the brain's cardiac and vasomotor centres, and a direct negative ionotropic effect on the heart. Gastrointestinal motility is also slowed, and ileus may develop. Barbiturates can also cause hypothermia by depressing the temperature-regulating mechanism in the pons.(5–7)

Treatment is mainly supportive in case of mild toxicity.American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists (AACT/EAPCCT) recommend MDAC as an useful adjunctive therapy and should be used in all cases of phenobarbital poisoning.Urinary alkalinization is no longer recommended as first-line treatment in cases of barbiturate poisoning because it does not increase renal clearance significantly and MDAC is considered superior.(8–11)

Extracorporeal treatment is recommended in long-acting barbiturate poisoning -if prolonged coma is present or expected;if shock is present after fluid resuscitation ;ifdespite MDAC treatment, toxicity persists;if despite MDAC treatment, serum barbiturate concentration rises or remains elevated ;if respiratory depression necessitating mechanical ventilation is present.Intermittent HD is the preferred mode of extracorporeal treatment of severe barbiturate poisoning.Cessation of hemodialysis is indicated when clinical improvement is apparent.(12)

IV. CONCLUSION :

Hemodialysis is indicated in severe cases of phenobarbital toxicity .Severity of phenobarbitone toxicity should be graded based on clinical assessment.Initial resuscitation and supportive care enhances recovery in phenobarbitone poisoning which has no antidote.Enhanced elimination techniques are recommended in refractory and severe toxicity of phenobarbitone poisoning.

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