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CASE REPORT

Effective Role of CVVH in Fatal Phenobarbital Overdose Clearance: A Case Report

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Abstract

We report affective utilization of continuous veno-venous hemofiltration for removal of phenobarbital in a patient who took twice amount of fatal dose and was hemodynamically stable. Historically treatment includes supportive care, activated charcoal and urinary alkalinisation along with the application of extracorporeal treatments such as charcoal haem perfusion or hemodialysis and continuous veno-venous hemodiafiltration are affective treatment for removal of drug. Early initiation of extracorporeal treatment and increasing blood flow rate effectively reduced half life of drug and improved patient outcome with fatal poisoning.

Background

Phenobarbital is a long-acting barbiturate in use reported since 1912 with a wide interindividual difference in rate of its metabolism and a narrow therapeutic index. Due to narrow therapeutic index close monitoring of drug level is mandatory. Overdose can cause coma, cardiovascular collapse, cardiac arrest, hypotonia, hyporeflexia, hypothermia, hypotension and respiratory depression. Historical treatment of a barbiturate overdose is based on supportive care, activated charcoal and urinary alkalinisation [1,2] along with the application of extracorporeal treatments such as charcoal haem perfusion or hemodialysis and continuous veno-venous hemodiafiltration [3-5] are affective treatment for removal of drug. We report affective utilization of continuous veno-venous hemofiltration for removal of phenobarbital.

Case Report

38-year-old man admitted with phenobarbital overdose from emergency department. He took 189 tablets of 100 mg cumulative dose of 18.9 gram taken at unknown time. He was brought unconscious had GCS of 3 blood pressure 120/75 pulse 85 per minutes' respiratory rate 12 per minutes' and temperature of 36.5 °C was intubated and ventilated and transferred to intensive care unit. His medical background history includes bipolar disorder, deliberate self harm.

His initial investigation showed positive blood and urine toxicology screen for barbiturates only and phenobarbital level of 160.5 mg/L, others investigation including full blood count, renal profile, liver function, arterial blood gases, calcium, phosphate, amylase, creatinine kinase and coagulation screen within normal limits (Table 1). His electrocardiogram showed prolonged QT. He remained hemodynamically stable without any inotropic support was started on supportive management with intravenous fluid and activated charcoal in intensive care unit as renal profile and acid base status remained within fair range with no evidence of renal failure. His repeat phenobarbital level after 48 hours was 221.8 mg/L likely due to redistribution of drug.

Management

It was decided to commence on CVVH (Plasma flex system Gambro) with initial blood flow of 200 ml/min and dialysate flow 2000 ml/hour and Gambro FX100 filter size in intensive care unit in view to improve clearance for phenobarbital level and recovery from coma. His phenol barbital level was measured after 48 hours from arterial port 80.4 mg/L venous port 79 mg/L and level in effluent fluid 58.5 mg/L. His blood flow rate was increase to 300 ml/min with same dialysate flow rate 2000 ml/hour, repeat levels after 4 hours were arterial port 72.9 mg/L venous port 79.3 mg/L and effluent 53.4 mg/L.

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After 72 hours on CVVH his repeat levels from arterial port 38.8 mg/L effluent 25.4 mg/Las shown in Figure 1. His GCG started to improve and it was decided to stop CVVH and planned to extubate him as he started to show respiratory efforts.

On CVVH elimination rate constant of 0.018/hr and half life of 39 hours was achieved.

Table 1: Laboratory Investigations on admission.

Test	Result	Reference
CREATININE	64	64-104 umol/l
UREA	2.8	2.5-7.8 mmol/l
SODIUM	135	133-146 mmol/l
POTASSIUM	3.7	3.5-5.3 mmol/l
CHLORIDE	100	95-108 mmol/l
BILIRUBIN	7	0-21 umol/l
ALT	15	0-50 I.U/L
ALP PHOS	141	30-130 I.U/L
AMYLASE	24	22-80 I.U/L
CALCIUM	2.25	2.20-2.60 mmol/l
PHOSPHATE	0.96	0.80-1.50 mmol/l
MAGNESIUM	0.84	0.70-1.00 mmol/l
pH	7.37	7.35-7.45
PCO_2	6.22	4.67-6.40 kPA
HCO_3	26.2	21-28 mmol/l
ALBUMIN	37	35-50 g/L
CK	63	0-210 I.U/L
TRICYCLICS	NOT DETECTED	
BENZODIAZIPINES	NOT DETECTED	
BARBITURATES	POSITIVE	
PARACETAMOL	< 10	mg/L
SALICYLATES	< 20	mg/L
ETHANOL	< 10	mg%
PT	14.6	12-15 seconds
INR	1.10	
APTT	34.5	24-38 seconds

Based on an initial blood level (C_1) of 221.8 mg/L and a subsequent level (C_2) of 96 mg/L and a time gap between these 2 levels of approx. 44 hours, an elimination rate constant (K) can be calculated using formula at $t_{1/2} = {}^{0.693}/_{K}$.

$C_2 = (C_1)\ (e^{-Kt})$

K = 0.018/hr

The half life can then be calculated from $t_{1/2} = {}^{0.693}/_{K}$ = 39 hours.

In theory these calculations could be done for any two blood levels of phenobarbital where C_1 is the earlier level and C_2 is the later level. The accuracy of such calculations is reduced when the time interval between blood levels is less than one half life.

His phenobarbital level after stopping CVVH 24, 48, 72 hours were 31.7 mg/L, 25.3 mg/L and 19.4 mg/L respectively there were no drug interactions which could interfere with half life of phenobarbital in treatment during admission in intensive care unit. There was progressive improvement in GCS with fall in blood phenobarbital levels. He was discharged from intensive care unit after mechanical ventilation of 5 days for duration of his coma and CVVH for 72 hours, specialist psychiatric team was also involved in his care before discharge from hospital.

Discussion

Phenobarbital is readily absorbed from the gastrointestinal tract, although it is relatively lipid insoluble; peak concentrations are reached in about 2 hours after oral administration. It is about 45 to 60% bound

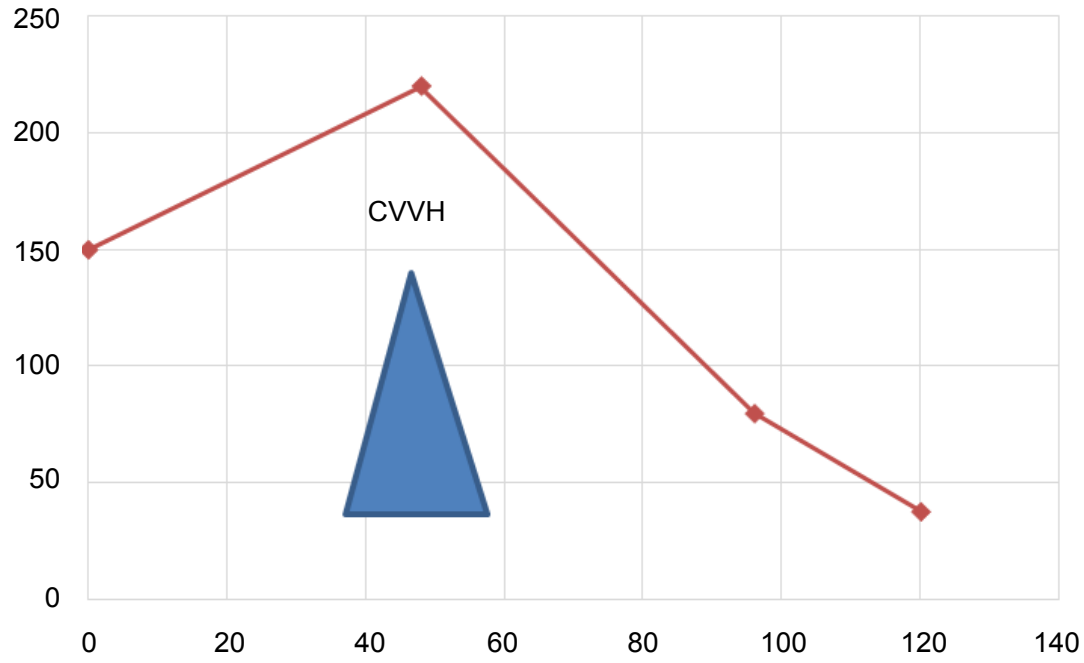

Figure 1: Triangle points at start of CVVH.
X-axis represents time in hours and Y-axis phenobarbital levels.

Table 2: Half life of drug with increase of blood flow.

	Prior to CVVH	Blood flow 200 ml/min	Blood flow 300 ml/min
Half Life of drug	> 140 hours	39 hours	32 hours

to plasma proteins. The plasma half life is about 75 to 120 hours in adults. There is considerable interindividual variation in phenobarbital kinetics. Phenobarbital in only partly metabolized in the liver and about 25% of a dose is excreted in the urine unchanged at normal urinary pH [6].

In different studies phenobarbital appears to have had inconsistent effects in suppressing experimental epileptic foci, and epileptic after-discharges, but it inhibits synaptic transmission, at least in the spinal cord. The drug's probable biochemical mechanism of action is through prolonging the opening time of Cl^- ion channels in postsynaptic neuronal membranes. This effect causes membrane hyperpolarization and thus impairs nerve impulse propagation. Phenobarbital also decreases intraneuronal Na^+ concentrations, and inhibits Ca^{2+} influx into depolarized synaptosomes. It raises brain serotonin levels, and inhibits noradrenaline (norepinephrine) reuptake into synaptosomes.

There have been previous case reports in medical literature where phenobarbital lethal dose has been managed with supportive, hemodialysis and continuous veno-venous hemodiafiltration with good outcomes. The reported fatal dose of phenobarabital in literature is 10 g with serum concentration of 80 mg/L [7]. Our patient took approximately twice the fatal dose was hemodynamically stable likely due to long-term tolerance to phenobarbital.

Balme, et al. presented a case in 1962, whereby a patient presenting with a barbitone level of 60 mg/100 mL was treated with hemodialysis for 8 h and responded with improvement of neurological status appropriate clinical responses sufficient to be extubated [8].

Le Quang Thuan, et al. study suggest that CVVH is an effective method to treat acute phenobarbital poisoning and additionally it is safer than HD. Moreover, it was found that one courses of HD was similarly effective on decreasing blood phenobarbital concentration compared to one course of CVVH. Nevertheless, Blood phenobarbital concentration fell more quickly with HD. Study found that duration of coma and mechanical ventilation in CVVH group was significantly shorter than hemodialysis group, revealing CVVH is more effective. Moreover, hypotension and recurrence of coma were not observed following CVVH, implying a safer method [9].

Recommendations on the use of extracorporeal treatment in poisoning of phenobarbital by EXTRIP (Extracorporeal Treatments in poisoning) workgroup in patients with barbiturate poisoning is based on a systematic review of relevant literature using a standardized evidence based process. Based on these recommendation supportive care is recommended as treatment of choice in all patients with barbiturate overdose. Extracorporeal techniques including hemodialysis and continuous veno-venous hemofiltration are recommended for use in patients who meet criteria of a fatal toxicity with long acting barbiturate phenobarbital.

Indication for extracorporeal treatment are coma, shock despite fluid resuscitation, persistent toxicity, rising serum barbiturate level non-responsive to supportive treatment and respiratory depression necessitating mechanical ventilation.

Treatment with theses modalities should be started as soon as available. As per EXTRIP intermittent hemodialysis is the preferred mode of treatment of severe barbiturate poisoning, continuous renal replacement modalities are valid alternatives, when clinical improvement is obvious cessation of hemodialysis or continuous veno-venous hemofiltration is indicated [10].

Ruhe M, et al. case report published in 2016, a patient took cumulative dose of 10 g and non-responsive to supportive treatment was started on continuous veno-venous hemodialysis on day five of admission with blood flow 100 ml/min and dialysate flow 2000 ml/h and total duration of continuous veno-venous hemodialysis was 37 hours and extubated on day 6 of admission [11].

In our case patient took cumulative dose of 18.9 g, continuous veno-venous hemofiltration was initiated after 48 hours of admission with higher blood flow rates of 200 ml/min later increased to 300 ml/min dialysate flow rate was similar 2000 ml/h, total duration of continuous veno-venous hemofiltration was 72 hours and patient was extubated on day five of admission.

In our case we started on extracorporeal treatment early in view of very high blood phenobarbital level. Duration of treatment was 72 hours and patient was extubated on day five of admission.

Conclusion

Our case report shows use of continuous veno-venous hemofiltration CVVH is effective and safer option to be considered early in fatal dose of phenobarbital. It also shows that CVVH can be used in management of phenobarbital overdose with good clearance, which resulted in improvement of neurological and clinical status of our patient. It also showed that drug clearance half life can be effectively reduced by increasing blood flow rate as shown in Table 2.

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References

1. Hauptman A (1912) Luminal bie epilepsia. Munch Med Wochenschr 59: 1907-1909.
2. Proudfoot AT, Krenzelok EP, Vale JA (2004) Position paper on urine alkalinisation. J Toxicol Clin Toxicol 42: 1-26.
3. Lal R, Faiz S, Garg RK, Baweja KS, Guntupalli J, et al. (2006) Use of continuous venovenous hemodiafiltration in a case of severe phenobarbital poisoning. Am J Kidney Dis 48: e13-e15.
4. Ellenhorn MJ, Barceloux DG (1988) Medical toxicology: Diagnosis and treatment of human poisoning. (1st edn), Elsevier Science Publishing Co, New York.
5. Jacobs F, Brivet FG (2004) Conventional hemodialysis significantly lowers toxic levels of phenobarbital. Nephrol Dial Transplant 19: 1663-1664.
6. Roberts DM, Buckley NA (2011) Enhanced elimination in acute barbiturate poisoning - a systematic review. Clin Toxicol (Phila) 49: 2-12.
7. Nitschke P, Stewart F (2010) The Peaceful Pill Handbook.
8. Balme RH, Lloyd-Thomas HG, Shead GV (1962) Severe barbitone poisoning treated by hemodialysis. Br Med J 1: 231-232.
9. Le Quang Thuan, Ngo Duc Ngoc, Pham Due (2013) Effectiveness of continuous veno-venous hemofiltration and intermittent hemodialysis in the treatment of severe acute phenobarbital poisoning. APJMT 2: 10-13.
10. Mactier R, Laliberté M, Mardini J, Ghannoum M, Lavergne V, et al. (2014) Extracorporeal treatment for barbiturate poisoning: Recommendations from the EXTRIP Workgroup. Am J Kidney Dis 64: 347-358.
11. Ruhe M, Grautoff S, Kähler J, Pohle T (2016) Suicide attempt by means of phenobarbital overdose. Effective treatment with continuous veno-venous hemodialysis. Med Klin Intensivmed Notfmed 111: 141-144.