

The Effectiveness of Continuous Venovenous Hemodiafiltration in Phenobarbital Intoxication

Yasemin Çoban, Dinçer Yıldızdas, Özden Özgür Horoz, Nagehan Aslan, Didar Arslan

Çukurova University, Faculty of Medicine, Balcali Hospital, Department of Pediatric Intensive Care, Adana, Turkey

Abstract

Phenobarbital continues to be widely used in childhood epilepsy. Incorrect drug prescription can sometimes lead to intoxication, particularly in young children. A 40-month-old female infant presented to our emergency department due to failure to awaken. The patient was assessed in terms of etiology of coma, and her history revealed that she had been given a 100 mg phenobarbital pill instead of 15 mg. Her blood phenobarbital level was high (>80 mg/dl). At physical examination, her Glasgow coma score was 6, the pupils were isochoric, pupillary light reflex was bilateral positive, deep tendon reflexes were absent, respiration was superficial, and pulmonary bilateral diffuse secretory rales were present, and the patient was intubated. Continuous venovenous hemodiafiltration (CVVHDF) was performed due to prolonged coma, intubation, and potentially fatal phenobarbital level. Blood phenobarbital levels at 4 and 12 h improved to >80 and 33.4 mg/dl, and the patient was extubated at 14 h. CVVHDF was effective in intoxication despite long-acting barbiturate phenobarbital not binding to protein. We think that this is a useful method capable of use in phenobarbital intoxications.

Keywords: Child, continuous venovenous hemodialysis, phenobarbital intoxication

INTRODUCTION

Phenobarbital is an old antiepileptic still widely used today.^[1] Drug intoxication is commonly encountered in the pediatric age group. Intoxication may also be observed as a result of incorrect prescription of continuously used medications.^[2] Although the incidence of phenobarbital intoxication is decreasing, it can still result in mortality and morbidity.^[3]

Extracorporeal methods have begun being used in cases of intoxication in recent years, and successful outcomes have been achieved. Hemodialysis is known to be effective in phenobarbital intoxication. However, continuous venovenous hemodiafiltration (CVVHDF) has been shown to be effective in only limited studies. We describe a patient admitted to our pediatric intensive care unit due to phenobarbital intoxication and receiving CVVHDF.

CASE REPORT

A 40-month-old female infant was brought by her parents to emergency service for unawakened. She was in coma when evaluated. We learned from the patient's history that she had been discharged 2 days earlier from the intensive

care unit from another hospital where she was status epilepticus under monitoring due to Dravet syndrome and had presented to the emergency department when her family was unable to wake her. Drugs used included daily were clonazepam (0.07 mg/kg), levetiracetam (50 mg/kg), and topiramate (1.6 mg/kg), while she had received phenobarbital at a dose of 40 mg/kg as a result of incorrect prescription. She took the last phenobarbital pills 18 h ago. Her blood phenobarbital level was >80 mg/dl (the highest level capable of measurement by the laboratory). On arrival at the intensive care unit, the patient's Glasgow coma score (GCS) was 6 (E:1, M:4, V:1), the pupils were isochoric and miotic, direct and indirect light reflexes were positive, deep tendon reflexes were absent, respiration was superficial, pulmonary sounds were bilaterally coarse, and secretory rales were present. Vital signs were heart rate of 130/min, arterial blood pressure of 85/50 mmHg, tympanic temperature of 36.8°C,

Address for correspondence: Dr. Yasemin Çoban, Balcali Hospital, Çukurova University, Sarıçam, Adana, Turkey.
E-mail: yasemincoban83@gmail.com

Access this article online

Quick Response Code:



Website:
www.actamedicainternational.com

DOI:
10.4103/ami.ami_20_18

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Çoban Y, Yıldızdas D, Horoz ÖÖ, Aslan N, Arslan D. The effectiveness of continuous venovenous hemodiafiltration in phenobarbital intoxication. Acta Med Int 2018;5:92-4.

capillary refill time of 2 s, and oxygen saturation of 92% with the patient receiving 15 l/min oxygen via an oxygen mask with a reservoir bag. NIRS values were left 59% and right 58%. The first arterial blood gas in the intensive care unit was pH 7.28, PCO₂ 65 mmHg, PO₂ 86 mmHg, HCO₃ 25 mEq/L, and lactate 1.4 mmol/L. The patient was intubated due to GCS <8, absence of gag reflex, and respiratory irregularity. She took phenobarbital 18 h ago; active charcoal was not used. Extracorporeal Treatments in Poisoning (EXTRIP) study^[2] recommends intermittent hemodialysis for prolonged coma. The patient was intubated. She had a prolonged coma and unstable hemodynamic. Also her phenobarbital level > 80 mg/dl. She was poisoned a long-acting phenobarbital. Thereby CVVHDF was planned. Informed consent was obtained from the patient parents. A 9 Fr hemodialysis catheter was inserted into the left femoral vein. CVVHDF for this 11-kg patient was performed using a HF20 (Gambro) polyarylethersulfone membrane with a Prismaflex continuous renal replacement therapy (CRRT) device. CVVHDF was applied with blood flow rate of 70 mL/min, dialysate flow rate of 450 mL/h, total replacement rate of 450 ml/h, predilution of 150 ml/h, and postdilution of 300 ml/h. Anticoagulation was established with heparin (10 U/kg/h). The patient's blood phenobarbital level of the procedure was >80 mg/dl at the 6th h and 33.4 mg/dl at the 12th h. Consciousness began to return after the 6th h of the procedure. NIRS values were left 70% and right 65%. The patient was extubated at approximately the 14th h. No further loss of consciousness or complication occurred during observation. The patient was then transferred to the pediatric neurology department for further treatment and medication adjustment.

DISCUSSION

Phenobarbital still causes frequent intoxications. Clinical evaluation is very important in terms of using extracorporeal therapeutic methods in severe phenobarbital intoxication. A sedative-hypnotic effect occurs in phenobarbital intoxication at low doses, coordination disturbance, slowed speech, dizziness and judgment impairment at moderate doses, and shallow breathing and coma at high doses. It depresses respiration and causes potentially fatal aspiration pneumonia, depression in the cardiovascular system by affecting the medullar vasomotor area, and congestive heart failure.^[4] The effectiveness of extracorporeal therapeutic methods declines during hypotension development due to decreased cardiac output.^[2] The therapeutic range for phenobarbital blood levels is 10–25 mg/L. Coma may occur if serum concentrations are >50 and <80 mg/L, and mortality may occur at levels exceeding 80 mg/L.^[5]

The general therapeutic approach in phenobarbital intoxication is optimal supportive care and multiple-dose active charcoal. Alkaline diuresis was once used in phenobarbital intoxication. However, this has now been shown not to significantly increase renal clearance and is no longer recommended as a primary therapy.^[6]

Extracorporeal methods have recently begun being employed in moderate and severe phenobarbital intoxications. Although there are no randomized controlled studies showing that one method is superior to other (intermittent hemodialysis, CVVHDF, hemoperfusion, and plasmapheresis), the EXTRIP workgroup reviewed 617 papers and offered recommendations concerning when extracorporeal treatment methods (four keys) to be used in barbiturate intoxications. The first is that extracorporeal treatment methods should only be used in the case of long-acting barbiturates. Second, they should be used in the case of prolonged coma, respiratory depression requiring mechanical ventilation, shock, persistent intoxication, or increasing or persistently elevated barbiturate levels despite the use of multiple-dose active charcoal. Third, intermittent hemodialysis is described as the preferred mode of extracorporeal treatment, and fourth, cessation is advised when clinical improvement is observed.^[2]

That study also determined a barbiturate clearance rate of 26–290 ml/min with hemoperfusion, 23–174 ml/min with hemodialysis, and 84 ml/min with multiple-dose active charcoal. It also recommends hemodialysis over hemoperfusion since hemoperfusion cannot be performed in many countries; Hemoperfusion is expensive, uncommon method. It needs to change very frequently the hemoperfusion column. In case of using hemodialysis method, thrombocytopenia and hypocalcemia rarely develop and heparin requirement declines. It particularly recommended intermittent hemodialysis as a hemodialysis technique but stated that CVVHDF can be performed if intermittent hemodialysis is not possible. Intermittent hemodialysis is regarded as superior to CRRT since it has been shown to have higher clearance in association with high dialysis rates and high blood flow rates.^[2] However, Rosenberg *et al.* showed that phenobarbital clearance in CVVHDF is six times greater than basal systemic clearance and that clearance is 7.5-fold greater if basal metabolism is also added.^[7] Thuan *et al.* compared intermittent hemodialysis with CVVH. They reported that blood phenobarbital decreased to comparable levels 4 h after intermittent hemodialysis and 16 h after CVVH (mean 3.9 and 3.2, respectively), while duration of coma and mechanical ventilation were shorter with CVVH. In addition, coma recurred and hypotension developed during the procedure in the IHD group.^[8] Different studies have also shown that CVVHDF is highly effective in severe phenobarbital intoxication and in the presence of hypotension.^[4,9]

Single pass albumin dialysis has also recently begun being applied in phenobarbital intoxication. Kılıtır *et al.* performed hemodialysis with 1% albumin-containing dialysate and described this as effective in one case report.^[3] Long-acting barbiturates bind to protein at a rate of 20%–60%.^[2] We applied high-flow CVVHDF due to our patient being a child, ventilation requirement, a disposition to hypotension, presence of prolonged coma, and phenobarbital levels being too high to measure. Our patient was extubated without complications on the 14 h of admission after CVVHDF.

CONCLUSION

CVVHDF therapy can be applied in severe phenobarbital intoxications. However, further studies are needed on this subject.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Yasiry Z, Shorvon SD. How phenobarbital revolutionized epilepsy therapy: The story of phenobarbital therapy in epilepsy in the last 100 years. *Epilepsia* 2012;53:26-39.
2. Mactier R, Laliberté M, Mardini J, Ghannoum M, Lavergne V, Gosselin S, *et al.* Extracorporeal treatment for barbiturate poisoning: Recommendations from the EXTRIP workgroup. *Am J Kidney Dis* 2014;64:347-58.
3. Kızırtır HS, Yıldırım HM, Yeşilbaş O, Duramaz BB, Şevketoğlu E. Single-pass albumin dialysis in a child aged six months with phenobarbital poisoning. *Turk Pediatri Ars* 2016;51:228-30.
4. Roberts DM, Buckley NA. Enhanced elimination in acute barbiturate poisoning – A systematic review. *Clin Toxicol (Phila)* 2011;49:2-12.
5. Mowry JB, Spyker DA, Cantilena LR Jr., Bailey JE, Ford M. 2012 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 30th Annual Report. *Clin Toxicol (Phila)* 2013;51:949-1229.
6. Mohammed Ebid AH, Abdel-Rahman HM. Pharmacokinetics of phenobarbital during certain enhanced elimination modalities to evaluate their clinical efficacy in management of drug overdose. *Ther Drug Monit* 2001;23:209-16.
7. Rosenborg S, Saraste L, Wide K. High phenobarbital clearance during continuous renal replacement therapy: A case report and pharmacokinetic analysis. *Medicine (Baltimore)* 2014;93:e46.
8. Thuan LQ, Ngoc, ND, Pham D. Effectiveness of continuous veno-venous hemofiltration and intermittent modality in the treatment of severe acute phenobarbital poisoning. *Asia Pac J Med Toxicol* 2013;2:10-3.
9. Lee JM, Lee YJ, Bang ES, Chu IS, Kim SH. Use of continuous venovenous hemodiafiltration to enhance the elimination of serum pentobarbital before diagnosis of brain death. *J Korean Soc Transplant* 2012;26:120-4.