Case Report

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Single-pass albumin dialysis in a child aged six months with phenobarbital poisoning

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Abstract

A girl aged six months was hospitalized because of resistant seizures and was discharged with phenobarbital and carbamazepine therapy. She was admitted to a state hospital with symptoms of inability to waken and difficulty in breathing. It was learned that phenobarbital had been used incorrectly and the patient was sent to our pediatric intensive care unit because of severe phenobarbital overdose. The decision was taken for hemodialysis. Single-pass albumin dialysis was planned because phenobarbital can bind to high levels of plasma protein. The process was undertaken with 1% albumin-containing dialysate, which was prepared manually. After 6 hours of dialysis, the phenobarbital blood level measured 62 mcg/mL (>140 mcg/mL on admission) and the patient's clinical findings were markedly regressed. There are no case reports about phenobarbital overdose treated with single-pass albumin dialysis in the literature. We conclude that single-pass albumin dialysis may be a useful treatment, especially with intoxications of drugs that bind protein at high levels. (Turk Pediatri Ars 2016; 51: 228-30)

Keywords: Continuous venovenous hemodialysis, phenobarbital intoxication, single-pass albumin dialysis

Introduction

Childhood is the period during which drug intoxications are observed most frequently. Although accession and ingestion of drugs by children outside the parents' knowledge is a common event, cases of intoxication also occur as a result of erroneous drug use by the parents or erroneously prescribed drugs. Extracorporal therapies are being used at increasing rates in cases of severe intoxication. Although hemodialysis is a well-known therapeutic approach in severe phenobarbital intoxication, we thought it was appropriate to present our case in order to draw attention to the possibility that more efficient results could be obtained with single-pass albumin dialysis (SPAD).

Case

In the history of a seven-month-old female patient who was admitted to the pediatric intensive care unit with a prediagnosis of phenobarbital intoxication, it was learned that she was recently followed up in the pediatric neurology ward because of seizures and her seizures were controlled with carbamazepine and phenobarbital. She had been discharged just one day before admission to the intensive care unit. A phenobarbital 100 mg tablet was erroneously prescribed instead of phenobarbital 15 mg and the mother gave the patient 2 tablets twice a day. It was learned that the child was transferred to a public hospital by the family when she could not be woken and breathed noisly approximately three hours after the second dose. The situation was distinguished there and gastric lavage was performed and active charcoal was administered. In the initial examination following admission to the intensive care unit, her general condition was poor, she was unconscious and the Glasgow Coma Score (GCS) was found as 7 (eye opening: 0, motor: 4, verbal response: 3). Her pupils were isochoric and myotic, the light reflex was bilaterally positive. The vital signs of the patient were as follows: heart rate: 98/min, arterial blood pressure: 73/41 mm Hg, body temperature: 36.2°C, capillary filling time: 3 seconds, and peripheral oxygen saturation (SpO2): 99%. The patient had spontaneous ventilation, but the airway protective reflexes (coughing, gagging) were assessed as decreased. Blood gasses were found as follows: pH 7.32, PCO2 46

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mm Hg, HCO3 23 meq/L, and lactate 1.2 mmol/L. The patient, whose blood gases and peripheral oxygen saturation values had a regular course, was monitored closely by giving oxygen with an oxygen mask with reservoir without intubation. The complete blood count, blood biochemistry and coagulometer tests were found normal. Sodium bicarbonate infusion was initiated for urine alkalinization and active charcoal treatment with repeated doses was initiated for gastrointestinal decontamination. We decided to perform hemodialysis when the blood phenobarbital level (BPL) was found as >140 mcg/mL (20-40 mcg/mL) and bradicardia and borderline hypotension accompanied and findings of neurologic supression were observed. Vascular access was achieved in the left subclavian vein with an 8 Fr dialysis catheter. We performed dialysis as SPAD, because phenobarbital could bind to plasma proteins at rates reaching up to 60%. With this objective, 250 mL was removed from 5 liter-Dialisan (Gambro) solution and 250 mL 20% albumin solution was added instead; thus, 5 L dialysate containing 1% albumin was prepared. An Hf20 (Gambro) polyarylethersulphon (paes) membrane was used for the procedure. Continuous venovenous hemodialysis (CVVHD) was initiated for the patient, who weighed approximately 9800 g and had a height of 72 cm (0.44 m^2), such that the blood flow rate was 60 mL/min (6 cc/kg/min) and the dialysate flow rate was 500 mL/h (2 000 cc/1.73m^2). Anticoagulation was provided with heparin (10U/kg/h) and titrated such that the activated coagulation time (ACT) was kept between 180 and 220 s. The blood phenobarbital level, which was measured in the sixth hour of the procedure, was found as 62 mcg/mL. Consciousness and respiratory findings started to improve after the six hours and consciousness was fully regained after the tenth hour of the procedure. No complications related with the catheter or procedure were observed during the procedure. In the follow-up, the patient had no hypotension and her apical heart beat was normalized. The SPAD procedure was completed when 5000 mL dialysate was finished. The patient was followed up for six hours after the procedure and no recurrent pathologic findings were observed. She was tranferred to the pediatrics ward for continuance of treatment. No problems were observed during follow-up in the pediatrics ward and she was discharged after her antiepileptic therapy was readjusted. Written informed consent was obtained from the family of the patient included in this study.

Discussion

Drug and non-drug intoxications occur frequently in children of young age. Children aged below five years constitute more than 2/3 of the cases and the agent of intoxication is frequently easily accesable drugs of the child or parents. Our patient was too young to have ingested any drug by herself and the reason of intoxication was erroneous prescription, which is a rare situation. Erroneous prescription has been blamed in many cases of intoxication in the mids of the twentieth century. In studies conducted in our country, phenobarbital intoxications constituted less than 1% of cases presenting to pediatric emergency deparments (1).

The clinical findings in phenobarbital intoxication are observed in a wide spectrum, ranging from deep sedation to coma and severe hypotension due to myocardial supression; reduced peripheral vascular resistance may also be observed. In addition, signs including apnea, areflexia, and hypothermia may also be observed. The classic therapeutic approach in phenobarbital intoxication includes urine alkalinization, active charcoal administered at repeated doses, and other supportive therapies (2). Impaired consciousness was the most prominent finding in our patient and the GCS was evaluated as 7 on admission. Although definite findings of cardiovascular supression were absent in our patient, she had bradycardia and borderline hypotension. With these findings, it was decided to perform SPAD in combination with classic therapeutic approaches considering the long half-life of phenobarbital (t1/2 80-120 hours) and high protein binding rate.

Dialysis in phenobarbital intoxication was reported with peritoneal dialysis in the 1960s and with hemodialysis and hemoperfusion applications after 1970. The number of cases of barbiturate intoxication in young children is considerably low in the literature and almost all are related with patients in the neonatal period who were accidentally given a high dose (3).

Single-pass albumin dialysis was reported for the first time in 1991 by Seige et al. Who used it in patients with hepatic encephalopathy (4). Single-pass albumin dialysis can also eliminate protein-bound toxins with high rates in addition to classic hemodialysis. The method can be applied with dialysates prepared with albumin in classic hemodialysis devices and therefore it seems that it will have a wider area of use compared with complex and high-cost systems including molecular adsorbent recirculating system (MARS). In the literature, there is no clear view related with dialysate albumin concentration in SPAD application. Adult cases where 4.4% concentrations were used in hepatic failure have been reported (5). However, albumin dialysates at concentrations of 1.85% and 5% were compared in a study conducted with patients with hyperbilirubinemia and no significant difference was found in terms of bilirubin clearance (6). Dialysate albumin concentrations may show variance by the objective of the application. In cases of hepatic failure, which require clearance of many toxins at the same time, albumin concentrations as high as 5% may be used, whereas lower concentrations of albumin may be sufficient in cases where clearance of only a single drug

or toxin is intended. In the literature, it was even reported that an albumin concentration of 0.2% was sufficient in a patient in whom only bilirubin clearance was intended to be increased (7). Reverse dialysis of preservative substances including caprylate (octanoate) or N-acetyl-tryptophan found in albumin solutions from dialysate solutions into the blood is possible, but there are insufficient data related with negativities that may be caused by this situation. In our case, we found it appropriate to use 1% albumin solution because of our drawbacks related with the potential negative effects of preservative substances and insufficient experience with pediatric cases in the literature. Phenobarbital binds to plasma proteins with rates reaching up to 60% and it appears that it can be cleared from the blood at higher rates with SPAD compared with classic hemodialysis because of this characteristic. As far as we know, application of SPAD in phenobarbital intoxication has not been reported in the literature. However, presentations related with successful use of SPAD in different cases of intoxication are present in the literature (8). Applications of hemodialysis and hemoperfusion in phenobarbital intoxications have been reported in the literature. Hoyland et al. reported that they used hemodialysis in 2 sessions of 2.5 hours in a patient who had phenobarbital intoxication (9). In their study, it was reported that blood phenobarbital levels were reduced from 115 mcg/mL to 84 mcg/mL in the first session and from 78 mcg/mL to 55 mcg/mL (approximately 30%) in the second session. In a case report of phenobarbital intoxication reported by Jacobs et al. (10), it was reported that the blood levels were reduced by 53% and 38%, respectively, following 6-hour hemodialysis applications performed in two sessions. The blood phenobarbital level of our patient measured before the procedure was found as >140 mcg/mL) (above the limit of measurement). This is a significant obstacle that causes difficulty in evaluation of the results of SPAD and in comparison with classic hemodialysis. However, the BPL was reduced more than 58% in our patient with a 6-hour SPAD procedure, the clinical findings improved nearly completely with an application of ten hours, and the need for intensive care monitoring was eliminated.

Conclusion

In conclusion, extrocorporeal therapies are usually not preferred in pediatric cases in Turkey because of potential complications. The increase in the number of pediatric intensive care units and raising of experienced pediatric intensive care specialists will potentially enable more widespread use of extracorporeal therapies in our country. In experienced centers, extracorporeal therapies can be applied with considerably low complication rates in children. Therefore, referal of eligible patients to these centers without delay may decrease the morbidity and mortality rates in cases of pediatric intoxication. Use of SPAD in cases of intoxication is novel information and large-scale randomized controlled studies are needed to show its efficiency and superiority compared with classic methods. However, we think the fact that it was used safely and efficiently in an infant aged six months would contribute to the literature.

Informed Consent: Written informed consent was obtained from the parents of the patients.

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