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CASE REPORT

Companion or pet animals

The use of haemodialysis for the treatment of phenobarbitone intoxication 30 h after ingestion

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Abstract

An 18-month-old male neutered Cocker Spaniel presented with a comatose mentation to his primary care veterinarian following the presumed ingestion of 216 mg/kg of phenobarbitone 2 h prior. Following a failure to improve with intravenous fluids, lipid emulsion therapy, and supportive care, the patient was then referred to a tertiary referral centre for further treatment 30 h following ingestion. Mechanical ventilation was initiated due to severe hypoventilation ($PvCO_2$: 69.9 mm Hg) before the patient underwent a 300-min prolonged veno-venous haemodiafiltration cycle performed using a continuous haemodialysis-based platform and a high-flux dialyser. The patient demonstrated rapid neurological improvement being extubated after 4 h, and becoming responsive and ambulatory 5 h from the initiation of the treatment. The patient was discharged 60 h following the completion of haemodialysis.

This is the first report in the veterinary literature of the effective use of veno-venous haemodiafiltration to treat phenobarbitone intoxication 30 h after ingestion using a high-flux dialyser.

KEYWORDS

critical care, poisoning, toxicology

BACKGROUND

Phenobarbitone is a long-acting barbiturate, widely used in veterinary medicine as an anti-convulsant. Similar to other barbiturates, phenobarbitone has been demonstrated to bind the gamma-aminobutyric acid (GABA)-sensitive ion channels in postsynaptic neuronal terminals of the central nervous system, resulting in the influx of chloride ions and subsequent neuronal hyperpolarisation[1], making neuronal cells less excitable thereby suppressing seizure activity. When given in large doses, barbiturates have also been demonstrated to stimulate GABA A receptors directly in the absence of GABA.[1,2]

Substantial depression of the central nervous and cardiovascular systems is well recognised in barbiturate toxicity.[1–3] Barbiturate-induced reduction of postsynaptic depolarisation results in the reduced contractility of smooth, skeletal and cardiac muscle.[2] At higher doses, depression of the medullary respiratory centres within the central nervous system may result in inhibition of respiratory drive, and in conjunction with the aforementioned skeletal muscle weakness, can lead to subsequent hypoventilation.[2,4] Additionally, central inhibition of the hypothalamic autonomic nuclei can result in hypotension and hypothermia.[1,5] Pharmacological studies using canine models have reported marked reduction in mentation at doses as low as 50 mg/kg, with a lethal dose in 50% of the population (LD_{50}) reported as low as 150 mg/kg.[6]

Veterinary species are typically intoxicated by barbiturates following the ingestion of pentobarbitone contaminated carcases,[7–9] or excessive ingestion of prescribed phenobarbitone.[10,11] The degree of cardiovascular and nervous system depression is typically proportional to the ingested amount, with some patients reportedly taking as long as 13 days to recover from severe intoxication using traditional decontamination techniques such as gastric lavage and repeated administration of activated charcoal.[11]

The case described documents the use of haemodialysis for the effective treatment of a patient with severe phenobarbitone toxicity 30-h post-ingestion.

CASE PRESENTATION

An 18-month-old male neutered Cocker Spaniel weighing 12.5 kg presented to its primary care veterinarian approximately 2 h after ingesting 216 mg/kg of phenobarbitone.

Initially unaware of its ingestion, the client presented for concerns for acute collapse. Upon returning home the owner discovered the empty remnants of a phenobarbitone bottle for another pet, which was known to have previously contained a total of ninety 30-mg tablets.

Upon presentation the patient was laterally recumbent, comatose with a reduced gag reflex, a heart rate of 120 beats per minute with normal pulse quality, systolic blood pressure of 120 mm Hg, an initial rectal temperature of 35.9°C, and respiratory rate of 12 breaths per minute, with no noted increased effort. Over the first 24 h of treatment the patient was actively warmed and given intravenous fluids with a single dose of intravenous lipid emulsion (ILE) as a 1.5 ml/kg bolus followed by a 0.5 ml/kg/min constant rate infusion (CRI) for 60 min. Given the patient's mentation, gastric decontamination with induction of emesis and/or administration of activated charcoal was considered inappropriate by the supervising veterinarian due to the risk of aspiration. Following a failure to improve the patient was then referred to a tertiary referral centre for further treatment approximately 30 h following ingestion.

On presentation to the tertiary referral centre the patient's neurological status had not changed from his initial presentation to his primary care veterinarian. His assessment demonstrated he had pink mucous membranes, capillary refill time of less than 2 s, and a heart rate of 100 beats per minute, with a regular rhythm, normal peripheral pulses, and systolic blood pressure of 120 mm Hg with a rectal temperature of 36.5°C. His respiratory rate was 20 breaths per minute with no adventitious lung sounds or increased effort. Initial venous blood gas[1], biochemistry,[2] and haematology[3] analysis demonstrated an acidaemia with respiratory acidosis (pH 7.223, RI: 7.350–7.470) with a $PvCO_2$ (69.9 mm Hg, RI: 37–47 mmHg), a moderate hypokalaemia (3 mmol/L, RI: 3.6–4.6 mmol/L), mildly increased ALP (180IU/L, RI: 0–130 U/L), mild hypoalbuminaemia (21.6 g/L, RI: 26.3–38.2 g/L), and mild neutrophilia of 12.45×10^9/L (RI: 3–11.5×10^9/L).

TREATMENT

Due to an absent gag reflex and hypoventilation the patient was immediately intubated to protect the airway, and mechanical ventilation[4] was instituted with a pressure controlled cycle (9 cm H_2O over positive end-expiratory pressure, PEEP), FiO_2 60%, respiratory rate 16 breaths per minute, and PEEP of 3 cm H_2O. Intravenous fluid therapy was provided with a balanced isotonic solution[5] supplemented with 30 mmol/L of potassium chloride[6] at 2 ml/kg/h.

Serum was collected for phenobarbitone serum concentration analysis[7]; however, results were not available for several days. Given the high index of suspicion of ingestion, respiratory depression and failure to respond to medical management, haemodialysis was performed to increase the clearance of phenobarbitone.

LEARNING POINTS/TAKE HOME MESSAGES

- Intoxication with phenobarbitone can be potentially life threatening in veterinary patients
- The use of continuous veno-venous haemodiafiltration can be used to effectively treat patients experiencing phenobarbitone intoxication, even with a prolonged elapsed time from exposure to presentation
- Continuous veno-venous haemodiafiltration can substantially reduce the length of hospitalisation for patients with severe phenobarbitone intoxication.

An 11.5Fr 19.5 cm dual lumen polyurethane dialysis catheter[8] was placed in the left jugular vein using a modified Seldinger technique. The tip of the dialysis catheter was positioned at the junction of the cranial vena cava and right atrium and confirmed with a single lateral radiograph. The patient was systemically anticoagulated with a bolus of 25 IU/kg IV of unfractionated heparin[9] followed by a CRI of 20 IU/kg/h. Appropriate systemic heparinisation was maintained using serial activated clotting times[10] between 180 and 200 s with adjustments in heparin CRI performed as previously described.[12]

Despite initial cardiovascular stability, prior to commencing haemodialysis the patient developed hypotension (75-mm Hg Doppler systolic blood pressure) and was started on a CRI of norepinephrine[11] at 0.1 μg/kg/min. In addition to vasopressor support, the patient received a total of three 5 ml/kg crystalloid boluses in an attempt to address documented hypotension throughout his dialysis session.

A 300-min veno-venous haemodiafiltration cycle was performed using a continuous renal replacement therapy-based platform[12] and a high-flux dialyser[13] at a blood flow rate of 70 ml/min (5.6 ml/kg/min). The treatment started with an initial dialysate flow rate of 2400 ml/h, before being increased to 7500 ml/h and a convective therapy of 150 ml/h of post filter replacement using commercially available dialysis solution[14] with a total effluent volume of 34.5 L. Flow settings were targeted to achieve a high efficiency which corresponded to a Kt/V (a dialytic adequacy index) of 4.75. Treatment duration was determined by the patient's response and neurological improvement.

Serum samples were collected for phenobarbitone serum concentration measurements when the treatment was initiated, hourly during the cycle and at 24 h post-cycle. Serum phenobarbitone at the initiation of therapy was 143 μg/ml (RI: 15–35 μg/ml). Over the course of the 5 h of treatment the patient's serum phenobarbitone level reduced to 64 μg/ml, demonstrating only a small increase to 68 μg/ml 24 h later (Figure 1).

[1] ABL90 FLEX, Radiometer UK, West Sussex, UK
[2] iLab 600, Instrumentation Laboratory, Cheshire, UK
[3] Advia 2120i Haematology System, Siemens Healthcare, Camberley, UK.
[4] Mindray SV300, Mindray, Huntingdon, UK
[5] Aquapharm 11 Hartmann's solution for infusion, Animalcare, York, UK
[6] Potassium Chloride concentrate 20%, Hameln Pharmaceuticals, Gloucester, UK
[7] Konelab 30i Chemistry Analyser, ASAMED Sp, Przezmierowo, Poland
[8] Mahurkar™ 11.5 Dual Lumen Acute Dialysis Catheter, Medtronic, Hertfordshire, UK
[9] Heparin Sodium1000 I.U/ml, Wockhardt, Wrexham, UK
[10] Hemochron™, Werfen, Cheshire, UK
[11] Noradrenaline (norepinephrine) 1 mg/ml, Hospira UK, Hurley, UK.
[12] Prismaflex System, Baxter Health Care, Berkshire, UK
[13] Prismaflex ST100, Baxter Health Care, Berkshire, UK
[14] Prismasol 4 Renal Replacement Solution, Baxter Health Care, Berkshire, UK

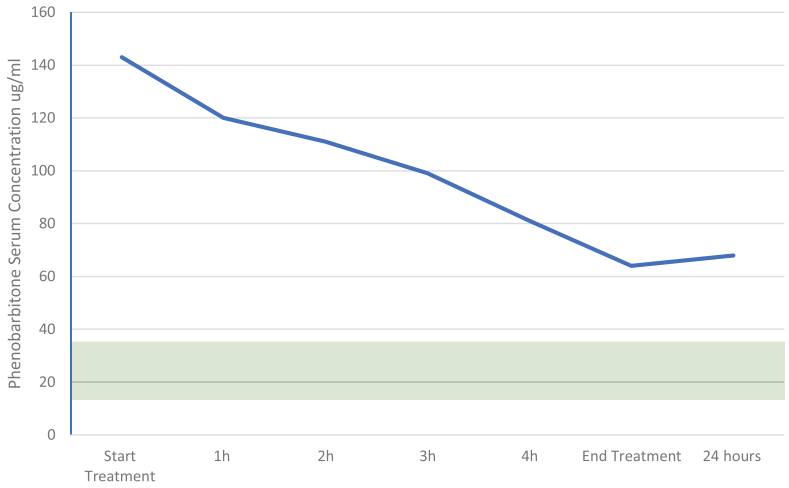

FIGURE 1 The reduction in phenobarbitone serum concentration level (μg/ml) following the initiation of haemodiafiltration therapy and 24 h later. Shaded area (green) demonstrates the recommended therapeutic phenobarbitone serum concentration level

Following 90 min of haemodiafiltration the patient began initiating spontaneous breaths and was transitioned from pressure controlled to spontaneous ventilation with pressure support, with further neurological improvement noted 90 min later with the return of the palpebral reflex and increased jaw tone. Four hours after starting haemodialysis the patient was noted to have increased respiratory noise on auscultation and an endotracheal wash was performed which later isolated a mixed population of *Staphylococcus pseudointermedius*, *Serratia marcescens* and *Enterobacter ludwigii*.

Following the endotracheal wash, the patient's neurological status continued to improve and he was extubated. At the end of the treatment the patient had regained consciousness but remained obtunded. Additional ILE[15] was administered with a 1.5 ml/kg bolus followed by a 0.5 ml/kg/min CRI for 60 min. Due to the septic endotracheal wash results the patient received 20 mg/kg of amoxycillin/clavulanic acid[16] intravenously that was continued every 8 h for a total 5-day course, with a transition to oral formulation upon discharge.

The patient's mentation continued to improve over the 12 h following the completion of haemodialysis, at which point he had commenced eating and was walking with a moderate degree of ataxia. The patient developed a substantial increase in urine output of > 12 ml/kg/h in the first 6 h following haemodialysis that was matched with an increased intravenous fluid rate. During the following 24 h the patient's ataxia and increased urine output resolved, and due to his increased ALP on admission, and expecting phenobarbitone-induced hepatic changes to be ongoing, he was started on oral ursodeoxycholic acid[17] and S-Adenosyl methionine[18]. Repeat biochemistry[b] and haematology[c] was performed on the day of discharge and demonstrated a mildly increased inorganic phosphate (1.75 mg, RI: 0.8–1.6 mmol/L), cholesterol (6.26, RI: 3.2–6.2 mmol/L) and ALP (402, RI: 0–130 U/L) with mild lipaemia and haemolysis. Notably, biochemistry prior to and after treatment failed to demonstrate any increase in ALT.

[15] Intralipid 20%, Fresenius Kabi, Homberg, Germany
[16] Augmentin intravenous, Beecham Group, Uxbridge, UK
[17] Desolit 150mg, Norgine, Uxbridge, UK
[18] Denamarin 225mg, Protexin® Veterinary, Somerset, UK

OUTCOME AND FOLLOW-UP

The patient was discharged 60 h following the completion of haemodialysis, and has no known long-term complications from his intoxication.

DISCUSSION

A variety of techniques are described in the human literature to enhance elimination of barbiturates following acute toxicity.[2,3] In humans it is recommended that patients suspected of barbiturate toxicity have serum concentrations obtained prior to therapy, and although serum levels are not reliable predictors of the duration or severity of toxicity, it is generally recognised that values greater than 50 μg/ml may induce a comatose state, while concentrations > 80 μg/ml can be reportedly fatal.[3,13] There is currently no reported correlation with serum concentration and clinical presentation in veterinary species, and these values in people may not directly translate to canine patients.

In patients with mild clinical signs, the use of multiple doses of activated charcoal is generally recommended as the mainstay of therapy.[2,3] Attempts at gastric decontamination and/or administration of activated charcoal orally alone however are limited to those individuals whom have recently ingested a toxic dose and have minimal neurological impairment given the potential risk of aspiration (3,14) thus were not appropriate in the case described here.

Several case reports in the veterinary literature describe similar techniques for the management of acute barbiturate toxicity. In these cases animals are typically intoxicated by the ingestion of pentobarbitone contaminated carcases,[7–9] or excessive ingestion of prescribed phenobarbitone.[10,11] This heterogenous population of cases all demonstrate a degree of depression of the central nervous and cardiovascular systems. In the majority of cases patients were successfully managed with supportive care and multiple doses of activated charcoal with a variable hospitalisation length of 2 to 13 days, which was typically proportional to the severity of clinical signs.[7–9,11]

The elimination half-live of phenobarbitone in dogs ranges from 12 to 125 h with an average of approximately 48 h (4,15); therefore, there is a reasonable time window to intervene after drug ingestion to reduce plasma concentrations significantly by extracorporeal removal.

Extracorporeal methods of enhanced elimination, namely haemodialysis, haemodiafiltration and haemoperfusion, are typically indicated in those human patients with severe long-acting barbiturate toxicity that demonstrate severe life-threatening clinical signs despite intensive supportive care.[3] Although other techniques such as urine alkalisation are described in the literature as a means of increasing renal excretion, in people they have been demonstrated to be relatively ineffective and have been superseded by the aforementioned techniques.[14,16,17]

The effectiveness of drug and toxin removal is greatly affected by the type of extracorporeal therapy used. Haemodialysis modalities can be generally divided into intermittent haemodialysis (IHD) and continuous renal replacement therapies (CRRT).[18] Standard IHD relies on the principle of a diffusion gradient across a dialyser (filter) to remove molecules from areas of high concentrations, such as in the blood, into a dialysate solution, consisting of a balanced isotonic solution with a lower or null concentration of that molecule.[19] The extent of exchange of drugs between the patient's blood and the dialysate is determined by the characteristics of that solute, especially size and protein binding, as well as structural characteristics of the dialyser membrane.[19]

CRRT modalities which more closely reflect endogenous renal function can use a mixture of diffusive and convective solute removal with the latter due to solutes being dragged with plasma water across the dialyser as a result of pressure gradients or hydrostatic pressure.[18] The rate at which a solute can be removed is dictated by the membrane's surface area, pore size and water movement across the membrane.

In order to be removable by diffusion, a molecule should have a low molecular weight (< 500 Da), and low protein-binding,[18] while convection allows for a more effective removal of medium molecular weight molecules (500—60,000 Da).[18,20] Phenobarbitone has a low affinity for protein (45% protein bound) and a molecular weight of approximately 232 Da.[3,4] Thus, in this case, to achieve a more rapid clearance of the phenobarbitone, the CRRT platform was used with high settings to maximise diffusive clearance and adding some convective clearance.

In a systematic review of the use of extracorporeal therapy in barbiturate toxicity in humans, a working group consisting of international participants from various fields (including nephrology, medical toxicology and emergency medicine) concluded that in cases of severe intoxication IHD was recognised as the preferred modality of extra-corporeal elimination, but CRRT modalities were considered a valid alternative if IHD is unavailable.[3]

The dialysis machine available at our centre cannot facilitate the high dialysate flow rates required for IHD therapies; however, a veno-venous haemodiafiltration technique was used to accelerate phenobarbitone clearance. The Prismaflex ST100^{m} extracorporeal filter used in this patient is indicated for renal replacement therapies and exogenous toxin removal, and can be used in a variety of veno-venous therapy options. The Prismaflex ST100 set contains a high flux AN 69 ST hollow synthetic fibre filter with an effective surface area of 1 m^2.[21] High flux dialysers have higher hydraulic conductivity and are able to remove small and middle weight molecules more efficiently compared to low-flux dialysers.[22] Therefore, the use of a high flux dialyser could enable more effective removal of specific non-protein-bound toxins, in particular when convective therapy is employed, and is the preferred dialyser type for the effective removal of barbiturates in intoxicated humans.[3]

Despite the phenobarbitone concentrations reducing significantly in only 5 h of treatment, it should be noted that in this case the use of a low convective therapy of 150 ml/h, compared with the diffusive therapy used, may have limited the potential advantage of using a high-flux dialyser.

In a recent case report the use of IHD was described to rapidly resolve acute phenobarbitone toxicity in two dogs with calculated half-life eliminations of approximately 1 h using extracorporeal removal.[10] When examining our patient's serial serum phenobarbitone concentrations (Figure 1), we demonstrate an elimination half-life clearance of approximately 5 h, a nearly 10-fold increase from reported natural clearance rates.[15]

The use of ILE for intoxications has become increasingly popular in the treatment of acute intoxications in veterinary patients. The mechanism of action in which ILE works to improve recovery rates with various lipophilic drugs is currently unknown.[23] One commonly described theory, coined the 'Lipid Sink' theory, describes the creation of an expanded lipid phase within the plasma that acts to sequester various lipophilic compounds within this lipid compartment and reduces the effective concentration at the target tissue.[23,24] The lipophilicity of an organic compound is described by the partition coefficient logP, defined as the ratio of the concentration of the compound at equilibrium between hydrophilic and lipophilic solvents.[24] LogP > 1 are described as lipophilic, with the greater the value, the more lipophilic the compound.[23] Phenobarbitone has a logP of 1.4[25], and theoretically would be amenable to ILE therapy.

In experimentally induced intoxication of rodents with phenobarbitone, ILE reportedly improved survival.[26] Its use in canine intoxications is limited to a single report in which ILE was used in conjunction with other decontamination techniques, such that the extent to which ILE can be attributed to the patient's recovery is unclear.[9] In our case, ILE was used on initial presentation and then again, following the completion of haemodiafiltration therapy. It is difficult to assess how much it may have contributed to the patient's overall recovery; however, it would appear that the initial dose provided at the primary care practice had minimal effect on the patient's condition.

In recent times, logD has become an increasingly more frequently used term by which to describe a substance's lipophilicity, and, unlikely logP, measures the lipophilicity of ionisable compounds and therefore accounts for variability in lipophilicity of weak acids and bases at different pH values.[27] Phenobarbitone, a weak acid, has a logD of 1.41 at pH < 4.6; however, this decreases progressively as the pH increases, with a logD of 0.96 at a pH of 7.4, which suggests that it is less lipophilic at physiological pH and therefore less amenable to ILE.[25] There is, however, currently no widely held consensus on a specific log D value to predict a toxin's responsiveness to ILE.

The patient experienced significant hypotension immediately prior to and during IHD therapy. Those changes noted prior to the time of dialysis could be attributed to the significant cardiovascular depressant effects of the phenobarbitone intoxication or to the institution of positive pressure ventilation which might have affected cardiac output.[2,28] While dialysis-induced hypotension (DIH) is one of the

most frequent complications of renal replacement therapy, its aetiology is often multi-factorial and complex.[29] DIH is most frequently the result of a rapid reduction of blood volume due to priming of the extra-corporeal circuit; however, other factors such as impaired cardiovascular compensatory mechanisms and production of vasoactive substances during dialysis are known to contribute.[29]

The patient also experienced a severe diuresis during and following the cycle, starting at 7.6 ml/kg/h during the procedure and peaking at 14 ml/kg/h after the procedure. It is unclear why the diuresis occurred, although there are multiple factors that might have contributed including positive fluid balance secondary to fluid therapy and potential fluid accumulation related to the dialysis procedure. Diuresis resolved over the following day, when intravenous fluid therapy rates were de-escalated to achieve a negative fluid balance.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest

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The authors received no specific funding for this work.

ETHICS STATEMENT

The following is a listed case report and describes the treatment of a specific patient. All treatments were performed at a university tertiary veterinary hospital under the direction of board-certified veterinary specialists. No explicit ethical committee approval is required at our institution for description of case reports; however, all treatments are performed in accordance with national welfare standards. Owner's consent has been given for the publication of this case report.

AUTHOR CONTRIBUTION

Conceptualization: TG, LC, SC
Data curation RT, SC
Formal analysis- RT, SC
Investigation/Treatment TG, LC, SC
Methodology- RT, SC
Resources-RT, SC, TG
Writing – original draft- RT, SC
Writing – review: RT, TG, LC, SC

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REFERENCES

1. Barile FA. Barile's clinical toxicology. Boca Raton: CRC Press; 2019.
2. Roberts DM, Buckley NA. Enhanced elimination in acute barbiturate poisoning – a systematic review. Clin Toxicol. 2011;49(1):2–12.
3. 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(3):347–58.
4. Donald C. Plumb. Plumb's veterinary drug handbook. 9th ed. Stockholm, WI: Wiley; 2017.
5. Murray L, Little M, Pascu O, Hoggett K. Toxicology handbook. 3rd ed. In: Armstong J, Pascu O, editors. Linvingstone, Australia: Elsevier; 2015. p. 560.
6. Lieske C, Volmer P. Illicit Human Drugs. In: Handbook of small animal practice. 5th ed. St. Louis: Saunders/Elsevier; 2008. p. 1227–32.
7. Campbell VL, Butler AL, Lunn KF. Use of a point-of-care urine drug test in a dog to assist in diagnosing barbiturate toxicosis secondary to ingestion of a euthanized carcass. J Vet Emerg Crit Care. 2009;19(3):286–91.
8. Brauer C, Tipold A, Desel H, Stein VM. Barbiturate intoxication in two dogs confirmed by toxicological urinalysis. J Small Anim Pract. 2009;50(8):423–5.
9. Bischoff K, Jaeger R, Ebel JG. An unusual case of relay pentobarbital toxicosis in a dog. J Med Toxicol. 2011;7(3):236–9.
10. Basile JK, Vigani A. Treatment of phenobarbital intoxication using hemodialysis in two dogs. J Vet Emerg Crit Care. 2020;30(2):221–5.
11. Khoutorsky A, Bruchim Y. Transient leucopenia, thrombocytopenia and anaemia associated with severe acute phenobarbital intoxication in a dog. J Small Anim Pract. 2008;49(7):367–9.
12. Edrees F, Li T, Vijayan A. Prolonged intermittent renal replacement therapy. Adv Chronic Kidney Dis. 2016;23(3):195–202.
13. Mowry JB, Spyker DA, Cantilena LR, 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(10):949–1229.
14. Mohammed Ebid A-HI, 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 Jun;23(3):209–16.
15. Pedersoli WM, Wike JS, Ravis WR. Pharmacokinetics of single doses of phenobarbital given intravenously and orally to dogs. Am J Vet Res. 1987 Apr;48(4):679–83.
16. Proudfoot AT, Krenzelok EP, Vale JA. Position paper on urine alkalinization. J Toxicol Clin Toxicol. 2004 Jan 15;42(1):1–26.
17. Frenia ML, Schauben JL, Wears RL, Karlix JL, Tucker CA, Kunisaki TA. Multiple-dose activated charcoal compared to urinary alkalinization for the enhancement of phenobarbital elimination. J Toxicol Clin Toxicol. 1996 Jan 25;34(2):169–75.
18. Monaghan KN, Acierno MJ. Extracorporeal removal of drugs and toxins. Vet Clin North Am Small Anim Pract. 2011;41(1):227–38.
19. Bloom CA, Labato MA. Intermittent hemodialysis for small animals. Vet Clin North Am Small Anim Pract. 2011;41(1):115–33.
20. Acierno MJ. Continuous renal replacement therapy in dogs and cats. Vet Clin North Am Small Anim Pract. 2011;41(1):135–46.
21. Baxter Health Care Ltd, Datasheet: Prismaflex sets with the AN 69 ST membrane for CRRT: Prismaflex ST60, ST100, ST150 sets, SE/MG120/16-0003, 2016.
22. Haroon S, Davenport A. Choosing a dialyzer: what clinicians need to know. Hemodial Int. 2018;22:S65–74.
23. Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. The use of intravenous lipid emulsion as an antidote in veterinary toxicology. J Vet Emerg Crit Care. 2011;21(4):309–20.
24. Bevavides K, Babyak J. Lipid "Rescue" therapy. In: Drobatz KJ, Hopper K, Rozanski EA, Silverstein DC, editors. Textbook of small animal emergency medicine. 1st ed. Hoboken, NJ: Wiley; 2019. p. 831–4.
25. Laxmi K. Calculation of properties of phenobarbital an antiepileptic drug using chemcalise software. Int J Sci Res Publ. 2019;9(11):p9524.
26. Moshiri M, Aftabi F, Esmaeili M, Etemad L, Hosseinzadeh H. Intravenousts. J Iranian Med Council. 2018;1(1):29-33.
27. Bhal SK, Kassam K, Peirson IG, Pearl GM. The rule of five revisited: applying log D in place of log P in drug-likeness filters. Mol Pharm. 2007;4(4):556-60.
28. Mahmood SS, Pinsky MR. Heart-lung interactions during mechanical ventilation: the basics. Ann Transl Med. 2018;6(18):349.
29. Sulowicz W, Radziszewski A. Pathogenesis and treatment of dialysis hypotension. Kidney Int. 2006;70(Suppl 104):S36–9.

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