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CASE SERIES

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Rescue strategies for valproic acid overdose poisoning: Case series and literature review

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Key Clinical Message

Valproic acid (VPA) is a wide-ranging anti-epileptic medication that primarily affects bipolar disorder, mania, and migraine. The leading causes of mortality associated with acute poisoning from VPA are nervous system toxicity, drug-induced shock due to encephalopathy from hyperammonemia, as well as acute liver and kidney failure, and respiratory depression that contribute to hemodynamic instability. Treatment of acute VPA poisoning primarily involves in vitro elimination methods, including hemoperfusion (HP), hemodialysis, and hemofiltration, as well as drug remedies such as L-carnitine and meropenem. Nonetheless, there are conflicting opinions regarding drug usage. This article details the three cases of acute poisoning from VPA. The fundamental approach to treatment employs HP assisted by blood concentration monitoring to alleviate shock and stabilize hemodynamics. This investigation presents guidance for the treatment and management of acute poisoning with VPA in clinical settings.

KEYWORDS

continuous renal replacement therapy, hemoperfusion, poisoning, rescue, therapeutic drug monitoring, valproic acid

1 | INTRODUCTION

Valproic acid (VPA) is a branched short-chain fatty acid derived from valeric acid, a low molecular weight carboxylic acid.[1] VPA is a broad-spectrum anti-epileptic drug. It is the first-line drug for various types of epilepsy and is the first choice for mandatory seizures.[2,3] VPA has also been effective in bipolar disorder, mania, anxiety, and migraine.[4–6] Because of its wide clinical use and narrow safety range, the effective concentration range is 50–100 mg/L,[7] We often encounter high doses of VPA for acute poisoning caused by suicide. The leading life-threatening toxicity and complications of VPA poisoning are central nervous system toxicity, hyperammonemia encephalopathy, acute liver, and renal failure.[8] Rescue of acute VPA poisoning mainly includes in vitro elimination such as hemoperfusion (HP), hemodialysis (HD), hemofiltration (HF),[9] and drug rescue such as L-carnitine, meropenem.[10,11] However, there are some disputes over the use of drugs. We reported three cases of HP, HD, and continuous renal replacement therapy (CRRT) based on blood concentration monitoring to eliminate VPA to rescue acute VPA poisoning, and provide a reference for emergency treatment of acute valproic.

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2 | CASE REPORT

Case 1: The patient, a 14-year-old female weighing 50 kg and measuring 160 cm in height, was discovered unconscious in bed at her home 3 h ago. She was unable to breathe or respond to stimulation. At the earlier time of 12 h before January 16, 2023, the patient's family members reported finding four bottles empty of sustained-release magnesium valproate tablets (120 tablets, 250 mg/tablet, 30 g) and two plates empty of quetiapine fumarate tablets (20 tablets, 0.1 g/tablet, 2 g). The patients were expeditiously taken to the emergency department for a routine gastric lavage with standard saline before being transferred to the ICU.

The patient had a history of depression. Magnesium valproate and quetiapine fumarate were used to treat depression. Medical examination: Body temperature: 36.8°C, Pulse: 102 times/min, Respiratory Rate: 14 times/min, Blood pressure: 106/56 mmHg. Laboratory examination showed that muscle enzymes, myoglobin, and elevated aspartate aminotransferase increased significantly, reducing glutathione to protect the liver from drug-related muscle damage. Blood ammonia showed plus aseptic ornithine acid and lactulose relief. The blood concentration of VPA was 635.77 mg/L. The doctor diagnosed VPA poisoning in the patient. To remove excess VPA, open venous channels, deep venous catheterization, HD combined with HP, and CRRT to release drugs. Blood drug concentrations at 12 h and 24 h after admission were 196.50 mg/L and 193 mg/L, respectively, significantly lower than before. However, the 36-h blood concentration was 263.2 mg/L, and the 48-h blood concentrations were 263.2 mg/L and 351.6 mg/L. On the third day of admission, the patient complained of a headache, a rapid heart rate of 120 beats per minute, and a blood pressure of 155/73 mmHg. The doctor considered intracranial hypertension as the patient's blood pressure increased several times. Therefore, the mannitol was used to reduce intracranial pressure. Laboratory tests showed increased pH, suggesting a high likelihood of metabolic alkalosis, slightly higher lactic acid, marginally lower blood potassium, and intravenous potassium chloride supplementation. Continue HP and CRRT to remove VPA. The blood concentration was 134.93 mg/L. On the fourth day, he was conscious and could answer questions accurately. The blood concentration was 71.05 mg/L and transferred from the ICU to the regular ward. The blood drug concentration was further reduced during hospitalization, the patient was discharged after finding no apparent abnormalities.

Case 2: The patient is a 13-year-old female, weighing 55 kg and measuring 167 cm in height. On March 7, 2021, the patient ingested sodium valproate (0.2 g * 68 tablets) and vitamin D (400 units * 4 tablets) 6 h ago. Three hours ago, the patient vomited with only food residue and no trace of drugs residues was seen. The patient reported feeling fatigued and drowsy, was unresponsive to questions, and had no other discomforts. The patient presented to our hospital with visible yellow gastric juice and received gastric lavage treatment. The patient had been experiencing symptoms of depression for over 5 months, sought treatment at a psychiatric hospital, was diagnosed with depression, and orally took sertraline dispersible tablets and Shugan Jieyu Capsule. The mood became more unstable and irritable after medication administration. On the day before admission, the doctor ceased the medication and switched to sodium valproate and vitamin D. The blood concentration of VPA was 507.00 mg/L, eliminated by HP apparatus. Heparin was administered for anticoagulation, while dopamine helped stabilize blood pressure. The blood pump speed was 150 mL/h. By the third day, the patient improved during their stay in the hospital without any apparent discomfort.

Case 3: The 14-year-old female patient weighed 58 kg and measured 160 cm in height. On October 3, 2022, she ingested 21 tablets of sustained-release sodium valproate (0.5 g/tablet) 4 h prior to admission, resulting in a disturbance of consciousness characterized by drowsiness and impaired wakefulness. Upon discovery, the patient was transported by the family to the emergency department, where immediate treatment involved gastric lavage. After being diagnosed with anxiety and depression in the hospital's psychological department, he was prescribed oral sertraline hydrochloride tablets, sodium valproate sustained-release tablets, and quetiapine fumarate tablets. He remained on this medication until his hospitalization. The blood concentration of VPA was measured at 317. An HP device was employed for HP treatment, with a blood pump speed of 150 mL/H. The initial blood concentrations of the patient were 178.78 mg/L and 176.88 mg/L at 6 h and 12 h post-admission, respectively, showing a significant decline compared to the readings before admission. However, the blood concentrations at 36 h and 48 h were 144.15 mg/L and 122.46 mg/L, respectively, indicating a slow clearance rate. The patient was administered a dose of furosemide with the intention of releasing diuretic protoxin. Naloxone was used to revive the patient. Additionally, 3000 U of heparin was administered intravenously as an anticoagulant, and dopamine was used to stabilize the patient's blood pressure. HP treatment was continued. On the third day of admission, the patient was conscious and able to answer questions accurately. On the fourth day, their blood concentration was 31.89 mg/L. The patient demonstrated improvement and was subsequently discharged.

The laboratory examination of each patient during the hospital is shown in Table 1, and the VPA blood concentration change is shown in Figure 1.

TABLE 1 The laboratory examination of each patient during the hospital.

	Case 1						Case 2		Case 3	
Investigations	**Day1**	**Day2**	**Day3**	**Day4**	**Day5**	**Day10**	**Day1**	**Day3**	**Day1**	**Day3**
Hemoglobin (110-150 g/L)	117	107	77	90	97	108	109	125	121	129
Serum creatinine (53.0–115.0 μmol/L)	57	48	54	39	39	48	52	39	51	36
Blood urea nitrogen (2.90–8.20 mmol/L)	4.1	2.7	2.2	2.4	1.3	4.3	2.6	3.4	2.3	1
Ammonia concentration (11.0–51.0 μmol/L)	53.4	54.6	25.3	NA	NA	NA	NA	NA	42.6	NA
White blood cell count (3.69–9.16*109/l)	8.09	5.29	8.58	6.08	5.52	12.8	5.03	6.15	8.92	8.52
Platelet count (101.0–320.0*109/L)	308	95	50	45	33	455	178	103	268	176
Sodium (135.00–145.00 mmol/L)	131	134	135	138	134	136	145	136	134	131
Potassium (3.50–5.10 mmol/L)	4.1	3.78	3.3	3.3	3.4	3.9	3.8	4.24	4.2	3.3
Aspartate transaminase (0.0–45.0 IU/L)	76.3	142.1	222.5	228.4	125.4	34.5	11.6	14.9	25.8	12.3
Alanine transaminase (0.0–40.0 IU/L)	22.3	40	66.5	65.7	53	37.9	7.1	9.2	4.7	2.5
pH (7.35–7.45)	7.43	7.43	7.51	7.48	7.45	7.45	7.41	7.36	7.4	7.46
PCO_2 (35.00–45.00 mmHg)	35	34	37	43	37	41	3.83	3.63	38	37
PO_2 (80.00–100.00 mmHg)	108	120	79	90	91	103	17.64	17.49	98	103
HCO3 (21.4–27.3 mmol/L)	23.2	22.6	29.5	32	25.7	28.5	19.8	17.4	23.5	26.3
Chloride (98–108 mmol/L)	NA	109	106	NA	NA	NA	105	102	NA	NA
Lactate dehydrogenase (114.0–240.0 IU/L)	303	440	600	554	449	443	115	171	367	167
Creatine kinase (25.0–195.0 IU/L)	10,476	16,427	16,549	9941	3723	192	74	51	137	66
Myoglobin (0.00–70.00 μg/L)	21,239	2327.6	1155.8	139	64.9	25.4	28	25	39.2	22.8
Amylase (10-200 IU/L)	327	973	558	96	58	40.8	77	71	40	NA

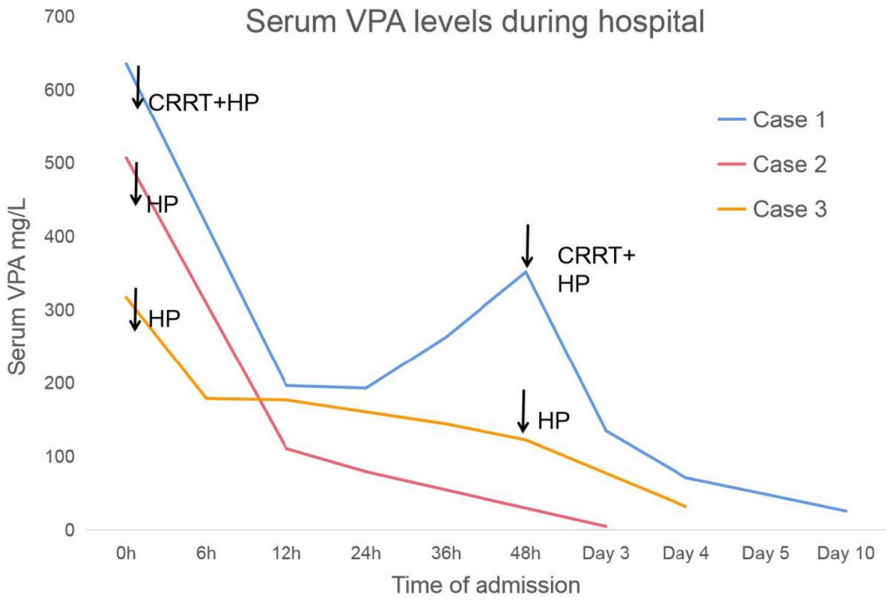

FIGURE 1 Serum VPA levels (mg/L) during hospital. HP, hemoperfusion; CRRT, continuous renal replacement therapy. The serum drug concentration in acute valproic acid (VPA) poisoning is well above the normal range. In case 1, the initial concentration reached 635.77 mg/L. HP and CRRT measures will rapidly reduce the serum drug concentration of VPA. As the drug concentration in the tissues and organs is still high, the drug redistribution leads to an increase in the blood drug concentration. It should be considered that HP and CRRT measures should be repeated or repeated to ensure rapid elimination of the drug.

3 | DISCUSSION

Acute intake of too much VPA, blood concentration greater than 125 mg/L often reduces white blood cells and platelets,[12] plasma concentrations above 180 mg/L often lead to central nervous system dysfunction in patients, such as tremors, agitation, brain edema, and other neurological damage. High VPA concentrations in tissues and organs can damage the liver, brain, kidney, and other vital organs.[13] It converted the median lethal dose of VPA in rats to 0.13–0.16 g/kg in humans,[14] the median lethal dose of patients in case 1 was about 0.6 g/kg, the median lethal dose of patients in case 2 was about 0.23 g/kg, and the median lethal dose of patients in case 3 was about 0.18 g/kg, which was of active life-saving significance.

VPA is a small molecule compound with strong water solubility. The drug has a relatively low molecular weight (144 Da). It can quickly absorb VPA after oral administration, its bioavailability is greater than 90%, and its sustained-release preparation is about 70%. The plasma protein binding rate ranged from 74% to 90%, mainly because of the saturation of its binding to plasma protein, which also made its pharmacokinetics present nonlinear metabolism.[15]

Each sustained-release magnesium valproate tablet contains 250 mg, and each sustained-release sodium valproate tablet contains 500 mg of sodium valproate. The absorption of VPA sustained-release tablets was slower than that of standard tablets after oral administration, and the blood concentration peaked at about 14 h, which could last for about 16 h. The release of sustained-release tablets is slower than ordinary tablets, so their absorption is slow, resulting in no linear relationship between blood concentration and drug dose. Gastric lavage is one method of removing poison poisoning from the digestive tract, it can reduce mortality in acute (especially severe) poisoning patients.[16] Although there is no specific antidote for excessive use of sodium valproate, there is no contraindication for gastric lavage. For patients with severe acute poisoning who do not have a specific antidote, elimination of VPA by gastric lavage, even if it has been over 6 h,[16] FDA guidelines also noted that gastric lavage treatment is still effective within 10–12 h of drug intake.[17]

Valproate is a strong alkali and weak acid salt. It is weakly alkaline after dissolution in water. The pH is 7.5 to 9.0. Strengthening diuresis may promote valproate release and elimination of VPA by CRRT combined with HP. HD and HP can speed up the elimination of VPA. In one case study, HD reduced the half-life of VPA from 8.5 h before treatment to 5.8 h after treatment. It extended the half-life to 22 h after discontinuation of HD.[18] Therefore, gastric lavage was performed on all three patients to eliminate any remaining VPA present in their stomachs.

HP is when blood flows through a perfusion column equipped with a solid-phase adsorbent (activated carbon

or resin) to remove exogenous drugs or poisons through adsorption to purify the blood. That is mainly used for toxicants with a high protein binding rate, high-fat solubility, and large and medium molecular weight. HP may not correct the water, electrolyte, and acid–base balance disorder and may cause platelets, white blood cells, clotting factors, glucose, and divalent cations to decrease, which should be monitored and supplemented promptly. In Case 1, the clinician urgently opened central venous access and performed CRRT+HP treatment to rapidly and stably reduce the concentration of free sodium valproate in the patient's blood. After 10 h of CRRT+HP treatment, the blood concentration of sodium valproate decreased from 635.77 mg/L to 193.00 mg/L, and the blood concentration rebounded to 263.20 mg/L after 12 h. The blood concentration of sodium valproate may rebound after one time of blood purification,[19] because drug concentration in tissues and organs is still significant, drug redistribution increases blood drug concentration again. The protein binding rate of sodium valproate is high. The CRRT is mainly used to remove toxic substances with high water solubility, small molecules, and low protein binding rate, and the removal effect of sodium valproate binding is not good. HP is mainly used for toxic substances with high protein binding rates, high-fat solubility, and relatively large molecular weight. The resin perfusion device has better removal of protein binding and fat-soluble molecules. Based on CRRT, combined with HP treatment, after 10 h of CRRT+ HP treatment, the blood concentration of sodium valproate decreased from 351.6 mg/L to 71.05 mg/L, and the removal effect was significant. In vivo, sodium valproate binds to the corresponding receptor in a free state to produce efficacy. Because of sodium valproate's high plasma protein binding rate, changes in plasma protein content can significantly affect the concentration of free sodium valproate, affecting efficacy or producing toxic adverse reactions.[20] Studies have confirmed that with the same amount of sodium valproate with the increase of plasma protein, free sodium valproate blood concentration showed a downward trend,[21] when the patient's plasma albumin decreases when appropriate, albumin supplementation can reduce the side effects of sodium valproate. For case 2, there was a significant decrease in the blood concentration of VPA after a single HP treatment. As for case 3, although the blood concentration decreased after HP was used, there was no significant decrease at 12 h and 48 h after treatment. However, after a second administration of HP, the blood concentration returned to the normal range. It should be noted that the concentration of the drug in tissues and organs remained high, resulting in a rise in the drug concentration in the blood due to redistribution.

Elevated blood ammonia is caused by sodium valproate and related hyperammonia encephalopathy, manifested as mental disorders, seizures, and lethargy. It can progress to coma or even death. It is material attention to the changes in blood ammonia in patients.[22] In case 1, on the day of admission and the second day, the blood ammonia of the patient was 53.4 and 54.6 μmol/L. The patient was treated with ornithine aspartate for an injection of 10 g every day. Ornithine aspartate may provide the substrate for the synthesis of urea and glutamine. Glutamine is the detoxification product of ammonia and the storage and transportation form of ammonia. Ornithine involves the activation of the urea cycle and the entire process of ammonia detoxification. Aseptic acid synthesizes nucleic acid in hepatocytes to facilitate the repair of damaged hepatocytes.[23] L-carnitine may treat hyperammonia by VPA, but there is no standard for treating VPA toxicity.[24] Some literature reported that meropenem was used to treat VPA overdose,[25] because meropenem significantly reduced VPA plasma drug concentration by inhibiting acyl peptide hydrolase, preventing reabsorption of VPA metabolites and leading to increased elimination.[25,26] However, because of some management reasons, meropenem cannot be used for outpatients and non-infected patients.

The first-line treatment for acute poisoning by VPA is to enhance excretion of the drug. Apart from using HP, CRRT, and gastric lavage, drug excretion can also be achieved by increasing blood volume and urine flow. In Case 1, infusion volume was expanded to increase blood volume, whereas in Case 3, furosemide was administered to enhance drug elimination. Hypokalemia is a common occurrence during acute drug poisoning. In Case 1, low blood potassium levels were observed during hospitalization and treated with potassium chloride.

4 | CONCLUSION

Acute poisoning by VPA often results from the ingestion of a single large dose. To prevent VPA poisoning, it is recommended to consider the following strategies. Reasonable storage of medication should be considered to prevent non-patients and children from accidentally consuming drugs. Additionally, for long-term use of VPA in antiepileptic and antipsychotic patients, physicians should avoid prescribing large amounts of medication at one time to prevent patients from potentially misusing VPA drugs to commit suicide, particularly if their depression is poorly controlled.

Acute VPA poisoning often damages organs, causes physiological dysfunction, and cause death. Monitoring the patient's blood concentration based on age, dosage,

discovery time, absorption, and renal function can guide the elimination of acute VPA poisoning and add symptomatic drugs to eliminate adverse reactions caused by VPA while using HP and CRRT.

AUTHOR CONTRIBUTIONS

Renzhu Liu: Conceptualization; writing – original draft. **Lu Xiao:** Methodology; writing – review and editing. **Yixiang Hu:** Data curation; software. **Qingzi Yan:** Investigation; visualization. **Xiang Liu:** Methodology; writing – review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The original data presented in the study are included in the article, and further queries can be directed to the corresponding authors.

INSTITUTIONAL REVIEW BOARD STATEMENT

Ethical approval was not required as this was a case report. Therefore, the Ethics Committee of Xiangtan Central Hospital waived the need for ethical approval.

CONSENT

Written informed consent has been obtained from the patient to publish this paper.

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REFERENCES

1. Romoli M, Mazzocchetti P, D'Alonzo R, et al. Valproic acid and epilepsy: from molecular mechanisms to clinical evidences. *Curr Neuropharmacol*. 2019;17(10):926-946.
2. Nelson SE, Varelas PN. Status epilepticus, refractory status epilepticus, and super-refractory status epilepticus. *Continuum (Minneap Minn)*. 2018;24(6):1683-1707.
3. Ascoli M, Mastroianni G, Gasparini S, et al. Diagnostic and therapeutic approach to drug-resistant juvenile myoclonic epilepsy. *Expert Rev Neurother*. 2021;21(11):1265-1273.
4. Yatham LN, Chakrabarty T, Bond DJ, et al. Canadian network for mood and anxiety treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations. *Bipolar Disord*. 2021;23(8):767-788.
5. Woo YS, Bahk WM, Jeong JH, et al. Korean medication algorithm project for bipolar disorder 2022, fifth revision: an executive summary. *Clin Psychopharmacol Neurosci*. 2022;20(4):747-761.
6. von Brevern M, Lempert T. Vestibular migraine: treatment and prognosis. *Semin Neurol*. 2020;40(1):83-86.
7. Hiemke C, Bergemann N, Clement HW, et al. Consensus guidelines for therapeutic drug monitoring in Neuropsychopharmacology: update 2017. *Pharmacopsychiatry*. 2018;51(1–02):e1.
8. Safdar A, Ismail F. A comprehensive review on pharmacological applications and drug-induced toxicity of valproic acid. *Saudi Pharm J*. 2023;31(2):265-278.
9. Ghannoum M, Laliberte M, Nolin TD, et al. Extracorporeal treatment for valproic acid poisoning: systematic review and recommendations from the EXTRIP workgroup. *Clin Toxicol (Phila)*. 2015;53(5):454-465.
10. Patel J, Berezowski I, Mazer-Amirshahi M, Frasure SE, Tran QK, Pourmand A. Valproic acid overdose: case report and literature review. *J Emerg Med*. 2022;63(5):651-655.
11. Cunningham D, Clark K, Lord K. Treatment of valproic acid overdose with meropenem in an epileptic patient. *Am J Emerg Med*. 2022;53:281-284.
12. Haymond J, Ensom MH. Does valproic acid warrant therapeutic drug monitoring in bipolar affective disorder? *Ther Drug Monit*. 2010;32(1):19-29.
13. Dupuis RE, Lichtman SN, Pollack GM. Acute valproic acid overdose. Clinical course and pharmacokinetic disposition of valproic acid and metabolites. *Drug Saf*. 1990;5(1):65-71.
14. Feng-jiao H, Ji-hong L, Dun-li T, Zi-ming J. Comparing the toxicity of valproate sodium with divalproex sodium. *Chin J Pharmacovigil*. 2012;9(1):7-8.
15. Patsalos PN, Spencer EP, Berry DJ. Therapeutic drug monitoring of antiepileptic drugs in epilepsy: a 2018 update. *Ther Drug Monit*. 2018;40(5):526-548.
16. Li Y, Tse ML, Gawarammana I, Buckley N, Eddleston M. Systematic review of controlled clinical trials of gastric lavage in acute organophosphorus pesticide poisoning. *Clin Toxicol (Phila)*. 2009;47(3):179-192.
17. U.S. Food and Drug Administration. Valproic acid [EB/OL]. Accessed June, 29, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/018081s070,018082s053lbl.pdf#page=41.
18. Comstock G, Kilgallon K, Wang GS, Bourne D, Blanchette E, Stenson E. Management and associated Toxicokinetics of massive valproic acid ingestion with high flow continuous venovenous hemodiafiltration. *J Med Toxicol*. 2022;18(3):239-242.
19. Al AZ, Yalamanchili P, Gonzalez E. Extracorporeal management of valproic acid toxicity: a case report and review of the literature. *Semin Dial*. 2005;18(1):62-66.
20. Dore M, San JA, Frenette AJ, Williamson D. Clinical importance of monitoring unbound valproic acid concentration in patients with hypoalbuminemia. *Pharmacotherapy*. 2017;37(8):900-907.
21. Guo J, Huo Y, Li F, et al. Impact of gender, albumin, and CYP2C19 polymorphisms on valproic acid in Chinese patients: a population pharmacokinetic model. *J Int Med Res*. 2020;48(8):1220751833.
22. Baddour E, Tewksbury A, Stauner N. Valproic acid-induced hyperammonemia: incidence, clinical significance, and treatment management. *Ment Health Clin*. 2018;8(2):73-77.
23. Pichon C, Nachit M, Gillard J, Vande Velde G, Lanthier N, Leclercq IA. Impact of L-ornithine L-aspartate on non-alcoholic steatohepatitis-associated hyperammonemia and muscle alterations. *Front Nutr*. 2022;9:1051157.
24. Nicholson C, Fowler M, Mullen C, Cunningham B. Evaluation of levocarnitine, lactulose, and combination therapy for the

treatment of valproic acid-induced hyperammonemia in critically ill patients. *Epilepsy Res*. 2021;178:106806.
25. Dreucean D, Beres K, McNierney-Moore A, Gravino D. Use of meropenem to treat valproic acid overdose. *Am J Emerg Med*. 2019;37(11):2120-2125.
26. Wen ZP, Fan SS, Du C, et al. Drug-drug interaction between valproic acid and meropenem: a retrospective analysis of electronic medical records from neurosurgery inpatients. *J Clin Pharm Ther*. 2017;42(2):221-227.

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