Case Report

Lacosamide poisoning improved by hemodialysis

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Background: Lacosamide (LCM) is a third-generation antiepileptic drug that has been proven to be effective and safe, with few side-effects.

Case Presentation: A woman aged in her 20s was transported to our hospital because of decreased consciousness. Many drugs, such as LCM (328 tablets) and perampanel hydrate (81 tablets), were found in her car. Her Glasgow Coma Scale score was 14. She was intubated and managed with mechanical ventilation, and she was treated with activated charcoal. Subsequently, hemodialysis (HD) was initiated due to the appearance of clonic convulsions. After 4 h of HD, no seizures were noted. The patient was weaned from the ventilator 18 h after admission and discharged on day 4. Her blood LCM level was 91.7 μg/mL on admission and 68.1 and 18.3 μg/ml before and after HD, respectively.

Conclusion: Hemodialysis was carried out in this severe case of LCM poisoning and was found to be effective.

Key words: Blood concentration, hemodialysis, lacosamide, poisoning, seizure

INTRODUCTION

LACOSAMIDE (LCM) IS a third-generation antiepileptic drug that has been approved for use in Europe and the United States. Lacosamide inhibits neuronal hyperexcitability by selectively promoting the slow inactivation of sodium channels.[1] Its effective blood concentration is 10–20 μg/ml, but the concentration is usually not measured in clinical practice and the intoxication dose is not specified. Here, we report a case of LCM poisoning in a patient who underwent hemodialysis (HD).

CASE REPORT

A WOMAN AGED in her 20s was transported to our hospital with altered consciousness. She started presenting transient loss of consciousness and seizures 9 months ago, but the cause was not identified.

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The patient's mother found her collapsed in her car and called for emergency services. Additionally, many drug packages were found in her car, and she was transported to our hospital due to suspected acute drug intoxication. Approximately 2 h 20 min had passed from the time she was seen in good health to the time of arrival at our hospital.

On admission, her height was 160 cm, weight was 58.5 kg, blood pressure was 118/88 mmHg, heart rate was 105 b.p.m., respiratory rate was 37/min, body temperature was 34.4°C, SpO2 was 100% (mask 5 L/min), Glasgow Coma Scale score was E4V2M4, and pupils were 6.0 mm/6.0 mm, with rapid light reflex; there were no other relevant findings. Electrocardiography (ECG) findings revealed a heart rate of 96 b.p.m., sinus rhythm, PR interval of 166 ms, QRS width of 100 ms, and QTc of 409 ms. The chest X-ray was normal. With regard to blood gases, 5 L/min of supplementary O_2 was provided, $PaCO_2$ was 44.9 mmHg, PaO_2 was 80.3 mmHg, and HCO_3^- was 21.7 mmol/L. Additionally, her blood pH was 7.353, Base excess BE was −1.0 mmol/L, glucose level was 178 mg/dl, and lactate level was 16.0 mg/dl. Her blood biochemistry was normal.

She had consumed: 328 tablets of 50 mg LCM (i.e., a total of 16,400 mg), 81 tablets of 2 mg perampanel hydrate (PER; i.e., a total of 162 mg), 54 tablets of 4 units of neurotropin, 26 tablets of 100 mg rebamipide, 18 tablets of

100 mg celecoxib, and 2 tablets of 60 mg loxoprofen sodium.

Subsequently, treatment for altered consciousness caused by acute drug intoxication was initiated. A gastric tube was inserted and yellow drug-mixed gastric content was aspirated (Fig. 1). This procedure was followed by gastric lavage and treatment with activated charcoal. Two hours after admission, her consciousness level decreased further (Glasgow Coma Scale score: E1V1M4). Therefore, we decided to intubate her and provide ventilator management in the intensive care unit.

Five hours after the patient's arrival, clonic convulsions appeared, and we initiated intravenous diazepam (5 mg) and continuous intravenous propofol as spasmolytic treatment. Hemodialysis was initiated 6 h after arrival at the hospital. A polysulfone membrane (VPS-18HA; Asahi Kasei Medical Co., Ltd., 1-1-2 Yurakucho, Chiyoda-ku, Tokyo 100-0006 Japan) was used with a 150 ml/min blood flow and a 500 ml/min dialysate flow. Hemodialysis was continued for 4 h under the same conditions. Propofol was discontinued 17 h after arrival. The patient could communicate immediately after discontinuing propofol, and she was weaned from the ventilator 18 h after her admission. On day 4 after psychiatric consultation, the patient was discharged without any seizure relapse or sequelae. We determined her blood LCM levels using the serum stored during her treatment (Fig. 2). After arrival at the hospital, her blood LCM level was 91.7 μg/ml, which was above the upper effective blood concentration limit (20 μg/ml). Six hours after admission, her blood LCM level decreased to 68.1 μg/ml; however, she experienced seizures. A total of 4 h of HD reduced the blood LCM level to 18.3 μg/ml. The LCM level continued to decrease slowly to 10.7 μg/ml 11 h after completing HD.

Fig. 1. Gastric contents of a woman aged in her 20s was transported to our hospital because of decreased consciousness (Glasgow Coma Scale score 14). A yellow drug-mixed liquid (approximately 400 ml) was collected.

DISCUSSION

LACOSAMIDE DOSES ARE adjusted depending on symptoms so that they do not exceed a value of 400 mg per day. It is assumed in this case that the patient took a high dose (16,400 mg [approximately 41 times higher than the upper limit of the usual dose]) of LCM. There have been few reports on LCM poisoning. Five hours after arrival at the hospital, the patient developed clonic convulsions. We could not determine whether the convulsions were caused by LCM or the primary chronic disease. As no seizures had been noticed due to chronic illness recently, we suspected that LCM poisoning might have caused convulsions. However, it remains unclear whether LCM poisoning induces seizures. Blood LCM levels take approximately 1 week to confirm the results of tests performed externally, making it difficult to determine a treatment plan based on blood LCM levels.

Hemodialysis was planned on the appearance of seizures in our patient because it has been reported that approximately 50% of LCM is removed from the systemic circulation by performing HD for 4 h.[2]

Retrospective consideration of the blood LCM level revealed that it was significantly elevated on admission at 91.7 μg/ml, being higher than the upper limit of the effective blood level (20 μg/mL). Six hours after admission, the blood LCM level decreased to 68.1 μg/mL; however, convulsions complicated the condition of the patient. After 4 h of HD, her blood LCM level was 18.3 μg/ml. Hemodialysis significantly reduced blood LCM levels.

The blood concentrations of other drugs (such as PER) taken simultaneously were not measured. Various reports on the prolonged disturbance of consciousness due to PER poisoning exist.[3,4] However, in this case, the effects of PER addiction and other medicines on seizures remain unknown.

In 2010, Bauer *et al.*[5] reported the first case of oral drug intoxication with multiple anticonvulsants, including 12 g LCM. The main symptoms reported were vomiting, convulsions, ECG abnormalities (prolonged PR interval and normal QTc), shock, and coma. The patient was successfully discharged without adverse effects after only ventilator management.

Based on the data from 2008 to 2013, the United States National Poison Data System reported that convulsions due to LCM overdose occurred in 17% of 208 cases, but the prognosis was good.[6] Malissin *et al.*[7] reported the case of a 56-year-old man who experienced cardiac arrest after he attempted suicide with 7 g LCM prescribed for symptomatic

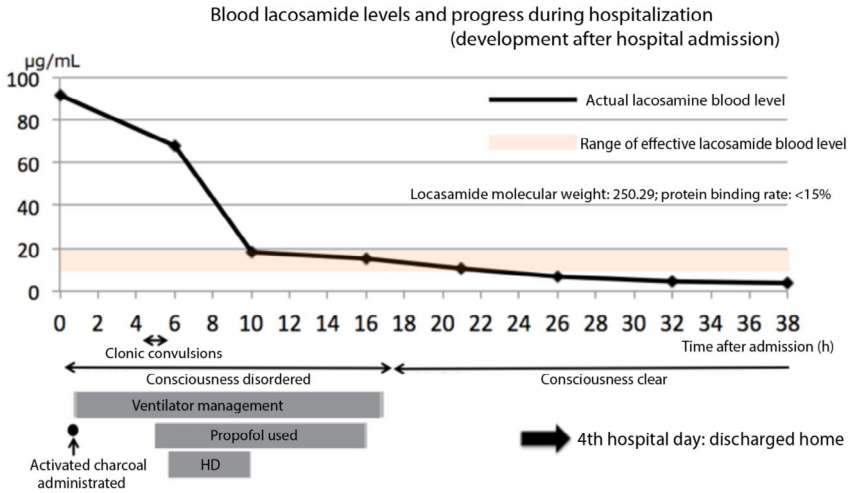

Fig. 2. Blood lacosamide levels during hospitalization of a woman aged in her 20s decreased on treatment with hemodialysis (HD).

epilepsy that occurred after cerebral infarction. Several reports describe the effect of LCM on QTc.[7,8] In our patient, a 12-lead ECG was performed three times, on admission and at 12 and 24 h after admission. The PR interval and QTc were within the normal range. The patient was a young woman and might have been highly tolerant of the drug. We believe it is necessary to pay attention to the occurrence of arrhythmias in cases of LCM poisoning in older patients or patients with a history of heart disease.

CONCLUSION

HEMODIALYSIS SHOULD BE considered in cases of LCM poisoning where there are convulsions or abnormal ECG findings. Hemodialysis was used in this severe case of LCM poisoning, and was found to be effective. However, the patient might have improved without HD, because LCM has a short half-life.

DISCLOSURE

APPROVAL OF THE research protocol: N/A.

Informed consent: The patient's parent provided consent for publication.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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