# Application of Hemodialysis in Rescuing Patients with Lithium Carbonate Poisoning

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**Purpose: Lithium carbonate, as a first-line mood stabilizer, is widely used in clinical practice, but its safety range is narrow, and its toxic dose is very close to the therapeutic dose We successfully saved the life of a patient with lithium carbonate poisoning by using hemodialysis method and reduced the side effects of lithium carbonate poisoning. Methods: The patient is a 42-year-old man. He was admitted to hospital because of "speech disorder, unsteady walking, incontinence of bowel and stool for 1 day". During this process, we used hemodialysis therapy. Results: After 11 days therapy, the patient was able to speak fluently and move moderately with help. After 22 days therapy, the patient was able to walk almost independently, and the blood lithium-ion level returned to normal. Conclusion: This paper reports the treatment of a case of lithium carbonate poisoning due to s aphasia, unsteady walking, fecal and urinary incontinence, providing reference for the clinical diagnosis and treatment of chronic poisoning with lithium carbonate drugs whose toxic dose is similar to the therapeutic dose for a long time.**

**Key words: lithium carbonate, side effect, aphasia, fecal and urinary incontinence, hemodialysis**
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Therapeutic dose and toxic dose of lithium carbonate is close[1,2]. Lithium carbonate is easy to damage the nervous system, urinary system, endocrine system, gastrointestinal system and so on, and even lead to lithium poisoning. Adverse reactions include dizziness, nausea and fatigue, muscle weakness, hand fibrillation, thirst and polyuria[3]. Encephalopathy syndrome occurs when poisoning, which is manifested as fuzzy consciousness, epileptic seizure and even coma, shock and renal failure.

At present, lithium carbonate combined with other antipsychotic drugs is often used in clinical treatment of mania, and the concentration of lithium in blood is often tested during the treatment to ensure the safety of medication[4-6].

There were no reports of side effects such as aphasia and incontinence of urine and excrement have not been reported in patients with lithium carbonate poisoning treated with hemodialysis in the early stage [7].

## CASE DATA

The patient is male and 42 years old. The patient was admitted due to "aphasia,,unstable walking, fecal and urinary incontinence for 1 day" on December 6, 2018.One day ago, the patient experienced slurred speech, unstable walking, falling from bed, trembling hands, fecal and urinary incontinence and other symptoms. On inquiry of medical history,

the patient was previously diagnosed with "bipolar disorder", and developed depressed mood, diminished interest, and decreased activity without obvious inducement 5 days ago. The patient bought the drug online, and orally took "Lithium Carbonate Tablets 1.0g Tid" for 4 days. Past medical history: the patient had a history of bipolar disorder for 15 years; the patient denied a history of hypertension, diabetes, coronary heart disease, hepatitis, tuberculosis and other infectious diseases; denied a history of blood transfusion, surgery, major trauma; denied a history of food and drug allergy. Personal history and marriage and childbearing history were unremarkable. Family history: The mother had a history of depression and was currently on medication with stable condition.

Nervous system: hazy consciousness, miosis, diameter 2 mm, presence of light reflex, gaze of both eyes, limited eye movement, inability to abduct and adduct, diplopia, no horizontal nystagmus and vertical nystagmus, significantly increased muscle tension of four extremities, refractor shape, tendon hyperreflexia, pathological signs were not elicited, and the rest could not cooperate.

Mental examination: hazy consciousness, uneven clothes, pushed by the family members into the ward by the flat car, can understand simple commands but can not speak, mostly nodding and shaking their heads. Auxiliary examination: lithium 18.10 mmol/L, glutamyl transpeptidase 66 U/L, creatinine 106.9 μmol/L, chloride 96.9 mmol/L, sodium 131.0 mmol/L. Electrocardiogram: sinus rhythm, 109 beats/min, QTC487 ms.

Diagnosis

Acute lithium carbonate poisoning. Diagnosis and treatment process: the patient was seriously ill, re-measurement of blood lithium concentration was 19.88 mmol/L, and the patient underwent the first hemodialysis treatment under local anesthesia on December 7, and was safely removed from the machine. Reexamination of blood lithium concentration was 6.74 mmol/L, the patient had delirium, limited eye movement, could not open mouth to eat, could not speak, significantly increased limb muscle tension, and could not move the trunk and limbs.

On December 8, the patient received hemodialysis for the second time, and re-examination showed lithium blood concentration of 1.29 mmol/L, the patient had hazy consciousness, limited eye movement, could not open mouth to eat, could not speak, significantly increased muscle tension of four extremities, and could not move trunk and four extremities. Meanwhile, the patient showed fever, T: 39℃; blood routine: C-reactive protein (CRP): 56.5 mg/L, lymphocyte: 0.083, absolute lymphocyte: 0.73 × 10 ^ 9/L, neutrophil: 0.848, absolute neutrophil: 7.46 × 10 ^ 9/L. Chest radiography: patchy high density shadow in the field under the left lung, inflammation? Aspiration pneumonia was considered, and symptomatic and supportive treatment such as expectorant therapy and potassium supplement and fluid replacement was given. On December 9, the patient received hemodialysis for the third time, and re-examination showed lithium blood concentration of 0.49 mmol/L. The patient had clear consciousness than before, with slight eye movement, could not open mouth to eat, could not speak, and the increased muscle tension of four extremities was slightly alleviated than before, and could not move.

Indwelling gastric tube + nasogastric feeding diet and indwelling catheter were prescribed by the doctor. On December 10, reexamination of blood lithium concentration showed 0.25 mmol/L.

During ward round, the patient had clear consciousness, more flexible eye movement, mouth opening and tongue extension, but could not speak. The increased muscle tension of four extremities was relieved than before, and the patient was still bedridden and could not walk. On December 12, the blood lithium concentration was 0.26 mmol/L after reexamination. During ward round, the patient had clear consciousness, flexible eye movement, liquid diet, vague words, reduced increased limb muscle tension than before, and could turn over, but could not walk.

During ward round on December 14, the patient had clear consciousness, could eat rice porridge and bread, could not spit clearly, complained of general weakness, significantly reduced increased limb muscle tension compared with admission, and could get out of bed with the help of his family for a few steps, and the stomach tube was pulled out according to the doctor's advice. On December 16, reexamination of blood lithium concentration showed 0.27 mmol/L. During ward round, the patient had clear consciousness, passive contact, appropriate questions and answers, less fluent speech, slightly higher limb muscle tension, good diet and sleep, normal urine and defecation. The doctor ordered to stop the disease and remove the urinary catheter. During ward round on December 18, the patient had good appetite and sleep, slightly higher muscle tension of four extremities, requiring assistance when walking, unstable gait and slow movement. On December 20, during ward round, the patient had clear speech, complained of generalized weakness, normal muscle tension of four extremities, could walk with the assistance of carers, and had stable gait.

On December 28, reexamination of blood lithium concentration was 0.23 mmol/L. During ward round, the patient had normal appetite during sleep and no abnormality in urination and defecation. The consciousness was clear, the expression was natural, the questions and answers were appropriate, the speech was fluent, the patient still complained of generalized weakness, and the patient could basically walk independently. The patient's symptoms of lithium poisoning were gradually controlled, and he was discharged automatically from the hospital 23 days after hospitalization at the strong request of his family and changed to outpatient treatment.

## DISCUSSION

Lithium ions are rapidly absorbed almost completely from the gastrointestinal tract, distributed in systemic fluids after absorption, and excreted by the kidneys[8-11]. The half-life of lithium is 12 to 17 hours in adults and up to 2 days in the elderly with decreased renal function or long-term lithium therapy[12].

The package insert recommends 0.25 g twice daily orally, which can be increased to 0.5 g twice daily if necessary. In this case, the patient orally took lithium carbonate 1.0 g three times daily for four consecutive days, which was severely excessive and easily led to accumulation of plasma concentration and poisoning events. The gap between therapeutic and toxic doses of lithium is relatively narrow, so routine blood and clinical monitoring is very important[13-16].

In addition, toxicity occurring close to or within the therapeutic serum lithium concentration range is a known risk. Failure to detect early signs of intoxication may delay treatment, lead to poor prognosis for the patient and, in the most severe cases, death[17,18].

Blood lithium levels ranged from 1.5 to 2.0 mmol/L in mild poisoning, 2.1 to 2.5 mmol/L in moderate poisoning, and ≥ 2.6 mmol/L in severe poisoning. The clinical symptoms of lithium intoxication are graded as follows: Grade 0: no symptoms; Grade 1: nausea, vomiting or tremor, tendon hyperreflexia, muscle weakness or ataxia, and patients with only somnolence are also classified as Grade 1; Grade 2: including stupor, rigidity, hypermyotonia, and hypotension; Grade 3: patients with coma, seizures, clonus, and severe cardiovascular symptoms (hypotension, arrhythmias), and creatinine above the normal range. In this case, the blood lithium level was 19.88 mmol/L, rarely increased.

The clinical toxic symptoms are very obvious, mainly including hazy consciousness, diplopia, limited eye movement, unfavorable speech, dysphagia, high muscle tension of four extremities, tremor of hand tremor, ataxia and fecal and urinary incontinence, with severity of grade 2, which may be life-threatening.

The relationship between blood lithium concentration and clinical manifestations of lithium poisoning may be related to the rate of increase in blood lithium concentration. Their data show that chronic poisoning is more severe than acute poisoning symptoms at the same blood lithium level[19]. It is found that lithium can be explained by the kinetic characteristics of lithium.

Lithium is absorbed in the upper gastrointestinal tract for about 8 hours, and the time to peak oral administration is 1 ~ 2 hours; the penetration rate of lithium through the blood-brain barrier is lower than that of other tissues of the body; the distribution of lithium is 24 hours slower than that of plasma. Therefore, the blood lithium concentration can be very high in acute lithium poisoning but the clinical symptoms are mild; on the contrary, the lithium concentration in patients with chronic poisoning has a sufficient development time, so neurological toxicity can occur with moderate blood lithium levels. This may explain why this patient had an abnormally high lithium level and a grade 2 severity.

At present, there is no special antidote for lithium poisoning, and management measures should immediately discontinue and remove excessive lithium, such as gastric lavage, infusion, correction of dehydration, and maintenance of fluid and electrolyte balance[12]. Lithium ions are very small and only 10% protein bound, so they are very suitable for hemodialysis treatment, and this method can remove about 90% of lithium from the blood circulation[19-23].

Hemodialysis should be performed as early as possible in patients who meet the treatment indications, and the specific criteria include: (1) clinical conditions: (complex symptoms, older age, electrolyte balance disorders, and poor cardiovascular conditions); (2) chronic overdose with acute poisoning; (3) manifestations of decreased lithium excretion: (renal insufficiency, congestive heart failure); (4) lithium blood level: in view of the risk of death or permanent neurological damage in 10% of patients with lithium poisoning, hemodialysis should be performed in all patients with lithium > 6 mmol/L; hemodialysis is recommended in patients with acute poisoning who take lithium for a long time, and lithium blood level > 4 mmol/L; lithium blood > 2.5 mmol/L, accompanied by renal failure, congestive heart failure, and hemodynamic instability, suggests the need for hemodialysis; hemodialysis should be

performed in patients with continued increase in lithium blood level (common in lithium sustained-release poisoning)[24].

In this case, the blood lithium concentration was more than 20 times beyond the normal range, and hemodialysis treatment was the best choice, which proved to be effective, and the blood lithium concentration quickly decreased to the normal range through three consecutive hemodialysis sessions.

Early hemodialysis treatment can rapidly reduce the drug concentration in the blood[20], but the improvement of clinical symptoms is not parallel to the level of plasma concentration reduction, usually lagging behind the change of plasma concentration, especially the symptoms of increased muscle tension and nervous system.

After three times of hemodialysis treatment, the patient's blood lithium concentration dropped to normal on December 9, 2018, and then the consciousness gradually became clear, with visible eye movements; 1 day later, the patient could open the mouth and stretch the tongue. 3 days later, the patient could eat liquid food, spit vaguely and turn over. 5 days later, the patient could eat normally, barely get out of bed with support. 7 days later, the speech was less fluent, and the patient could defecate spontaneously. 9 days later, the patient could move a small amount with assistance, had unstable gait. 11 days later, the speech was fluent, and the patient could move an appropriate amount with help. 22 days later, the patient could basically walk independently.

Lithium blood concentrations often "rebound" after hemodialysis in patients with lithium carbonate poisoning, so daily monitoring of plasma concentrations is required, and continuous daily hemodialysis can continuously remove lithium blood and avoid another increase. In this case, the patient had no "rebound" symptom by closely monitoring the change of blood lithium concentration. When the concentration of lithium ion in the blood reaches 0.25 mmol/L, the patient can open the mouth and extend the tongue (lingual nerve and facial nerve recovery); When the concentration of lithium ion in the blood reaches 0.26 mmol/L, the patient can take liquid food through the mouth, speak vaguely, and turn over (recovery of upper limb strength); When the concentration of lithium ion in the blood reaches 0.27 mmol/L, the patient can pass urine and feces autonomously.

When the lithium ion concentration in the blood reached 0.23 mmol/L, the patient was able to walk independently.

**Table 1**
**Changes in the blood concentration of lithium and clinical symptoms**

| Date | Blood lithium concentration (mmol/L) | Symptom change |
|---|---|---|
| **12-06(Before 1st dialysis )** | 19.88 | Haziness |
| **12-07(Before 2nd dialysis )** | 6.74 | Haziness |
| **12-08(before the 3rd dialysis)** | 1.29 | Haziness |
| **12-09(After the 3rd dialysis)** | 0.49 | The consciousness gradually became clear, and eye moveme was observed (oculomotor nerve recovery) |
| **10-Dec** | 0.25 | Tongue extension with mouth opening (recovery of lingual n and facial nerve) |
| **12-Dec** | 0.26 | Liquid diet via mouth, slurred speech, can turn over (recover upper limb muscle strength) |
| **14-Dec** | --- | Eat normally and get out of bed with support |
| **16-Dec** | 0.27 | Spontaneous defecation |
| **18-Dec** | --- | Walking requires support, slow movement (recovery of lowe limb muscle strength) |
| **20-Dec** | --- | Fluent in speech and assist with moderate activities |
| **28-Dec** | 0.23 | Able to walk independently |

## CONCLUSION

Hemodialysis is very good at addressing the aphasia, unsteady walking, fecal and urinary incontinence associated with adverse drug reactions in patients with lithium carbonate poisoning. It is worthy of early clinical application.

Lithium carbonate, as a first-line mood stabilizer, is widely used in clinical practice, but the safety margin is narrow, in which the toxic dose is very close to the therapeutic dose.

Lithium ion levels in the blood declined over time and the patient's symptom changes returned to normal (Table 1)

Early continuous hemodialysis in patients with Early continuous hemodialysis in patients with severe lithium carbonate poisoning can improve the success rate of rescue, and the blood lithium concentration often increases again after hemodialysis. Clinicians need to closely monitor the dynamic changes of plasma concentration.

This paper reports the treatment of a case of lithium carbonate poisoning due to s aphasia, unsteady walking, fecal and urinary incontinence, providing reference for the clinical diagnosis and treatment of chronic poisoning with lithium carbonate drugs whose toxic dose is similar to the therapeutic dose for a long time.

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**Authors' contributions**

X Chen, CQ Ai, CH Wang and H Gao attended to the patient. X Chen wrote the manuscript. Q Sun, X Wang, ZC Liu, L Pan, LZ Liu and HM Chen gave conceptual advice. All authors read and approved the final manuscript.

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**Availability of data and materials**

The datasets analyzed in this case report are available from the corresponding author on request.

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Competing interests**

The authors declare that they have no competing interests.

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