

Grand Mal Seizure After Hemodialysis for Acute-On-Chronic Lithium Intoxication

Huib van Dijk*, Neuteboom O, Hendrix MRS and Kamps MJA

Intensive Care Unit, Catharina Ziekenhuis Eindhoven, Michelangelolaan 2, 5623 EJ, Eindhoven, the Netherlands

*Corresponding author: Huib van Dijk, MD, Intensive Care Unit, Catharina Ziekenhuis Eindhoven, Michelangelolaan 2, 5623 EJ, Eindhoven, the Netherlands

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Abstract

A 55-year-old female patient with a history of bipolar disorder, for which she uses mirtazapine and lithium, presented with severe lithium intoxication for which hemodialysis was started. During hemodialysis the patient suffered a grand mal seizure most likely due to the rapid decline of the lithium plasma level. Grand mal seizures are described as a possible complication of hemodialysis, which is a life-threatening complication. Although, hemodialysis is described as the first line treatment of a severe lithium intoxication.

With this case and literature study we would like to emphasize the consideration of hyperhydration without hemodialysis in case of a severe acute-on-chronic lithium intoxication in the absence of severe life-threatening neurological symptoms.

Keywords: Lithium intoxication; Hemodialysis; Grand mal seizure

Introduction

Lithium is commonly used for bipolar disorder (30.000 users in the Netherlands in 2021) [1] and has a high risk of toxicity due to the small therapeutic range. The Dutch poisoning information center (NVIC) reported 552 consultations for lithium intoxication in 2022, but the exact number of lithium intoxications leading to hospital presentation or admission is unknown [2]. There are different types of lithium intoxication: acute, acute-on-chronic and chronic. The treatment for severe lithium intoxication is hemodialysis and hyperfiltration [3]. This case report illustrates that hemodialysis should be initiated with caution, since rare but life-threatening complications can occur.

Case Report

A 55-year-old female patient with a history of bipolar disorder, for which she uses mirtazapine and lithium, presented with tremors, weakness and reduced consciousness to the emergency room. She reported a feeling of malaise, coughing, sneezing, sweating and reduced intake in the days before presentation.

On physical examination she showed a tachycardia (110 beats per minute), hypertension (160 / 95 mmHg), a fever of 38.1 degrees Celsius and a normal oxygenation saturation and respiratory rate. Glasgow Coma Score (GCS) was 12 (E3M6V3), responding only with "yes" and "no". Furthermore, she had hypertonia of the muscles and generalized tremors.

Laboratory testing was performed, with a creatinine of 99 $\mu\text{mol/L}$, sodium of 139 mmol/L hypophosphatemia of 0.39

mmol/L and an elevated lithium concentration of 2.64 mmol/L . Her lithium concentration 6 weeks prior in regular follow-up was 0.82 mmol/L , with a creatinine of 74 $\mu\text{mol/L}$. The electrocardiogram (ECG) presented sinus tachycardia, elongated QTc time of 580 milliseconds with no signs of ischemia.

In conclusion we saw a patient on chronic lithium use with a symptomatic acute-on-chronic lithium intoxication due to acute kidney injury most likely caused by dehydration

The patient was admitted to the Intensive Care Unit for hemodynamic monitoring and treatment, that consisted of fluid and phosphate supplementation. The myoclonus and reduced consciousness were considered to be signs of a severe intoxication and the patient was treated with intermitted hemodialysis. Thirty minutes after hemodialysis was started the patient rapidly deteriorated. The patient was tachypneic (40-50 breaths per minute) with hypoxemia (peripheral oxygen saturation 80-85%), tachycardic (140 beats per minute) with hypertension (165 / 65 mmHg) and unresponsive. Blood testing showed elevated lactate concentration of 18 mmol/L and hypokalemia of 2.8 mmol/L .

After sedation, intubation and termination of hemodialysis the patient stabilized. Point of care ultrasound showed normal left and right ventricular function, a non-collapsible vena cava and no free fluid in the abdomen. There was no clinical suspicion of sepsis, hypovolemia or cardiac failure. Lactate levels completely normalized after one hour. Within 13 hours the sedation could be stopped, and patient was extubated. The serum lith-

ium levels at that moment were 1.3 mmol/L. In retrospect the patient most likely suffered a grand mal seizure, which terminated with the sedatives that were given to facilitate intubation.

Discussion

Lithium is a small cation and acts similar like sodium. Lithium is almost completely absorbed after oral administration [5]. Like potassium, intracellular concentrations are higher than extracellular concentrations. It distributes widely in total body water and accumulates in the kidney, bones, thyroid and certain areas of the brain [6,7].

Lithium does not bind to serum proteins and is excreted unchanged by the glomerulus for 89-98% [8]. Just like sodium, lithium is reabsorbed for 70-80% by the proximal tubule and by the thick ascending limb of the loop of Henle [4]. Volume depletion and diuretics will increase proximal tubule reabsorption of sodium and lithium and therefore cause toxic lithium concentrations in the blood [4]. Normally, the half-life of lithium is 12-27 hours. However, it can be up to 58 hours in older patients, patients with renal dysfunctions or chronic lithium users [4]. Three types of lithium intoxication are distinguished: acute poisoning (in a lithium-naive patient), acute-on-chronic and chronic poisoning (in a patient already on a daily dose of lithium). Symptoms are mostly gastro-intestinal (nausea, vomiting) and neurological (tremors, confusion, agitation). Severe symptoms like coma, seizures, hypotension and arrhythmias have been described. Due to slow diffusion of lithium into the central nervous system (up to 24 hours) gastro-intestinal symptoms usually precede neurological symptoms in acute poisoning. The neurological symptoms can occur at lower lithium levels in acute-on-chronic or chronic poisoning, because of the already increased lithium level in the central nervous system [9]. Symptoms can even occur at normal or slightly increased lithium levels, especially in chronic poisoning. For supportive measures stopping the lithium, whole bowel irrigation (activated charcoal is not useful) and volume resuscitation (in case of volume depletion due to gastro-intestinal or renal losses) are suggested.

Hemodialysis (HD) or Continuous Renal Replacement Therapy (CRRT) has long been recommended for severe lithium intoxication.

Hemodialysis uses the concentration gradient between the blood and a dialysate in counter-current flow over a semi-permeable membrane to excrete waste products and toxins via diffusion. CRRT uses hydrostatic pressure over a filter to achieve the same effect via convection.

Due to its low molecular weight, predominant renal excretion, absence of metabolism, good solubility in water and lack of binding to plasma proteins, hemodialysis is an effective way of reducing lithium levels. Lithium clearance up to 106.9 ml/min can be reached via hemodialysis (with a reduction of 1 mEq/L per 4 hours of hemodialysis) [10], compared to 10.6 ml/min via endogenous renal clearance and 43.1 ml/min via CRRT [4]. A rebound effect of distribution from the tissues to the plasma can occur.

In the literature diverse indications for hemodialysis have been described, ranging from criteria purely based on symptoms, blood levels and a combination of both. Evidence-based consensus recommendations of the Extracorporeal Treatments in

Poisoning (EXTRIP) Workgroup recommended hemodialysis with a) impaired kidney function and a lithium level > 4.0 mEq/L, b) the presence of a decreased level of consciousness, seizures or life-threatening dysrhythmias and suggested hemodialysis in case of c) a lithium level > 5.0 mEq/L, d) significant confusion, e) or the expected time to reduce lithium level < 1 mEq/L is > 36 hours [4]. Later retrospective analyses suggested that the EXTRIP criteria are too broad and created narrower criteria (a lithium level > 5.2 or a creatinine level > 200 µmol/L) [11] or created different criteria for chronic toxicity and acute-on-chronic poisoning [12].

Earlier case reports have described both cerebral seizures as a complication of hemodialysis for lithium intoxication and progressive encephalopathy and unresponsiveness after starting peritoneal dialysis for lithium intoxication [13,14]. Gradual onset of encephalopathy during hospital admission after stopping lithium has been described as well [5]. A clear pathophysiological cause of the seizures has not been described. An analogy to the neurological symptoms of osmotic demyelination in too rapid correction of chronic hyponatremia has been made, with high lithium levels leading to intraneuronal hyponatremia and thus the lithium removal to correction of this unmeasurable intraneuronal hyponatremia [15].

Our patient presumably suffered a grand mal seizure after starting hemodialysis for an acute-on-chronic lithium intoxication. Although the literature is scarce and there is no clear physiological mechanism, after this literature study we think that in this case hyperhydration should have been given and hemodialysis should only be considered after failure of hyperhydration or with severe life-threatening neurological symptoms.

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References

1. Zorginstituut Nederland. Het aantal Gebruikers van anti-psychoptica, 2003 - 2022 | gipdatabank.nl. GIPdatabank.nl.
2. Nugteren-van Lonkhuyzen JJ, Mulder-Spijkerboer HN, van Velzen AG. NVIC Jaaroverzicht 2021, 2023. <https://nvc.umcutrecht.nl/nl/jaaroverzichten>.
3. Perrone J, Mudan A. Lithium poisoning, 2022.
4. Decker BS, Goldfarb DS, Dargan PI, Friesen M, Gosselin S, Hoffman RS, et al. Extracorporeal treatment for lithium poisoning. *Clinical Journal of the American Society of Nephrology*, 2015; 10(5): 875-887. <https://doi.org/10.2215/cjn.10021014>
5. Oruch R, Elderbi MA, Khattab HA, Pryme IF, Lund A. Lithium: A review of Pharmacology, clinical uses, and toxicity. *European Journal of Pharmacology*, 2014; 740: 464-473. <https://doi.org/10.1016/j.ejphar.2014.06.042>
6. KNMP. Lithium. In *Informatarium Medicamentorum*, 2023; (53rd ed.).
7. Okusa MD, Crystal LJ. Clinical manifestations and management of acute lithium intoxication. *The American Journal of Medicine*, 1994; 97(4): 383-389. [https://doi.org/10.1016/0002-9343\(94\)90308-5](https://doi.org/10.1016/0002-9343(94)90308-5)
8. Sombogaard F, van Berlo-van de Laar IRF, Shak Shie M, Touw DJ. Monografieën. TDM Monografie, 2014.
9. Hansen HE, Amdisen A. Lithium intoxication (report of 23 cases and review of 100 cases from the literature). *QJM: An International Journal of Medicine*, 1978. <https://doi.org/10.1093/oxfordjournals.qjmed.a067533>

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10. Timmer RT, Sands JM. Lithium intoxication. *Journal of the American Society of Nephrology*, 1999; 10(3): 666–674. <https://doi.org/10.1681/asn.v10i3666>
11. Vodovar D, Beaune S, Langrand J, Vicaut E, Labat L, Mégarbane B. Assessment of extracorporeal treatments in poisoning criteria for the decision of extracorporeal toxin removal in lithium poisoning. *British Journal of Clinical Pharmacology*, 2019; 86(3): 560–568. <https://doi.org/10.1111/bcp.14087>
12. Buckley NA, Cheng S, Isoardi K, Chiew AL, Siu W, Vercellio E, et al. Haemodialysis for lithium poisoning: Translating EXTRIP recommendations into practical guidelines. *British Journal of Clinical Pharmacology*, 2020; 86(5): 999–1006. <https://doi.org/10.1111/bcp.14212>