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Lithium poisoning: A case report

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Abstract

Introduction: Lithium is a mood-stabilizing drug, mainly used for the treatment of bipolar affective disorder, with a narrow therapeutic range that facilitates intoxication, being an important cause of morbidity and mortality.
Case report: A 66-year-old male patient with a history of diabetes mellitus, arterial hypertension, chronic renal insufficiency and heart failure, under chronic treatment with lithium carbonate for bipolar affective disorder, consulted the emergency department for progressive neurological deterioration secondary to lithium intoxication, elevated lithemia (1.76 mEq/L) was identified and other causes of neurological deterioration were ruled out. The patient evolved favorably after discontinuation of the drug and use of hemodialysis.
Conclusion: Lithium intoxication should be suspected in patients with chronic use of the drug attending the emergency department for neurological symptoms, drug discontinuation, hydroelectrolytic correction and hemodialysis in indicated cases are the treatment of choice.
Keywords: lithium; lithium compounds; poisoning

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Intoxicación por litio: a propósito de un caso

Resumen

Introducción: El litio es un medicamento estabilizador del ánimo, utilizado de forma principal para el tratamiento del trastorno afectivo bipolar y cuenta con una ventana terapéutica estrecha que facilita cuadros de intoxicación, lo cual es una causa importante de morbilidad y mortalidad.

Caso clínico: Hombre de 66 años con antecedente de diabetes mellitus, hipertensión arterial, insuficiencia renal crónica y falla cardiaca, en tratamiento crónico con carbonato de litio por trastorno afectivo bipolar. Consultó a urgencias por un deterioro neurológico progresivo secundario a intoxicación por litio. Se identificó litemia elevada (1,76 mEq/L) y se descartaron otras causas de deterioro neurológico. El paciente evolucionó de modo favorable posterior a la suspensión del medicamento y el uso de hemodiálisis.

Conclusión: La intoxicación por litio debe sospecharse en pacientes con uso crónico del medicamento que asisten a urgencias por síntomas neurológicos. La suspensión del medicamento, la corrección hidroelectrolítica y la hemodiálisis en casos indicados son el tratamiento de elección.

Palabras clave: litio; compuestos de litio; intoxicación.

Intoxicação por lítio: a propósito de um caso

Resumo

Introdução: O lítio é um medicamento estabilizador do humor, usado principalmente no tratamento do transtorno afetivo bipolar, e possui uma janela terapêutica estreita que facilita quadros de intoxicação, o que é uma causa importante de morbidade e mortalidade.

Caso clínico: Homem de 66 anos com histórico de diabetes mellitus, hipertensão arterial, insuficiência renal crônica e insuficiência cardíaca, em tratamento crônico com carbonato de lítio para transtorno afetivo bipolar. Ele procurou atendimento de emergência devido a um deterioro neurológico progressivo secundário a intoxicação por lítio. Foi identificada uma litemia elevada (1,76 mEq/L) e outras causas de deterioro neurológico foram descartadas. O paciente evoluiu favoravelmente após a suspensão do medicamento e o uso de hemodiálise.

Conclusão: A intoxicação por lítio deve ser suspeitada em pacientes em uso crônico do medicamento que procuram atendimento de emergência devido a sintomas neurológicos. A suspensão do medicamento, a correção hidroeletrolítica e a hemodiálise nos casos indicados são o tratamento de escolha.

Palavras-chave: lítio; compostos de lítio; intoxicação.

INTRODUCTION

Lithium poisoning is a significant cause of morbidity, mortality, and increased costs for healthcare systems (1). From December 2001 to March 2017, 1914 cases of adverse reactions to lithium were reported in older adults in Europe, accounting for 21.8% of the total cases in which medical prescriptions containing lithium were prescribed. Similar data were documented in the United States, with 22.7%, and in Canada, with 26.2% (2). In Colombia, there are no epidemiological data on the frequency of this type of poisoning (3). Since the 1940s, lithium has been the treatment of choice for Bipolar Affective Disorder (BAD) (4,5), being effective in counteracting depressive and manic episodes and reducing the risk of suicide (6). Its mechanism of action is not fully elucidated. Still, it is believed that its mood-stabilizing effect involves the modulation of neurotransmitters such as serotonin and norepinephrine, regulation of intracellular calcium, neuroprotection, influence on synaptic density and function, as well as its activity on cell signaling proteins (6-8). Together, these effects may contribute to its ability to prevent manic and depressive episodes in individuals with BAD (7).

Lithium has a narrow therapeutic window, with a therapeutic range of 0.6 to 1.2 mEq/L, and is sensitive to modest changes in renal function (6,7,9); hence, symptoms of intoxication occur with levels higher than 1.5 mEq/L (7). The initial symptoms of intoxication include nausea, vomiting, diarrhea, muscle weakness, intense tremors, muscle spasms, ataxia, dysarthria, and drowsiness (6,8). Late intoxication symptoms include excitement, hypertonia, fasciculations, hyperreflexia, nystagmus, seizures, loss of consciousness, and oliguria or anuria (8). In cases of severe intoxication, hemodialysis is required (10), and a delay in diagnosis can lead to death (6,8,10). This case presentation aims to describe the clinical evolution, diagnosis, and treatment of a patient with lithium poisoning at a high-complexity hospital in Popayán, in the department of Cauca, Colombia. Informed consent was obtained from the patient to allow for case documentation.

CASE PRESENTATION

The case involves a 66-year-old man with a history of BAD treated with *carbonato de litio* (300 mg orally every 8 hours for the past 4 years), type 2 diabetes mellitus with diabetic nephropathy managed with *vildagliptin/metformin* (50/1000 mg orally once a day), arterial hypertension, heart failure secondary to ischemic-valvular heart disease with a left ventricular ejection fraction of 25%, moderate to severe mitral insufficiency, and moderate tricuspid insufficiency under management (with *carvedilol* 6.25 mg orally once a day), *furosemide* (40 mg orally once a day), *acetylsalicylic acid* (100 mg orally once a day),

and *Spironolactone* (25 mg orally once a day), without another significant medical history.

The patient was admitted to a high-complexity hospital in Popayán, Colombia due to a clinical picture evolving over six days, consisting of a syncopal episode and loss of consciousness of undetermined duration, followed by neurological deterioration with bradylalia, prostration, and loss of control of the bladder sphincter. On admission physical examination, vital signs included blood pressure of 100/60 mmHg, heart rate of 75 bpm, respiratory rate of 16 rpm, axillary temperature of 36.5 °C, oxygen saturation in ambient air of 96%, and Glasgow Coma Scale score of 14/15 (eye-opening 4, verbal response 4, motor response 6).

Initially, a plain Computed Tomography (CT) scan of the brain was ordered due to suspicion of cerebrovascular disease. This revealed age-related involutional changes in the absence of other abnormalities. Upon admission, laboratory tests showed leukocytosis and neutrophilia on the complete blood count, elevated serum creatinine (3.03 mg/dl), elevated blood urea nitrogen (62.9 mg/dl), slight hyponatremia (130 mEq/L) and mild hyperkalemia (5.02 mEq/L) on the electrolyte panel, and normal central glucose (118 mg/dl).

Electrolyte correction was initiated, and further tests were requested to search for any infectious focus. A pathological urinalysis with Gram stain showed gram-negative bacilli; chest X-ray and lumbar puncture yielded normal results. Treatment with 1 gram of intravenous cefazolin every 6 hours was started for a urinary tract infection as the cause of the delirium; however, 5 days after antibiotic treatment, the patient developed altered consciousness with the presence of stupor.

Given the patient's torpid clinical course, a medical board considered the suspicion of lithium intoxication, due to the history of BAD being treated with said medication, and in the context of chronic renal insufficiency, lithium levels were requested, and discontinuation of *carbonato de litio* was indicated. Subsequently, the patient presented marked neurological deterioration with a Glasgow score of 8/15 (eye-opening 2, verbal response 2, motor response 4), Cheyne-Stokes breathing with 25-second apneas, oxygen saturation of 90% with supplemental oxygen at 3 liters/minute via nasal cannula, decreasing to 80% during apnea episodes, arterial blood gases showing metabolic acidosis, lactate at 1.2, and mild respiratory dysfunction with a PaO_2/FiO_2 ratio of 273. The airway was secured with orotracheal intubation and invasive mechanical ventilatory support was provided. The exact cause of the neurological impairment was unknown; therefore, the patient was transferred to the intensive care unit, and antibiotic therapy was escalated to

meropenem due to leukocytosis and increasing acute phase reactants.

On the ninth day of hospitalization, blood lithium concentrations were reported with elevated values at 1.78 mEq/L (reference value: 0.6-1.2). In conjunction with the nephrology service, the initiation of dialysis therapy was considered, and the following day successful extubation was achieved with progressive clinical improvement. The post-dialysis lithium level was reported as 0.06 mEq/L. On the 14th day of hospitalization, the patient was discharged without neurological sequelae and with paraclinical exams within normal limits.

Currently, the patient is stable with adequate control of underlying conditions, including the psychiatric pathology, which continued to be managed with lithium. Dose adjustment was necessary along with periodic monitoring of lithium levels and renal function.

DISCUSSION

Lithium is an inorganic monovalent cation that is rapidly absorbed, has a low volume of distribution (0.6 to 0.9 L/kg), and is eliminated via the renal route (11). Lithium is a mood-stabilizing medication (12), used in the prevention of cluster headaches, BAD, and Kleine-Levin syndrome (13). In the present case, the patient had been on lithium medication for 4 years for BAD. The therapeutic opportunity of lithium can be influenced by factors such as excessive drug intake, renal insufficiency, drug interactions, age, and comorbidities (5,12,14).

In our case, the patient was an elderly individual with multiple metabolic, cardiac, and renal comorbidities, who was also chronically taking lithium, and the intoxication was precipitated by the progression of his renal disease, data that are consistent with the literature, where modest changes in renal function can lead to intoxication (6,7,9).

Toxicity occurs due to the accumulation of lithium in the affected organs, mainly the brain, kidneys, and thyroid gland (15). In turn, lithium intoxication can be classified as acute, chronic, or acute-on-chronic (11). Acute toxicity occurs when a patient who previously did not take the medication regularly experiences an overdose. Clinical manifestations include nausea, vomiting, diarrhea, and abdominal pain. Neurological symptoms usually do not manifest early in these cases (16); however, these symptoms may include tremors, hyperreflexia, dystonia, and ataxia. It is important to note that, on rare occasions, cardiac involvement can also be observed, manifested by flattening of the T wave and prolongation of the QT interval (17).

In cases of chronic intoxication, the patient has been taking lithium for a long period, and lithium levels are affected due to volume loss, renal failure, or a recent change in medication dosage. The clinical signs of chronic intoxication mainly manifest in the nervous system, as they encompass a wide range of manifestations ranging from tremors to alterations in mental status, encephalopathy, coma, and seizures. Additionally, other clinical manifestations that may occur include SILENT syndrome (irreversible neurotoxicity syndrome caused by lithium), thyroid dysfunction, hyperparathyroidism, leukocytosis, and nephrogenic diabetes insipidus (13,16,18).

In this case, chronic intoxication was considered, and neurological involvement was the main clinical manifestation of lithium intoxication, which was evidenced by the progressive deterioration of the level of consciousness and alteration in the Glasgow Coma Scale, requiring airway protection through orotracheal intubation and mechanical ventilation. Leukocytosis and increasing neutrophilia were also identified. The diagnosis was confirmed by elevated lithium concentrations (1.76 mEq/L), above the known therapeutic range (up to 1.2 mEq/L), which confirmed the diagnostic suspicion. According to Martínez et al. (13), the diagnosis of lithium intoxication requires consideration and study of other pathologies that may present with similar symptoms, such as cerebrovascular disease, electrolyte disorders, central nervous system infections, and delirium exacerbated by an infectious process (13). In this case, these conditions were also evaluated and ruled out, with the diagnostic approach being similar to what is reported in the literature (2,13).

The treatment of lithium intoxication involves discontinuation of the medication and initiation of intravenous hydration to restore euvolemia (15). In acute cases, gastric lavage is indicated if ingestion occurs within the first hour, and activated charcoal is only administered when ingestion is mixed (17). Hemodialysis may be necessary in cases of severe toxicity and is recommended for lithium levels greater than 4 mEq/L or in patients with altered consciousness, seizures, or life-threatening cardiac arrhythmias (7). In our case, due to neurological involvement with progressive deterioration of consciousness, hemodialysis was indicated, in addition to volume correction and suspension of lithium carbonate intake. Table 1 describes the relevant findings related to the clinical case and provides comments according to the literature.

Table 1. Main findings in the case presentation and comments

Main findings	Comments
Elderly patient presents to the emergency department with syncope, bradylalia, prostration, urinary incontinence, and progressive deterioration of consciousness.	In the chronic form of intoxication, the main clinical symptoms focus on neurological manifestations that can range from tremors to alterations in mental status, encephalopathy, coma, and seizure episodes (13,16,18).
History of chronic use of Lithium carbonate for BAD.	Lithium is used in the treatment of BAD, as well as in the prevention of cluster headaches and Kleine-Levin syndrome (12,13).
Physical examination revealed progressive deterioration in the Glasgow Coma Scale, apneas, and Cheyne-Stokes respiration.	In the physical examination of patients with lithium intoxication, alterations in consciousness, seizures, nystagmus, hyperreflexia, hypertonia, and fasciculations may be observed (8).
Diagnostic tests showed the following findings: leukocytosis and neutrophilia, renal insufficiency, metabolic acidosis, hyponatremia, and mild hyperkalemia. The plain brain CT scan showed no lesions indicative of cerebrovascular disease or space-occupying lesions, the lumbar puncture was negative for neuroinfection, and the lithium levels were elevated (1,76 mEq/L).	Lithium has a therapeutic window with a range of 0.6 to 1.2 mEq/L. Intoxication symptoms manifest when levels exceed 1.5 mEq/L (5,7,12,14); additionally, leukocytosis and renal insufficiency may be observed (13,16,18).
The patient was treated with discontinuation of Lithium carbonate, electrolyte correction, and hemodialysis.	Treatment for lithium intoxication involves immediate discontinuation of the medication, correction of electrolyte imbalances, and, in severe cases, when lithium levels exceed 4 mEq/L or there are symptoms such as altered consciousness, seizures, or potentially life-threatening cardiac arrhythmias, hemodialysis may be required (7).

BAD: Bipolar affective disorder; CT: computed tomography.

CONCLUSION

Lithium intoxication should be considered in patients who are taking the medication and present neurological symptoms. It is vital to regularly monitor lithium concentrations, especially in elderly patients with multiple concomitant diseases and risk of renal function deterioration, as this could increase the risk of intoxication. In this case, discontinuation of Lithium carbonate, restoration of electrolyte balance, and hemodialysis were effective measures that contributed to the patient's recovery.

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CONFLICT OF INTEREST

The authors of the manuscript declare no conflicts of interest.

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