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A Case Report On Lithium Toxicity

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Abstract

The drug of choice for the management of bipolar disorder is Lithium.It is a narrow therapeutic index drug with a range of 0.6-1.5 mmol/L.A 58 year old male who was on chronic lithium therapy for bipolar disorder presented with decreased sleep, confused behaviour, irrelevant talk and breathlessness for 1 week with elevated lithium levels. The patient was treated symptomatically and his antipsychotic medications were withheld.This case illustrates the need for closely monitoring of the serum lithium levels in patients who are on chronic lithium treatment.

Keywords: Lithium Toxicity, Bipolar disorder, Serum lithium concentration

Introduction

Lithium, a monovalent cation, is the drug of choice for the treatment of bipolar disease.(1) It has a restricted therapeutic index and a range of 0.6–1.5 mmol/L. Its use as a mania therapy and mood stabiliser was originally authorised by the US FDA in 1970(2). Lithium poisoning can present clinically as nausea, vomiting, diarrhoea, dysrhythmia, bradycardia, neurological symptoms such as cerebellar signs, ataxia, sluggishness, disorientation, delirium, seizures, and coma, as well as long-term neurological sequelae like dementia(3).A blood lithium content of 1. 5 mEq/L or greater was considered as poisoning. We report a case of a 58 year old male patient who presented with complaints of decreased sleep, confused behaviour, irrelevant talk for 1 week after the chronic intake of lithium.

Case Report

A 58 year old male patient with a known case of Bipolar disorder (32years), COPD, CAD, Type 2 Diabetes Mellitus and with a social history of smoking (32 years) presented to the Emergency department with complaints of decreased sleep, confused behaviour, irrelevant talk and breathlessness for 1 week. On arrival, the patient was drowsy and not oriented. On physical examination, he had an irregular heart rate (38bpm), BP of 160/80mmHg, SPo2 level of 90%, RR of 16 breaths/min, GRBS of 107 mg/dL. He was also found to have bilateral pitting edema, clubbing, tobacco stains in nails and ulcers in toe. The patient was on 600mg of Lithium Carbonate daily for 32 years. He had continued the drug without review after his first visit with the consultant. He had a history of tremor and hallucinations for a few days.He was also on carbamazepine 200 mg thrice daily, Aripiprazole 10 mg and clonazepam 0.25mg at bedtime. All the psychotic medications were withheld.

ECG and ECHO were taken outside and ECG appeared to have first degree AV block, RBBB,AV dissociation, where ECHO showed severe LV systolic dysfunction(EF:27%) and bradycardia and was brought here for further management.He was admitted in ICU in view of bradycardia and arrhythmia.Adrenaline infusion was given for bradycardia and one hemodialysis was done in suspicion of Lithium toxicity. Lithium level was

monitored and it was elevated (2.4 mmol/L), and lithium toxicity was diagnosed. On laboratory findings, creatinine value was 2.78mg/dL, urea 58.8mg/dL, Sodium 132 mmol/L, potassium 4.39mEq/L, CRP 23.6mg/L, Total count 11700/µL, Hb 11g/dL, Ammonia 47.60µmol/L. Thyroid function tests were also altered with an increased TSH value of 55.23µIU/mL and a low T4 value of 2.35µg/dL. Chest X- ray showed cardiomegaly. ECG showed AV dissociation, sinus tachycardia, LVH, ST depression V5 V6, IVCD(+). Lithium levels were repeated with a decreasing level down to 1.3mmol/L after 3 days.He was shifted to HDU and Inj Levipil was added in view of myoclonic jerks. As the day progressed, he became more agitated and exhibited restlessness and myoclonic jerks. Hence administered Inj. Levetiracetam 500mg BD. Inj. Haloperidol 2.5mg, T. Clonazepam 0.25mg OD. The patient's condition deteriorated dramatically on the 7th day of hospitalisation. He was shifted to ICU in view of uremic encephalopathy. Then he was intubated in view of GCS drop (E1V1M3)and tachypnoea. Then some of his parameters were deranged: procalcitonin 4.79ng/mL, Urea 142.7mg/dL, Creatinine 3.10mg/dL, SGOT 56 U/L , SGPT 53 U/L, Ammonia 56.8µmol/L. Brain CT showed mild cerebral atrophy. Cardiology consultation was sort out in view of heart failure and recommended to do cardiac synchronisation therapy once the patient becomes stable. The Nephrology team consulted for the need to do hemodialysis. EEG showed a mild degree of generalised non specific disturbance of electrical function. Repeat lithium report sent after 8 days and it was normal (0.54 mmol/L).After 17 days, patient was discharged as he was symptomatically better and hemodynamically stable.

Discussion

Since 1970, Lithium has been licenced by the U.S. Food and Drug Administration as a mood stabiliser for the treatment of bipolar illness. It is also used off-label to treat a variety of psychiatric and non-psychiatric issues, including acute mania, PTSD, schizoaffective issues, and neuropathic pain.[(1)] Lithium targets the inositol monophosphatase enzyme in the phosphatidylinositol signalling pathway and the protein kinase glycogen synthase kinase 3 enzyme.Lithium inhibits these enzymes by replacing the normal magnesium cofactor, a vital regulator of many signalling pathways.

The severity of lithium toxicity can be divided into 3 types: mild, moderate and severe. Mild signs and symptoms include nausea, vomiting, lethargy, tremor, and fatigue(lithium level:1.5-2.5mEq/L).Moderate intoxication shows confusion, agitation, delirium, tachycardia, and hypertonia (lithium level:2.5-3.5 mEq/L). Severe intoxication which may result in Coma, seizures, hyperthermia, and hypotension (lithium level>3.5 mEq/L)[(1)]. In our case the patient's lithium level was monitored and the level was 2.4 mmol/L. The typical medical signs and symptoms diagnosed are as follows: chronic cerebellar dysfunction, chronic extrapyramidal syndrome, chronic brain-stem dysfunction, or dementia with various natural intellectual syndromes. Lithium has an elimination half-life of 12-27 hours after a single dose, although in elderly people or those taking lithium continuously, this time can extend to up to fifty-eight hours[(4)].

We present a case of a 58 year old male patient with bipolar disorder, who developed lithium toxicity and was admitted under the general medicine department due to decreased sleep, confused behaviour, irrelevant talk and breathlessness. In a case report by Arnaoudova MD et al, the patient presented with nausea, weakness, unstable gait, memory difficulties and severe anxiety[(2)].

In an older population, the dosage and serum concentration of lithium must be adjusted[(2)].Renal toxicity and thyroid dysfunction are known side effects of lithium administration. Thus it is advisable to monitor creatinine and TSH levels periodically in patients on lithium. Lithium distributes to a steady-state concentration in the brain and serum with continuous lithium usage, it should be noted that there may be interindividual variation in the relative concentrations. Lithium will build up in the CNS tissue to a hazardous level in patients receiving high doses of the drug over an extended period of time[(5)].

Lithium poisoning is treated in general the same as other poisonings, which includes managing the airway, especially in situations of changed mental status, inserting a nasogastric tube, and performing gastric lavage, particularly in cases where patients appear soon after intoxication. Most patients with lithium toxicity are volume depleted hence fluid therapy is one of the main treatments given.In cases of ingestion with sustained-release medications,

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studies on lithium preparation advice employ polyethylene glycol for entire bowel irrigation[7]. In our case, the patient was managed with administration of adrenaline infusion, anticonvulsant agents and hemodialysis.

This case highlights that the patients who are on lithium for a long term should monitor their serum lithium level and should undergo regular follow up at appropriate intervals. Elderly people have higher ratios of brain-to-peripheral lithium concentrations, which could make them more susceptible to CNS damage[2].On review, the patient was stable and the psychiatrist advised to start on Divalproate as mood stabiliser and Bupropion as antidepressant.

If a patient shows signs of toxicity, lithium should be stopped immediately and the serum lithium levels, creatinine and urinalysis should be investigated. Patients with renal failure who are unable to excrete lithium should receive hemodialysis. Additionally, it is advised for individuals who exhibit severe neurotoxic symptoms[2].

Conclusion

Since it necessitates thorough monitoring and detection of neurologic side effects, narrow therapeutic index continues to be a significant constraint of lithium treatment. It is important to closely monitor lithium levels in patients on chronic lithium and to identify any potential toxicity risk factors. Proper medical history should also be considered while suspecting any toxicity. To prevent lithium toxicity, it is necessary to monitor drug plasma concentration and should provide education to the patient and caregivers on vigilant follow-up and recognition of early signs of intoxication.

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