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A Case Report of Lithium Overdose and Delayed Severe Neurotoxicity: Time to Recomence Lithium and to Think of Renal Replacement Therapy

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Keywords

lithium toxicity, renal replacement therapy, neurotoxicity.

Abstract

In this case report, a female in her 60s presented to a tertiary care hospital with lithium toxicity. 24 hour monitoring was done, nephrology team opinion was obtained and patient was put on renal replacement therapy. Patient was started on lithium again, once the lithium levels fell within the normal therapeutic range (between 4.7mEq/L and 0.67 mEq/L). In this particular instance, patient devoloped slurring of speech followed by catatonia a little later. This case report is meant to discuss the factors that predispose the respective group of patients to neurotoxicity.

1. Introduction

Lithium is used in the treatment of patients with depressive disorders, biploar illness. Chronic usage of lithium as a medication in patients can lead to renal and neurological impairments. The predominant form of chronic kidney disease associated with lithium therapy is chronic tubulointerstitial nephropathy. Lithium neurotoxicity may be reversible or irreversible.Lithium toxicity can be classified into 3 subtypes namely acute, subacute, and chronic. Acute toxicity usually presents in patients who have had suicide attempts with lithium.

Clinical use of lithium in a hospital setting

Lithium is an alkaline material available naturally in the environment which was identified incidently to relieve mood disorder and hence it was brought into use since the mid 20th century [1]. As suggested by the popular psychiatry guidelines such as the Maudsley rules for prescription and the guidelines suggested by National Institute for Health and Care Excellence, it is now routinely applied as a primary line drug for bipolar affective disorder maintenance therapy [2,3]. Other disorders, where lithium is employed in treatment include depressive disorders (recurrent in nature), headaches especially migraines, violent behaviour and cluster headaches [3,4]. One of the most significant disadvantages of using lithium is its limited therapeutic index, which causes overdose, particularly in the kidneys. This overdose could be due to an unintentional or deliberate overintake or an intoxication owing to decreased kidney clearance (as more than 90 percent of lithium taken is excreted via kidneys).

Neurotoxicity caused by lithium: Caution, Clinical presentation andetiopathogenesis

Inspite having used lithium in clinical practice for

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greater than 6 decades, neurotoxicity caused by the drug is still not clearly understood. Lithium overdose affecting nervous system comprises of a broad range of neuropsychiatric symptoms that are rarely linked to brain harm caused by lithium consumption [5]. Confusion, Altered sensorium, Slurring of speech, mood changes, impaired memory, epilepsy, and stupor are among the symptoms documented in earlier case reports [6-8]. These side effects are usually caused by serum intoxication, however toxicity levels affecting nervous system has been recorded at curative levels on rare occasions [7]. In this case report, we elaborate lithium toxicity, which has occurred on an acute background where symptoms pertaining to nervous system appeared later than expected. The time of renal replacement therapy and lithium resumption is also discussed here.

2. Case Report

HISTORY

A female in her 6th decade of life who had sustained several depresssive disorders in the past at regular intervals was admitted to the hospital after taking a large dose of lithium. She was on lithium carbonate 800 mg one time at night (HS), clomipramine 75 mg HS, and quetiapine 200 mg HS as suggested by her psychiatrist before her admission. She gave a history of having three hospitalizations prior to this one, the latest one was for neglect in self with depression which was severe in nature in 2008. She gave a history of self reporting an overdose of zopiclone few years prior to admission. But there was no details of such reporting. During those months when patient was on lithium, patient was identified to have an uncommon skin cancer in her leg and she had to go through a surgery, which she described it to be a disastrous experience. Following a relationship breakup about a year before to admission, she was socially isolated.

This woman had prepared for death by self-administering 25 X 800 mg lithium carbonate with 1 litre of water. She contacted an ambulance 10 hours later owing to giddiness, continous vomiting, loose stools and stomach ache.The incident was reported to the paramedical team and the primary admitting medical team. On presentation, the individual was going through a depressive episode, severe in nature and she presented with insomnia, poor food intake, feeling of no hope, suicidal thoughts and withdrawal from surroundings. Patient did not have any past alcoholism history

INVESTIGATIONS

This female was clinically dehydrated when he was admitted, and a proper examination of the nervous system revealed ataxia of cerebellar origin and had post pointing without any other abnormalities. On admission, venous blood gas revealed pH 7.40 (7.35–7.45), bicarbonate 28.3 mmol/L (22–26), base excess 2.9 mmol/L (2 to +2), and lactate 1.6 mmol/L (0.6–1.4), all of which were higher than baseline (1.7 mg/dl). 12 hours after the overdose, the serum lithium level was 4.7 mEq/L (typical therapeutic range 0.4–1.0 mEq/L). He had a increased corrected QT (QTc) of 490 ms and ECG had right bundle branch block. Other tests were reported to be normal.

TREATMENT

The admitting medical team began haemofiltration twenty-four hours following his presentation, and he had three episodes. All psychotropic medicines were taken out of the equation. After two haemofiltration events, the level of lithium in serum was lowered to 2.0 mEq/L, and it was reduced to 0.88 mEq/L after the next hemofiltration.

OUTCOME AND FOLLOW UP

Post overdose on 6th day, patient was recommenced on lithium at a dose of 400mg HS and the serum level of lithium during that time was 0,67mEq/L. The patient acquired tremors bilaterally, slurring of speech, and dystonia within 24 hours, which were all absent at the time of admission. Lithium therapy was abruptly discontinued after consultation with the psychiatric team. At this point, serum lithium level was repeated and was found to be within the therapeutic level (0.24 mEq/ L). Following that, a Computerized tomography scan of brain and MRI of the brain revealed no abnormalities. Electrocardiography which was repeated revealed a QTC of 442 milliseconds and no Right bundle branch block. Because the patient's mood remained poor and she had suicidal ideas, 50 mg HS of quetiapine was begun and 15 mg HS mirtazepine

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was started to cure the relapse of a depressive episode.

3. Discussion

Neurotoxicity assosiated with lithium: The risks and etiopathogenesis

Oakley et al did a retrospective examination of 97 lithium overdose case files at one regional facility in Australia over a 13-year period. Toxicity to nervous system was found to be dependant on the dosage, with more serious symptoms occurring at larger concentration (2.3 versus 1.6 mmol/L, p=0.02) [5]. Patients on longterm lithium who had subtle or acute toxicity were at the greatest risk of neurotoxicity. Chronic overdose (chronic or acute-on-chronic) was linked with a increased risk of severe neurotoxicity than a single acute lithium overdose [5]. They also discovered that being over 50, having kidney disease (nephrogenic diabetes insipidus or kidney failure), and having any thyroid issue were all significant risk factors for neurotoxicity. The female in her sixties reported in this case report with acute-on-chronic severe overdose (lithium level of 4.7 mEq/L) may be at significant risk of high toxicity to nervous system as a result of their findings and our observations.

Neurotoxicity can be either reversible or irreversible. Ataxia and slurred speech are examples of cerebellar symptoms that are more prone to be irreversible [9]. Cognitive and visuospatial abnormalities can continue even after other cognitive functions have been restored, according to one case study. An Electroencephalography has been shown to show broad slowing after neurotoxicity [6]. As in our instance, imaging studies of the brain (including MRI) may not suggest any specific abnormality and isn't always finished. It's been difficult to define the underlying neural area malfunction induced by lithium overdose because of these characteristics, and also the patients' current physical problems. According to Bartha et al., [6] the consequences could be severe neuronal pathways of both cortical and subcortical part in both halves show a mixed, multifocal functional impairment. In cerebellum, Internalgranule layer and purkinje layers showed high extent of degeneration with Bergmann gliosis in postmortem examination. Changes similar Alzheimers disease was found in lentiform nuclei and thalamus. These changes have been reported in one case report of acute or chronic toxicity, which could due to terminal uremia.

'Lithium rebound' may have played a part in the clinical deterioration that happened after haemodialysis was halted in this case. After extracorporeal therapy is no longer used [10]. The term "lithium rebound" describes a rise in lithium serum concentrations as well as the likelihood of poisoning symptoms recurring. This occurs over the next 10 hours on average, though it may take more time if absorption is delayed or gastrointestinal motility is limited [10].

Managing a case of lithium toxicity associated with neurtoxocity

In 2015, the Extracorporeal Treatments in Poisoning (EXTIP) workgroup in the United States issued guidelines on how to use kidney replacement therapy for poisoning [10]. The EXTIP workgroup looked at 167 articles (mainly articles with approximately 420 patients), and they were able to extract patient-level data from 228 of them. The criteria which warrants the clinicians to use extracorporeal treatment in serious lithium overdose are, if the function of renal system is decreased and if the level of lithium is more than 4.0 mEq/L or in the If the level of lithium is greater than 5.0 mEq/L, there is severe disorientation, or the time taken to lower the level of lithium to less than 1.0 mEq/L is longer than predicted (more than 36 hours) extracorporeal treatment is recommended. Extracorporeal therapy should be continued until clinical status of the patient improves or the serum levels of lithium falls below 1.0 mEq/L. If serum lithium is not easily quantifiable, extracorporeal treatments should be continued for at least 6 hours [11]. Although there are no UK official recommendations relating to lithium and renal replacement treatment, the UK Poisons Advice Service provides similar advice to physicians practicing in the United Kingdom.

Specific signs of toxicity to nervous system, such as epilepsy, episodes of unconsiousess, or disorientation, should be treated with renal replacement therapy, according to US guidelines, regardless of serum lithium levels. Extracorporeal

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therapy is also recommended for patients with multiple ingestions or high serum levels of lithium, even if no symptoms are present. Other than care of delirium, convulsions, and agitation, additional management of lithium neurotoxicity is unknown. As a result, taking these suggestions to our case, we may conclude that renal replacement medication was appropriate in our patient's instance due to the high levels of lithium and acute renal failure. But still, there are no clear guidelines over whether to start renal replacement treatment (i.e., should it be started right away in an accident and emergency or delayed for up to 1 day following admission in under medical team, as this decision could have a significant impact on clinical outcomes). Levels of lithium in serum and its pharmacokinetics can be used to determine the best time to restart lithium treatment [12].

4. Conclusion

Toxicity to nervous system on account of lithium usage is a possible side effect of lithium medication, more commonly seen in people on long-term lithium who have a serious overdose or have decreased kidney clearance of lithium. The exact mechanism of toxicity to nervous system at the regional level of the brain is unknown; however cerebellum and basal ganglia involvement fits the presentation. According to US recommendations, symptoms of severe toxicity to nervous system (independent of blood lithium levels) or a lithium level greater than 4.0 mEq/L with poor kidney function (regardless of symptoms due to toxicity of nervous system) should be strongly considered for renal replacement treatment to avoid complications. Some toxicity symptoms will improve with treatment, but others, particularly cerebellar problems, may be irreversible. There is a distinct lack of information on the underlying areas of brain affected by toxicity due to lithium, as well as if any particular management, such as the time of renal replacement therapy, can influence the prognosis of neurotoxic symptoms and their resolution. However, earlier renal replacement is likely to be the best option.

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ETHICAL CONSENT :

Informed consent was taken from the patient regarding this study .

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CONFLICT OF INTEREST :

The authors declare that there was no conflict of interest.

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