

Lithium: contributor to movement disorder sensitivity after anoxic brain injury?

SAGE Open Medical Case Reports
Volume 7: 1–3
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DOI: 10.1177/2050313X18823101
journals.sagepub.com/home/sco



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Abstract

Although lithium-induced dystonia has been well documented in the literature, conflicting evidence discusses whether a patient may be susceptible to adverse effects from the drug after an anoxic brain injury. More recent literature discusses that lithium may, in fact, be neuroprotective. This case report presents a 35-year-old male who, after an anoxic brain injury after a suicide attempt, developed lithium-induced dystonia with characteristic symptoms of sustained muscle contractions, repetitive movements, and postures, which was not markedly improved with benzotropine or benzodiazepines. It is postulated that because this patient received a depot neuroleptic with a subsequent anoxic brain injury, he may have become more sensitive to lithium and its rare complications.

Keywords

Lithium, dystonia, anoxia, brain injury

Date received: 19 December 2016; accepted: 13 December 2018

Introduction

Lithium carbonate is a first-line, mono-therapy drug for those with bipolar disorder.¹ It has been found to be the drug of choice for both the prophylaxis and treatment of depressive and manic states in the disorder and at therapeutic doses can exercise a favorable influence on various cognitive functions by protecting against the occurrence of affective episodes and improvement of neural plasticity.² However, the potentiation of lithium induced neuroleptic-related side effects has been established in the literature, although usually with minor degree of effects.³ First described several decades ago, Kane et al.⁴ researched 38 outpatients who had received lithium without neuroleptics for 3 months and examined them for side effects. Their literature found that two of those examined exhibited evidence of cogwheeling. Notable side effects that are described in more recent literature include ataxia, dysarthria, delirium, tremor, polyuria, polydipsia, diarrhea, nausea, weight gain, euthyroid/hypothyroid goiter, acne, rash, and leukocytosis.^{5,6}

While research into lithium and its effectiveness for bipolar disorder has been widely available, its discussion on the effects of those with brain injury appears to be less certain. While rare in the brains of healthy adults, early research into those who have had a brain injury discussed an increased sensitivity to the neurotoxic effects of lithium.⁷ This was researched mostly in

patients who had become aggressive as a result of a brain injury and discussed using lithium as a treatment for aggression. This literature has more recently been discussed in a positive light with the possibility of lithium having a neuroprotective effect.⁸ The authors describe emerging evidence that lithium can stimulate neurogenesis and provide anti-inflammatory effects, angiogenesis, as well as decrease oxidative stress and mitochondrial dysfunction. While these are experimental models, the authors report exciting findings regarding lithium and brain injury. This article presents a patient in the context of this information who experienced a dystonic reaction after an anoxic brain injury and lithium therapy.

Ethics

Prior to commencement, this case report was reviewed for ethical compliance by Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board and was granted approval. The patient was capable to provide

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consent and gave full written informed consent to participate in this case report.

Case presentation

The patient is a 35-year-old male with bipolar I disorder who presented initially to his family physician with complaints of low mood and so was started on sertraline. When he presented to psychiatry 4 months later, his mood was significantly elevated and he reported symptoms of mania including gross overspending and sexual indiscretions and had committed several crimes and so was admitted to an inpatient forensics psychiatric facility. He was started on aripiprazole 10 mg PO daily and eventually given aripiprazole 400 mg IM and was discharged with follow-up with a mood disorders specialist.

Approximately 5 days after discharge from the forensics facility, the patient attempted suicide by means of overdose and lacerations to his wrists. He was admitted to the Intensive Care Unit (ICU) with a Glasgow Coma Score of 3. Electroencephalography (EEG) showed an abnormality possibly associated with anoxic brain injury. Once discharged from the ICU, the patient was transferred to an acute care Psychiatry service. He was noted to be dystonic on transfer with several movement concerns. He described muscle contracture in his arms which kept them angled at 90° and a consistent need to walk around the unit due to restlessness. He displayed repetitive movements of the arms and hands and reported stiffness in his neck and back. At times, the movements of his hands would display a tremor. He was started on regular benzotropine.

On the acute care Psychiatry unit, the patient was started on lithium up to 900 mg PO QHS for mood stabilization, which he initially tolerated well. Vortioxetine was added for antidepressant effects at a starting dose of 10 mg PO QHS. Due to continuous complaints of poor sleep, quetiapine, clonazepam, oxazepam, temazepam, nozinan, zopiclone, and lorazepam were all trialed with only lorazepam effective. He required as needed benzotropine throughout his stay. Approximately 64 days after receiving IM aripiprazole and 41 days after starting lithium, the patient developed another acute dystonic reaction, and all medications were discontinued. Librium, clonazepam, and benzotropine were trialed to treat the symptoms with only mild relief.

Neurology provided two consults with the impression that the patient was sensitive not only to antipsychotics but also to lithium after suffering an anoxic brain injury after his suicide attempt. A magnetic resonance imaging (MRI) head was completed at the time and was found to be unremarkable. The patient was then transferred to a Mood Disorders Inpatient specialty facility for further treatment.

Discussion

The present case is characterized by bipolar disorder compounded by an anoxic brain injury and sensitivity to antipsychotics and lithium. Of note was that the patient was started on aripiprazole IM which has an approximate

terminal half-life of 30–40 days (Stahl, 2008). This would disclose that the antipsychotic would continue to be a factor during his entire acute care stay, a feature that may have contributed to his sensitivity to other agents, including lithium. Past literature has discussed that brain trauma may contribute to increased sensitivity to both neuroleptics and lithium, and as such, it may be difficult to attribute the onset solely to lithium. These patients are particularly susceptible to dystonias, akathisias, and other Parkinsonian side effects, even at very low doses of antipsychotics.⁹

Lithium is a complex medication with multifaceted mechanisms of action and its study over the last decade and a half as a neuroprotective agent in regard to its mechanics is promising. Leeds et al. (2014) show promising research in their discussion regarding lithium's protective effects in rodent models. First, lithium reduces protein kinase C activity, which may explain genomic expression associated with neurotransmission. It also increases cytoprotective proteins and activates signaling cascades utilized by endogenous growth factors which increases gray matter content via neurogenesis and enhances trophic actions that maintain synapses.⁵ Chronic lithium exposure can block neuronal apoptosis and control inflammatory conditions in both the peripheral and central nervous systems.⁸ While human trials have not yet begun, the authors show interesting research potential for the future.

This case was highlighted to promote discussion regarding antipsychotics, anoxic brain injury, past literature, and the advances and current considerations regarding lithium and neuroprotective effects. It appears that there are possible new developments on the horizon.

Acknowledgements

This case report has not been published and is not under consideration for publication elsewhere.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval to report this case was obtained from the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board Approval Number #6018108. ID PSYI-523-16.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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