



Case Report

The Impact of Increasing Manic Episodes in Bipolar 1 Disorder and Patient Noncompliance with Lithium: A Case Report

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Abstract

Bipolar 1 disorder involves recurrent episodes of mania and depression. Mania is severe and sustained in bipolar I disorder. The effects of recurring manic episodes are costly and prevention has utmost importance. A subset of patients present with a progressive course of cognitive impairment and changes to the brain known as neuroprogression after an increasing amount of manic episodes. Studies reveal that the recurrence of episodes tends to accelerate over time and leads to shortening of inter-episodic intervals. Changes to the brain include reduction in hippocampal volumes, cortical thickness, gray matter volume in the frontal and temporal lobes, and corpus callosum. Cognitive changes include worse performance in semantic clustering, executive function, and working memory. Prevention of recurrence of manic episodes requires early intervention and medication compliance. We report a case of a 32 year old female with bipolar 1 disorder with significant past medical history of 8 prior hospitalizations for manic episodes and 9 prior suicide attempts. She was admitted to an acute psychiatric ward after her latest manic episode due to medication noncompliance for 8 months for reasons of adverse side effects of lithium and the desire to get pregnant. Despite being admitted for 8 weeks on an intensive treatment regimen she has been refractory to treatment. This case highlights the impact of recurring manic episodes. Physicians also need to discuss with patients their concerns with side effects and pregnancy regarding lithium as newer research shows lithium is much safer to use during pregnancy than previously thought.

Keywords: Recurrence of manic episodes; Bipolar 1 disorder; Lithium; Lithium usage and pregnancy.

Introduction

Bipolar disorder has a lifetime prevalence of 2% among the adult population worldwide with a similar prevalence in men and women. It is a chronic disease of abnormal mood with episodes of elevated mood or depression. Lithium remains the gold standard to treatment for maintenance of mood. With lithium there can be noncompliance for a number of reasons with the chief among these being its adverse side effects. The most common reasons for discontinuing are diarrhea, weight gain, and tremors.

Lithium usage during pregnancy is another topic of concern for patients. Older research in the 1970s seemed to indicate a much

greater chance of developing Ebstein's anomaly but newer research shows this is much less probable than previously believed.

Despite apprehension with lithium, it remains a first-line treatment for bipolar disorder. Its prominent use is due to its greater effectiveness compared to other drugs. Usage of lithium is associated with reduced risk of mood-episode recurrence.

Recurrence of manic episodes has been linked to changes in the brain in areas important for emotional processing and regulation, executive function, and memory.

Cognitive changes are also seen in these patients that are not seen in those with lesser amounts of manic episodes.

Prevention of recurrence might minimize these changes and requires early intervention. Achieving this goal also requires

identifying patients who might be prone to more manic episodes based on past trauma, number of prior manic episodes, and medication noncompliance.

We present a case of a patient with a history of multiple manic episodes who has been more refractory to treatment than usually seen with our patients. It highlights the importance of medication compliance especially with those already having multiple manic episodes. While there is growing research demonstrating the affects of recurring manic episodes, studies are still limited on this matter.

Case Presentation

A 32 year old female veteran with a significant past medical history for bipolar 1 disorder with 8 prior manic episodes and 9 prior suicide attempts presented with insomnia and was admitted for mania. At an IVF OBGYN clinic with her boyfriend she was asking if everyone was real. Stated that she quit her job but wasn't able to produce a reason. She said that she and her boyfriend were going to play pickle ball all day and just have fun. Patient said there were spirits with them in the clinic. Stated she had little sleep for the last 4 nights. OB provider advised to present to the VA for evaluation. Patient only agreed to go by Uber Tesla claiming that was the only safe way of getting there.

At the VA the patient explained she stopped taking her medications, including lithium, 8 months prior because she wanted to get pregnant. She also expressed displeasure with the side effects of hypothyroidism and weight gain. Although patient stated her psychiatrist assisted her in tapering off medications, clinical notes reflected that this was against psychiatric advise. The patient said she was going to save the world and needed to quit her job. She declined to get back on medication. The patient was diagnosed with a current manic episode and admitted into inpatient psychiatric care.

Patient was started on lithium and aripiprazole for treatment. Patient had little sleep during the first week. She would frequently be combative with staff and went into patient rooms. She still maintained that she didn't want treatment. She reiterated multiple times she did not want to be on lithium due to the side effects of hypothyroidism and weight gain. She also expressed concerned about what lithium would do to any future pregnancy. After one week in a mental health court day she was ordered to have additional days of treatment.

Over the course of 8 weeks of treatment patient showed little improvement. Several medications were used in attempt to get more improvement. Patient had been treated with haloperidol, lamotrigine, chlorpromazine, lithium, olanzapine, and risperadone throughout the 8 weeks. Patient was later being given 1,500 mg of Lithium daily. Patient had recently started clozapine with some improvement.

She continued with minimal sleeping, pressured speech, delusional thoughts, and bizarre statements. She consistently had pressured speech and flight of ideas. She also displayed delusions of grandeur.

Patient would say she was a little girl who was missing and to tell people she had been found. She often said she had a chip put into her brain and people were listening to her conversations. Some days patient thought she was on a ship and other days thought she was at a construction site. She had delusions about frozen embryos and seeing her partner at the parking lot and feeling his spirit in the unit. Patient was to have another court date to extend her treatment in the inpatient psychiatric unit.

Discussion

Here we present a difficult case of bipolar 1 disorder in which our patient has a significant past medical history of 8 prior manic episodes requiring hospitalization and 9 suicide attempts. This patient has been refractory to treatment thus far after being admitted for 8 weeks. Growing research shows that each successive manic episode can lead to further changes in the brain, further cognitive decompensation, and resistance to treatment. This phenomena has been termed neuroprogression. While this is not a general rule with bipolar 1 disorder it is seen in some patients.

MRI changes to the brain are seen in patients after an increasing number of manic episodes. Gray matter volume reduction in the left frontal and bilateral temporal regions is seen in patients with multiple episodes that are not seen at illness onset [4]. One study involving 173 subjects demonstrated hippocampal volume loss in patients with 10 or more manic episodes and was significantly greater than those with 5 or less [1]. Longitudinal studies show changes in the frontal cortex and episode acceleration [3]. A cross sectional study showed that lateral ventricles were significantly larger [1].

An analysis showed significantly worse memory performance during immediate recall [1]. Patients also show worse semantic clustering scores [1]. Patients with 3 or more manic episodes are more impaired in attention and executive function [6]. There is also a decrease in working memory and visual memory [8]. Patients in their first few episodes not only reach recovery or remission more often, but do so more rapidly [8]. Even when similar illness severity is present, patients with more manic episodes require longer hospital stays [8].

Our patient's latest manic episode and hospitalization was due to noncompliance with her medications due to concerns with side effects and the desire to become pregnant. Lithium compliance has been problematic despite its proven benefits preventing severe manic episodes and suicide. One study reports out of 873 patients that 54% discontinued lithium with 2/3 of those discontinuing due to adverse side effects [5]. Overall men and women are equally likely to discontinue lithium with women three times more likely to discontinue due to weight gain [5]. The five most common reasons are diarrhea, tremors, polyuria/polydypsia, diabetes insipidus, and weight gain [5]. Our patient discontinued lithium due to her weight gain and hypothyroidism. But some studies show that side effects can lessen over time [5]. These findings call for further development of strategies and communication of physicians with their patients to improve medication compliance. It is important

to talk to patients about weighing the risks and benefits of taking lithium, especially for those who have already had multiple manic episodes and therefore being prone to more.

Our patient stopped lithium treatment due to concerns of congenital heart defects. Recent research shows the risk for Ebstein's anomaly is much lower than previously suspected [2]. One study of 663 women exposed to lithium during pregnancy compared to an unexposed group only had one additional case per 100 live births [2]. A 2018 meta-analysis looking at 21,397 pregnancies found no association between lithium exposure during pregnancy and major pregnancy complications. Some studies show a 66% relative risk reduction of manic episodes during pregnancy in those taking lithium [2]. In one study, only 24% of bipolar women who continued lithium relapsed into a manic episode, whereas 70% who discontinued lithium did [2]. Manic episodes during pregnancy are associated with poor prenatal care, placental abnormalities, antepartum hemorrhage, preterm birth, low birthweight, and small for gestational age [7]. It is much more likely that one cause harm during pregnancy due to a manic episode occurring than the small chance of Ebstein's anomaly. Discussions need to take place with patients regarding pregnancy and the harm that can be done not taking lithium. Ebstein's anomaly can also be treated surgically and ultrasounds can monitor fetal cardiac changes during pregnancy. A lower dose of lithium can also be used during the 1st trimester.

Physicians will need to take into account the patient's illness severity, the number of prior manic episodes they've had, and the likely but weak association of lithium to Ebstein's anomaly. Women and their physicians need to balance the risks and benefits of treatment with the likelihood of another manic episode. Given our patient's significant past medical history she is someone that needs to remain on lithium treatment.

Treatment rates using olanzapine are significantly lower among patients with > 5 episodes and patients with more than 7 episodes have worse outcomes with psychoeducation [8]. Clozapine has shown the most promising efficacy in patients with more manic episodes [6]. Several medications had not made significant progress with our patient. But some progress has been made with clozapine in recent weeks. It might be good practice to start a patient with increasing manic episodes on clozapine.

Conclusion

Increasing amounts of manic episodes can lead to shorter interval between episodes, changes in the brain, permanent changes in cognition, and resistance to treatment. Early treatment intervention and medication compliance can prevent further manic episodes and therefore prevent neuroprogression that is seen in some patients.

It is important to have discussions and provide reassurance to patients in regards to side effects. Physicians also need to discuss with patients their concerns regarding lithium use during pregnancy as newer research shows lithium is much safer to use during pregnancy than previously thought.

Declarations

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