



## International Journal of Psychiatry and Mental Health

Case Report

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### Quetiapine associated tics in a pediatric patient post overdose on re-initiation: An interesting clinical scenario

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**Received Date:** Mar 01, 2021 / **Accepted Date:** Mar 19, 2021 / **Published Date:** Mar 22, 2021

**Cite this article as:** Thomas Barrett, Emma Wu, Nirmal Singh M, et al. 2021. Quetiapine associated tics in a pediatric patient post overdose on re-initiation: An interesting clinical scenario. Int J Psychiatr Ment Health. 3: 10-15.

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### Introduction

The COVID-19 pandemic has led to a multitude of new medical and psychiatric complications and new presentations that were either never seen before or not seen to the extent that they are presenting now. [1,2]. Increased number of suicide attempts and worsening severity of suicide attempts have been noted in the past year since the COVID-19 pandemic has started [1]. Psychotropic medications can often have lesser-known side effects and movement

disorders, including tics, can be one of them [3]. Tics are recurrent, simple or complex behaviors that can be motor or phonic in nature [4,5]. Simple motor tics are often observed as rapid movements while complex motor tics are more synchronized and elaborate. Additionally, noises or brief sounds are examples of simple vocal tics, while speaking a string of words or syllables are more characteristic of a complex vocal tic [4]. The underlying pathogenesis of tics and tic disorders has not been well elucidated, dopaminergic hypothesis being the most widely accepted; however, multiple areas of the brain are speculated to be involved [4,6].

Common treatment options for tic disorders include alpha-2 agonists, clonidine and guanfacine, and antipsychotics [4,7]. Previous literature identifies two case reports that documented tics related to quetiapine. One report described a pediatric bipolar patient who developed tics proportional to quetiapine dose [8], and the other report identified an adult patient with schizophrenia who developed tics during quetiapine therapy [9]. In this article, we describe a pediatric patient who presented after overdosing on quetiapine, lamotrigine and sertraline and developed tics after re-initiation of quetiapine at a much lower dose. To the best of our knowledge, this is the first case of its kind where tics, which were previously absent, developed on re-initiation of quetiapine after an overdose.

## Case Report

### Presentation

Patient is a 16-year-old Caucasian female with history of major depressive disorder, generalized anxiety disorder, and cannabis use disorder, who presented to the hospital after overdosing on quetiapine 2000 mg, lamotrigine unknown quantity, sertraline unknown amount. Afterwards, she suffered cardiac arrest and required cardiopulmonary resuscitation, and then was hospitalized in the ICU. Basic investigations showed a normal CT scan of her brain and initial electrolyte abnormalities with respiratory acidosis, which were corrected during the medical hospitalization. After being stabilized medically, she was transferred to inpatient Psychiatry for further management.

### History

Patient's home medications were quetiapine 100 mg and lamotrigine 100 mg per day, prior to hospitalization. Patient reported a longstanding history of depression as well as symptoms pertinent to PTSD in context of alleged verbal and physical abuse at the hands of her coach a few years prior. The patient also

reported an intermittent history of having panic attacks in the context of worsening anxiety. There was history of regular marijuana use and LSD use on 2 occasions in the past year. The patient did not endorse having any specific stressors at the time of her overdose; however, said that ongoing arguments at home were a contributing factor along with Covid-19 related stressors of not being able to enjoy the activities that she used to do until last year [1].

### Treatment Course

Upon admission to the inpatient psychiatric unit, the patient was not re-started on any of her psychotropic medications for the first week, due to the recent overdose. Baseline labs including EKG at the time of admission were reviewed and were noted to be within normal limits. The patient requested re-initiation of quetiapine to address her insomnia, as it had been helpful in the past. Quetiapine was started at a dose of 25 mg at bedtime and was gradually titrated up to the dose of 75 mg, at which point the patient reported having tics. The tics increased in frequency over the next day, to the point that the patient was twitching her neck every 15-20 seconds towards her left. The abnormal involuntary movement scale was completed on her, and other than tics in her neck and urges to whistle, no other extrapyramidal symptoms were noted. Using the Yale Global Tic Severity Scale (YGTSS) [10], the Total Tic Score (Motor and Phonic) was 16/50 at the time of assessment and 25/50 for the worst experienced in the past week. The YGTSS Impairment score was 0/50 for both the current time of assessment and at the worst in the past week. Following this, the patient was started on clonidine to address her motor tics. Clonidine was started at a dose of 0.05 mg twice daily, but there was no relief in her tics and the medication was discontinued due to hypotensive episodes. Guanfacine extended release 1 mg at bedtime was also tried, but it did not relieve her symptoms. Finally, on arriving to the most probable conclusion that the tics might be secondary to quetiapine, which is not a common offending agent to cause tics, the

patient was slowly weaned off quetiapine down to 50 mg and then up to 25 mg over the course of the next 2-3 days. Drastic improvement in patient's tics was noted, and when the patient was finally weaned off her quetiapine, her tics completely resolved by the end of her hospital stay. The patient was started on buspirone 10 mg twice daily along with oxcarbazepine 300 mg twice daily and trazodone 75 mg at bedtime to address her anxiety, mood lability and insomnia respectively. All of these medication changes were made once the tics had resolved. The patient had no other pertinent medical or surgical history. The patient did not have a previous history of side effects from her psychotropic medications including extrapyramidal side effects. To the best of our knowledge, this is the first reported case of a patient developing tics on quetiapine re-initiation following an overdose on it. Previous case reports have been noted in patients who were on maintenance doses of quetiapine or lamotrigine [8,9,11,12].

## Discussion

Quetiapine, Sertraline, and Lamotrigine, have been previously documented to have induced tics in a pediatric patient at therapeutic dosages [8,11-13]. However, to our knowledge, there have been no reports of quetiapine, lamotrigine, or sertraline overdoses to have induced tics in a pediatric patient. Determining the etiology of tics was challenging, as the overdose involved three different medications. We took a systematic approach to establish the association of tics with quetiapine. The clinical picture is complicated by polypharmacy, hypoxic injury, and overlapping phenomenology of tics and EPS, which are common side-effects of antipsychotic medications.

## Plausible explanation

The tics appeared after restarting quetiapine and disappeared with lowering the dose. Confounding medication lamotrigine and sertraline are less likely causes, as the timeline

is more consistent with quetiapine re-initiation. At physiological level, sertraline, an SSRI, and lamotrigine, a sodium channel blocker, are contrary to the most recognized hypothesis of dopaminergic dysregulation in tics. The patient experienced cardiac arrest requiring CPR and raising the concerns for a hypoxic injury to basal ganglia or thalamic structures. In our case, initial CT scan of the brain showed no abnormalities. In case of hypoxic-injury, one would expect a longer recovery process with more complicated neurological sequelae; however, in our case, tics immediately resolved after lowering quetiapine. Based on the careful evaluation, we believe that tics are most likely associated with quetiapine overdose and then subsequent reinitiation.

## EPS possibility

A potential side effect of Quetiapine is the development of Extrapyramidal Symptoms (EPS) [14]. EPS are movement disorders that can be induced by dopaminergic medications, of which the antipsychotics are the largest group [14-16]. Therefore, we considered the possibility of acute EPS that could account for the newly observed movement and phonic behaviors. However, the behavior was isolated to the face and neck, not accompanied by an urge to move, did not mimic movements characteristic of EPS, and normal vital signs, making the clinical picture more indicative of tics than EPS.

## Why Quetiapine

Quetiapine is classified as an atypical antipsychotic. It has antagonistic activities at serotonin, dopamine and adrenergic systems. Quetiapine is also a potent antihistaminergic drug. At low doses, it has antihistaminic and adrenergic blocking agent. In the medium dose range, it binds to the adrenergic and serotonin receptors. At the higher dose ranges, the drug provides dopamine blocking action, making it useful in psychotic disorders [17]. The abnormalities in dopamine transmission have an important role in pathophysiology of tics in

Tourette disorder [18]. The role of dopamine in pathophysiology of tics is supported by multiple fMRI studies and clinical observations reported in previous case studies [8,9].

## Dopamine Supersensitivity

Dopamine supersensitivity, long term D2 suppression leading to increased sensitivity at postsynaptic D2 receptors, is widely believed to be the mechanism involved in antipsychotic associated tics. Given the low dose of quetiapine and unknown period of use, this is less likely. Other potential mechanisms could be involved. The mechanism most likely to occur at a low dose is an imbalance of presynaptic and postsynaptic dopamine antagonism, that is more presynaptic dopamine release than postsynaptic antagonism [19,20]. Another possible mechanism could be involvement of adrenergic system. Tics have been successfully treated by alpha-2 adrenergic agonists, leading to possibility of development of tics in case of antipsychotic's high affinity at adrenergic receptors, as quetiapine [21].

## Conclusion

This case has the important clinical implication of keeping an open mind to lesser-known side effects when prescribing psychotropic medications. Quetiapine, which is one of the lesser-known agents to cause movement disorders and tics, is often used as a treatment for tics in patients with Tourette's disorder [22]; however, was noted to be the offending agent leading to significant tics in this patient. It is important for clinicians to pay careful attention to the timeline and chronology of events when prescribing these complex medications. Another important learning objective is to be more mindful of worsening of mental health crisis in teenagers in the times COVID-19 and be mindful of children and adolescents who were either diagnosed with COVID-19 and had worsening of their mental health in context of mandatory quarantine or otherwise feel trapped because of social distancing protocols [23].

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DOI: <https://doi.org/10.36811/ijpmh.2021.110011>

IJPmh: Mach-2021: Page No: 10-15

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