


Baclofen Withdrawal–Induced Psychosis in the Setting of Renal Insufficiency

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Abstract

Baclofen is used to treat muscle spasticity, acting at GABA B receptors in the central nervous system. The abrupt cessation of baclofen causes baclofen withdrawal–induced psychosis. The risk is exacerbated if the patient has renal insufficiency or if the drug has been taken for a long time at high doses. Gradual tapering of baclofen usually does not produce symptomatic adverse effects. However, abrupt termination of the drug, especially in an inpatient hospital setting, can lead to symptoms such as increased spasticity, agitation, confusion, hallucinations, and seizures. We present a case of a patient who initially presented with seizures and experienced hallucinations after abrupt cessation of the medication. She had baseline chronic kidney disease but presented with acute worsening of her renal function. Impaired renal function decreases baclofen clearance and causes increased concentration of baclofen in circulation. This put the patient at higher risk of developing baclofen withdrawal, even at a lower dose.

Keywords

baclofen; withdrawal, psychosis, renal insufficiency

Introduction

Baclofen is a centrally acting γ -aminobutyric acid (GABA) agonist with clinical indications in treating spasticity and rigidity.¹ Sudden withdrawal of baclofen has been found to reveal a range of adverse reactions, including behavioral, perceptual, emotional, and movement disturbances.³ Given that oral baclofen is renally excreted, insufficiency of the renal system can cause increased drug concentrations and predispose the patient to withdrawal if abruptly stopped, a phenomenon commonly seen in the inpatient setting. This case report demonstrates the clinically significant consequence of psychosis in withdrawal of oral baclofen in the setting of renal insufficiency.

Case Presentation

The patient is a 58-year-old woman with a past medical history of cerebrovascular accident (CVA) with left-sided hemiplegia and associated spasticity, chronic kidney disease (CKD), and hypertension who was brought to the hospital for a witnessed tonic-clonic seizure and found to have incidental COVID-19 infection. Collateral obtained from the daughter reported that the patient was found on the bed confused, frothing at the mouth, and had twitching muscles that lasted approximately 10 to 15 seconds, subsequently in a

post-ictal state. The review of systems was negative for headache, dizziness, tongue biting, and urinary incontinence. Her last seizure episode was 8-years ago secondary to alcohol withdrawal. Before that episode, she had no seizures and remained seizure-free with a solid commitment to her sobriety. She has a past medical history of CKD stage 3 and hypertension. Her home medications were cholecalciferol 50 μ g, aspirin 81 mg, baclofen 20 mg twice daily, hydralazine 25 mg twice daily, and metoprolol tartrate 25 mg twice daily. The family reported that the patient is compliant with all home medications. She is a daily smoker of 0.25 packs/day and denies illicit drug use.

Physical examination revealed left-sided weakness and was otherwise unremarkable. On initial encounter, vitals were as follows: the patient had a temperature of 36.7°C, a heart rate of 93 bpm, a blood pressure of 164/90 mm Hg, a

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respiratory rate of 19 breaths per minute, and oxygen saturation of 95% on room air. Labs demonstrated an acute-on-chronic kidney injury with elevated creatinine of 2.80 mg/dL with a blood urea nitrogen (BUN) of 45 mg/dL. The patient's NasalSwab returned COVID-19 positive. Computed tomographic head/brain without contrast showed moderate parenchymal volume loss out of proportion to age but no acute intracranial findings. The patient was started on levetiracetam in the emergency room, and a sonogram of the abdomen was performed. The patient was kept nothing by mouth until bedside swallow evaluation was completed. The patient was admitted to the medical floor for further management.

The patient was accepted to the medical floor and was at baseline and alert and oriented $\times 3$. Renal ultrasound done on the day of admission showed no acute pathology. Neurology was consulted on the same day, and recommended magnetic resonance imaging brain seizure protocol, EEG, and levetiracetam were held until electroencephalogram (EEG) was performed. Nephrology was consulted on day 2 of admission and noted an acute kidney injury (AKI) likely multifactorial, including prerenal azotemia and acute tubular necrosis. On day 4 of hospitalization, the patient was disoriented to time and situation and had hallucinations. She reported seeing individuals in her room and believed she was in the hospital's morgue. She was disoriented to time and situation. Her mental status improved, and her hallucinations resolved after she was restarted on baclofen at 10 mg twice a day. The patient was continued on baclofen at 10 mg twice a day and was started on low-dose Ativan every 6 hours. The patient was mentating well, and her hallucinations resolved on day 6, and was downgraded to the floor.

Discussion

Oral antispasmodics are commonly prescribed to reduce muscle tightness and spasms in patients with a known CVA associated with spasticity. Oral baclofen, a GABA B agonist, exerts its effects at the spinal cord level, making it the first-line treatment for spasticity.¹ Patients with baclofen withdrawal often exhibit neurologic symptoms or mental status changes similar to alcohol withdrawal, which sometimes leads to mistaking baclofen withdrawal for alcohol withdrawal.² Factors influencing vulnerability to baclofen-withdrawal delirium include the duration of exposure to the medication and the abruptness of baclofen cessation.³ According to a single published case report from 1986, using high-dose baclofen chronically, patients with CKD are at increased risk of baclofen withdrawal-induced psychosis.⁴

The patient presented in this case had a previous CVA with associated hemiplegia and spasticity, for which she was on oral baclofen 20 mg twice daily for 4 years. Not only does this patient have a history of chronic baclofen use, but she also was found to have acute-on-chronic kidney injury. Her

labs demonstrated an AKI with elevated creatinine of 2.80 mg/dL, increased BUN of 45 mg/dL, and a creatinine clearance of 28 ml/min. Although she was not prescribed significantly high doses of baclofen, her acute-on-chronic kidney injury inhibits the drug's metabolism, causing increased baclofen levels. The liver is responsible for 15% of baclofen clearance. In total, 69% to 85% of baclofen is excreted intact in the urine.⁵ Glomerular filtration rate is the primary determinant of baclofen filtration, and creatinine clearance is similar to baclofen clearance.⁶ Impaired renal clearance of baclofen increases the concentration of baclofen in circulation, leading to increased baclofen levels. This leads to an increased amount of the drug entering the central nervous system. When baclofen is abruptly stopped, it causes an abrupt reduction in GABA B activity, with symptoms developing within 12 to 72 hours after the baclofen cessation.⁷ Our patient was put on nothing by mouth status with abrupt cessation of baclofen therapy. Shortly thereafter, she experienced hallucinations and seizures. Hallucinations and seizures occur more commonly if the drug is abruptly withdrawn.^{8,9}

Treatment approaches consist of reinstatement of baclofen in most cases, and occasionally this is combined with adding antipsychotics and benzodiazepines.^{3,10}

Reinstating the offending drug led to the hallucinations, making baclofen withdrawal a likely etiology of her psychotic symptoms. This would not rule out alcohol withdrawal as baclofen is used to treat acute alcohol withdrawal syndrome and delirium tremens.¹ Although she has a history of alcohol use, the patient has refrained from alcohol use for many years and denied any current alcohol use. Thus, alcohol withdrawal-induced hallucinations are less likely. Infection was less likely as the patient presented with stable vital signs and had no other clinical signs suggestive of infection. The patient was afebrile on presentation and saturating well on room air. She had no signs of symptomatic infection, making an infectious etiology of her hallucinations unlikely.

Conclusions

Baclofen withdrawal may exhibit an array of signs and symptoms such as disorientation, hallucinations, impaired thought processes, abnormal movements, and seizures.^{9,10} Baclofen withdrawal and toxicity may be underdiagnosed and need to be considered in patients with impaired kidney function who present with such symptoms. It is crucial to rule out other etiologies, past medical or psychiatric history, and other pharmacological causes. Although symptomatic management of withdrawal symptoms with antipsychotics and benzodiazepines has been demonstrated, reinstating and slowly tapering off baclofen has been shown to be a more favorable and effective approach in the resolution of psychotic symptoms.

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Ethics Approval

Our institution does not require ethical approval for reporting individual case or case series.

Informed Consent

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

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