


Severe Case of Oral Baclofen Withdrawal Resulting in Mechanical Ventilation

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Abstract

Abrupt baclofen withdrawal may be life-threatening with varied neuropsychiatric manifestations. We present a case of baclofen withdrawal necessitating intubation. A 58-year-old female with a history of undiagnosed muscle spasticity presented with worsening extremities tremors, paresthesia, and weakness for 2 days. Initial vitals included temperature 103 F, tachycardia, hypertension, and tachypnea. Examination revealed coarse tremors of all extremities. Inflammatory markers, blood, and urine culture were negative. Head and spine imaging were non-diagnostic. Meningitis and seizure were ruled out. She continued worsening with hallucinations, hyperpyrexia, ocular clonus, and profound muscle rigidity. The patient was intubated for respiratory distress and transferred to intensive care unit (ICU). Further history revealed running out of oral baclofen 3 days ago. Baclofen was restarted with symptomatic improvement. The patient was extubated after 2 days and discharged to a rehabilitation facility. Oral or intrathecal baclofen is thought to inhibit spinal nerves reducing muscle spasm and pain. Abrupt stoppage causes activation of dopamine and noradrenergic receptors causing muscle spasms, tremors, hyperpyrexia, delusions, hallucination, and delirium. Severe cases can mimic meningoencephalitis, seizure disorder, or neuroleptic malignant syndrome. Symptoms usually develop in 1 to 3 days of cessation and can be life-threatening if unrecognized timely. Treatment includes supportive therapy, re-administration of baclofen, or use of benzodiazepines, propofol, dexmedetomidine; however, no specific guidelines have been established. To the knowledge of the authors, this is the first case of oral baclofen withdrawal requiring intubation. We found only 3 reported cases of intrathecal baclofen withdrawal necessitating intubation.

Keywords

baclofen, baclofen withdrawal, intubation, muscle spasticity, tremor

Introduction

Baclofen is a commonly used medicine in patients with severe muscle spasticity, but symptoms of withdrawal can often be missed. Abrupt withdrawal of baclofen regardless of the route of ingestion may be life-threatening and can present with varied neuropsychiatric manifestations. The symptomatic presentation can mimic various clinical scenarios like severe sepsis, meningitis, neuroleptic malignant syndrome, seizure disorder, or alcohol withdrawal. Here, we present a severe and rare case of oral baclofen withdrawal in a middle-aged female necessitating endotracheal intubation.

Case Presentation

A 58-year-old female with history of hypertension, stage 3 chronic kidney disease, undiagnosed muscle spasticity presented to the emergency department (ED) with a complaint of worsening upper extremities tremors associated with paresthesia, limb weakness and pins and needle sensation on her upper and lower extremities for 3 days. ED vitals were

significant for temperature of 103 F, tachycardia to 103 beats per minute, hypertensive to 150/90 mmHg, tachypneic to 21 breaths per minute saturating 97% in room air. Patient was ill-appearing with coarse tremors noted on all 4 extremities. Neurology examination revealed $\frac{3}{5}$ strength in bilateral upper extremities and $\frac{4}{5}$ strength in bilateral lower extremities with decreased sensation in all 4 extremities. Lungs were clear to auscultation. Initial impression was sepsis versus fever of unknown origin and the patient was started on broad spectrum antibiotics with cefepime, vancomycin, and metronidazole. Laboratory work including white blood cell (WBC) count, lactic acid, inflammatory markers

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were non-significant. Blood, urine and respiratory cultures were negative. Lumbar puncture and cerebrospinal fluid analysis ruled out meningitis. Chest x-ray and abdominal ultrasound were unremarkable. Magnetic resonance imaging of head and spine were non-diagnostic and thus ruled out intracranial pathology and osteomyelitis of spine. Neurology was consulted and electroencephalography (EEG) was done which ruled out seizure disorder. Neurology also ruled out Guillain Barre Syndrome and Alcohol withdrawal syndrome. Toxicology was consulted with the concern of anticholinergic toxicity which was ruled out.

On day 4 of the hospital stay, she continued to have persistent fever with worsening mental status to the extent of experiencing visual hallucinations, hyperpyrexia with ocular clonus, profound muscle rigidity despite being on broad spectrum antibiotics. On examination she was somnolent, was unable to follow command, and had continuous tremors. A total 7 mg of lorazepam and 250 mg of phenobarbital was given with no improvement. Intravenous haloperidol was given which caused further decline in the patient's condition. Rapid response was called, and the patient was evaluated by the intensive care unit (ICU) team. She continued to be minimally responsive with tachypnea to 40 breaths/minute. ABG showed pH of 7.3, PCO₂ of 28.6, PaO₂ of 70 on room air. Patient was intubated due to respiratory distress and continued worsening of the mental status and transferred to the ICU with possible diagnosis of neuroleptic malignant syndrome versus baclofen withdrawal. Laboratory work for serum creatinine kinase and lactic acid was within normal range. Bromocriptine was started for possible neuroleptic malignant syndrome with no improvement of symptoms. In the ICU, history and home medications were reviewed again. It was found that the patient was on oral baclofen 10 mg 3 times a day for the last 2 years and she was not taking it for the last 3 days. Baclofen was restarted immediately followed by the resolution of fever, improvement in mental status and complete cessation of tremors in the next 48 hours. Patient was extubated after 2 days. She was transferred to the medical floor and, then discharged to an acute rehabilitation facility.

Discussion

Baclofen is a gamma amino butyric acid (GABA) derivative thought to inhibit the reflex of the spinal nerves reducing muscle spasm and pain.^{1,2} Baclofen can be administered orally or intrathecally. Baclofen withdrawal can be intentional or unintentional. Risk factor for baclofen withdrawal includes duration and abrupt interruption as seen in our patient. Half-life of baclofen is 3.5 hours and 85% or more of baclofen is excreted by the kidney after 24 hours of drug consumption, remaining is excreted in feces. The baclofen plasma to cerebrospinal fluid (CSF) ratio is variable in human beings when used orally, so withdrawal may not be dose-dependent.²⁻⁴ On an average, 5 months of baclofen consumption may result in delirium when withdrawn.³

Abrupt stoppage of baclofen causes activation of autonomic system by loss of inhibition of monoamine pathway causing activation of dopamine and noradrenergic receptors.⁴ The symptoms of baclofen withdrawal include muscle spasm, tremors, hyperpyrexia, delusions, hallucination, and delirium. In severe cases, it can cause rhabdomyolysis and presentation can be similar to meningoencephalitis, seizure disorder, or neuroleptic malignant syndrome as seen in our case.⁴ The symptoms of withdrawal usually last for 1 to 3 days. It can be life threatening if not recognized early.⁵ It has been found that patients on oral baclofen usually present with worse delirium than patient on intrathecal baclofen pump because pump failure is recognized early but patient on oral baclofen may not seek medical help unless they are symptomatic.⁴

To the knowledge of authors, this is the first case of oral baclofen withdrawal requiring intubation. From the literature review, till date, the authors could find 3 cases of intrathecal baclofen withdrawal requiring intubation due to intrathecal baclofen (ITB) pump failure. All 3 patients presented with increased spasticity; however, delirium and hallucination were not reported in any cases.⁶⁻⁸ Unlike our case, withdrawal was suspected early; however, no improvement was seen despite receiving oral baclofen.^{6,7} Like our case, patients presented with hyperthermia, tachycardia, hypotension, and respiratory distress requiring mechanical ventilation. As seen in our case, these patients showed no improvement with benzodiazepine and broad-spectrum antibiotics.⁶⁻⁸ Two of 3 cases were complicated with multiorgan failure.^{6,7} The ITB pump was restarted, and the patients eventually returned to a full functional baseline as early as 2 days to latest by 3 months of hospital stay.⁶⁻⁸

In a case review of 23 cases by Leo and Baer, delirium resolved after restarting baclofen and none of them had residual symptoms. Our patient's symptoms resolved in 48 hours after re-starting home dose of baclofen.⁴ Treatment options may involve re-administration of baclofen along with supportive therapy including intravenous hydration, antipyretics, anti-epileptics, benzodiazepines, propofol, or dexmedetomidine; however, no specific guidelines have been established for management of baclofen withdrawal till date.^{5,9} When a decision is made to stop baclofen, it is advised to taper gradually to avoid withdrawal symptoms.¹⁰

Conclusion

Baclofen is a very commonly used medication. When not reviewed properly at admission, discharge or at clinic; the baclofen withdrawal can be easily ignored. This simple error has the potential to present as a life-threatening complication. We presented this article to emphasize the severity and importance of early diagnosis of baclofen withdrawal which can easily be missed, neglected, or misdiagnosed. The author also wants to emphasize the need for more research in this

field as currently there are no robust and well-defined guidelines for the management of baclofen withdrawal.

Authors' Note

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Ethics Approval

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


Informed Consent

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References

1. Meythaler JM, Steers WD, Tuel SM, Cross LL, Haworth CS. Continuous intrathecal baclofen in spinal cord spasticity: a prospective study. *Am J Phys Med Rehabil.* 1992;71:321-327.
2. Alvis BD, Sobey CM. Oral baclofen withdrawal resulting in progressive weakness and sedation requiring intensive care admission. *Neurohospitalist.* 2017;7(1):39-40.
3. Terrence CF, Fromm GH. Complication of baclofen withdrawal. *Arch Neurol.* 1981;38(9):588-589.
4. Leo RJ, Baer D. Delirium associated with baclofen withdrawal: a review of common presentations and management strategies. *Psychosomatics.* 2005;46:503-507.
5. Coffey RJ, Edgar TS, Francisco GE, et al. Abrupt withdrawal from intrathecal baclofen: recognition and management of a potentially life-threatening syndrome. *Arch Phys Med Rehabil.* 2002;83:735-741.
6. Reeves RK, Stolp-Smith KA, Christopherson MW. Hyperthermia, rhabdomyolysis, and disseminated intravascular coagulation associated with baclofen pump catheter failure. *Arch Phys Med Rehabil.* 1998;79(3):353-356.
7. Mohammed I, Hussain A. Intrathecal baclofen withdrawal syndrome- a life-threatening complication of baclofen pump: a case report. *BMC Clin Pharmacol.* 2004;9(4):6.
8. Sampathkumar P, Scanlon PD, Plevak DJ. Baclofen withdrawal presenting as multiorgan system failure. *Anesth Analg.* 1998;87(3):562-563.
9. Ross JC, Cook AM, Stewart GL, Fahy BG. Acute intrathecal baclofen withdrawal: a brief review of treatment options. *Neurocrit Care.* 2011;14:103-108.
10. Terrence CF, Fromm GH. Complications of baclofen withdrawal. *Arch Neurol.* 1981;38(9):588-589.