

Case Report

Extended Phenobarbital Taper for the Management of Recurrent, Delayed Benzodiazepine Withdrawal Syndrome in a Patient with Acute Alcohol Use Disorder

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- Withdrawal
- Delayed
- Protracted
- Phenobarbital

Abstract

Background: Alcohol withdrawal and benzodiazepine withdrawal present in similar fashions, but can be difficult to differentiate with a muddled history of polysubstance use and psychiatric disorders especially in acute settings.

Case presentation: We report the case of a 44-year old man with history of Bipolar disorder who presented with acute onset delirium, visual and auditory hallucinations, and autonomic instability after years of heavy alcohol and benzodiazepine use. He was unresponsive to benzodiazepine therapy, yet had profound improvement with a 7-day phenobarbital taper. Unfortunately, with completion of therapy he continued to present with intermittent episodes of agitation, delirium, and persistent hallucinations. This case outlines the necessary importance of a clear historical timeline and the variability of presentation of withdrawal when confronted with polysubstance abuse. It was eventually concluded that the etiology of presentation was attributed to alcohol withdrawal syndrome with subsequent prolonged benzodiazepine withdrawal.

Conclusions: It remains a difficult task to correctly identify alcohol versus benzodiazepine withdrawal, especially when a prior psychiatric diagnosis could be clouding clarity of diagnosis. Importance remains on a thorough history with emphasis of timeline and detailing of drug use. Benzodiazepine withdrawal can present with various symptomatic patterns with variance in timing after discontinuation of the drug.

ABBREVIATIONS

AWS: Alcohol Withdrawal Syndrome

INTRODUCTION

Alcohol and benzodiazepine use disorder results in a direct alteration in gamma-aminobutyric acid (GABA) neurotransmission and its receptor complex. As an inhibitory neurotransmitter, heightened GABA activity leads to widespread decreased neural signaling. Thus, leading to clinical symptoms such as somnolence, syncope, slurred speech, depressed respiratory effect, ataxia, and many others. Withdrawal from these drugs allows for an increase in NMDA-receptor activity due to lack of inhibition, as well as a dopaminergic surge. It has been proposed that during active drug use, neurons will compensate for the inhibition of excitatory NMDA receptor activity by upregulating the number of NMDA receptors in the brain. Sensibly, withdrawal of such drug(s) allows for excess

excitatory stimulation resulting in symptoms such as diaphoresis, autonomic instability, psychomotor agitation, with possible confusion or hallucinations.

With an increase in Emergency Department visits involving the non-medical use of sedative hypnotics, it is of more importance than ever to obtain the skills to recognize use patterns, physical dependence, or withdrawal of these substances.

CASE PRESENTATION

A 44-year old male presented to the Emergency Department for alcohol withdrawal presenting with symptoms of altered behavioral status and acute-onset delirium. He was tremulous and anxious with intermittent episodes of agitation. He admitted to having vivid visual, tactile, and auditory hallucinations. While in the ED, the patient was found to have aggressive outbursts nonresponsive to Alprazolam, Midazolam, and Diazepam. At this point in time he was transferred to the Medical Intensive Care Unit

for airway protection via intubation as well as successful sedation with Propofol and Dexmedetomidine. He was transitioned in a timely fashion to a phenobarbital taper while in the MICU. After being extubated and weaned from mechanical ventilation 2 days following, imaging studies were ordered. On physical exam, decreased breath sounds and bilateral crackles were heard upon auscultation of the lung fields. A chest x-ray suggested atelectasis and/or the possibility of aspiration pneumonia. Sputum cultures confirmed pneumonia with both Gram-negative bacilli and gram-positive cocci grown. He was treated appropriately.

He was then transferred to an adult inpatient medicine service due to stability and termination of behavioral threat. The patient began to complain of shortness of breath and orthopnea. An Echocardiogram performed on this floor resulted in the new diagnosis of Congestive Heart Failure with evidence of an ejection fraction of 25-30% and grade 1 diastolic dysfunction, as well as inferior vena cava dilation. Subsequently, the patient was placed on Lisinopril, Spironolactone, Aspirin, and Lipitor. It was recommended that he continue phenobarbital with necessary use of Ativan only with CIWA score greater than 8 or for seizure-like activity. He completed his 7-day taper of Phenobarbital and was transferred to the inpatient rehab service.

Three days following transfer, the patient began to have episodes of delirium, anxiety, and agitation. He was given 14 mg of Lorazepam with 10 mg of Haloperidol and was readmitted to the inpatient medicine service for work-up of delirium. With completion of the phenobarbital taper, it was not well understood why he was continuing to present clinically with intermittent hallucinations. For the next ten days on this floor, he continued to have intermittent episodes of autonomic instability, tremor, and agitation with temporary resolution by Lorazepam. On the 10th day of stay on this floor, the patient began to become extremely agitated, diaphoretic, and delirious. In order to once again protect his airway, the patient was intubated and transferred to the MICU. Following two days later, the patient was extubated and transferred to the Medicine service.

A complete psychiatric history revealed that the patient had a vast history of polysubstance use including Cocaine, LSD, Percocet, Ecstasy, Xanax, Suboxone, and heavy alcohol use. His addiction to alcohol began at 17-years of age due to family stressors at home. He stated he would drink several 6-packs of beers a night until he would "black out". At this age, the patient was also seeing a psychiatrist for a diagnosis that was unknown to him. He admits to attempting suicide at this time by means of self-harm. He describes taking Seroquel, Trazadone, and Haldol for a 4-month period. Without agreement of his Psychiatrist, he discontinued his regimen due to significant weight gain. He discontinued his mental health care at this time. At 19 years of age, the patient admitted to attempting suicide for the second and third times by means of overdosing on pain medication. He did not choose to seek out treatment even though he admits to anhedonia and a depressed mood. He begins to understand that his drinking is a problem and seeks out Alcoholic Anonymous with success in the program. He admits to staying sober until 39-years of age. At age 39, he fractured several ribs after a motor vehicle accident. He was later prescribed Xanax for anxiety and soon became addicted to it, with the seriousness of seeking out alternate sources when

he would run out of his prescription. He admits to purchasing 40 2-mg bars of Xanax monthly, with range of dose between 0-4 bars per day. He states he was also abusing Percocet as well. At this point in time he was re-referred to a Psychiatrist. He states being managed for diagnosis of Bipolar Type II and ADHD. He was prescribed Lamotrigine, Adderall, and Zoloft. At age 41, he was referred for Opioid detoxification treatment and began Suboxone therapy. At age 43, he discontinued previously prescribed psychiatric medications due to lack of access to the clinic. The most important details of his history for this specific admission were the fact that he had abruptly stopped taking Xanax two weeks prior to presenting in the ED. He admitted to cutting down in his alcohol use over two weeks prior to presentation, but that his last drink was on the day of presentation. He also emphasizes that his hallucinations began only a few days before presentation with no prior history or events.

With this new information, the patient was started on a Phenobarbital taper for 7 additional days, and Carbamazepine and Gabapentin were started for seizure prophylaxis for one month. The patient tolerated this regime very well and was discharged to the inpatient rehabilitation unit.

DISCUSSION

In this current case, it was important to review differential diagnosis of delirium tremens from recent cutting down of alcohol, delayed benzodiazepine withdrawal, and the possibility of a new psychotic break from previously diagnosed psychiatric conditions; or the co-occurrence of all three possible etiologies. Despite escalating doses of various benzodiazepines, his severe alcohol withdrawal syndrome showed no improvement. It is understood that treatment with benzodiazepines plus the use of Propofol increases the median time to Alcohol Withdrawal Syndrome (AWS) resolution from 5 days to 7 days [1]. This may have played a role in his continuing, intermittent symptoms.

After completing a 7-day phenobarbital taper status post extubation, he continued to be symptomatic. Alcoholic hallucinosis could be thought to play a role due to his classic paranoid schizophrenic presentation, but he presented with symptoms outlying just hallucinations. The onset of alcoholic hallucinosis is also seen one to two days after alcohol consumption has been terminated or decreased. Of note, these hallucinations have been found to recur for months to years in some patients [2]. An

Table 1: Risk Factors for Protracted/Delayed Benzodiazepine Withdrawal.

Risk Factors for Protracted Benzodiazepine Withdrawal
High Dosage
Increased duration of use*
Short half-life Benzodiazepines**
Concurrent depressant use
Improper management of initial withdrawal presentation***
Abrupt cessation
*Leading to GABA receptor tolerance
** Alprazolam, Lorazepam, Oxazepam, Triazolam
***Such as discontinuing therapy too early

atypical, delayed presentation of delirium tremens due to alcohol use was not necessarily congruent with the patient's history in terms of timing. The probability of delirium during alcohol withdrawal increases with varying risks which include CIWA scores above 15, recent withdrawal seizures, prior withdrawal delirium, older age, abuse of other depressant agents, and concurrent medical problems. This particular case did have many of these variables for which may have also increased his risk of delirium during AWS [3]. It has also been proposed that intake with a greater percentage of alcohol ratio per serving comes a greater imbalance in GABA and NMDA receptor expression. This may cause a prolonged presentation of withdrawal. But, this specific case involved mild to moderate ratios of alcohol percentage being consumed per history obtained [4].

Withdrawal from benzodiazepines has been shown to present in a differentiating timeline versus alcohol. Various authors have provided evidence for both an acute and protracted phase of benzodiazepine withdrawal. Acute withdrawal defines its boundaries between 5-28 days of length while protracted withdrawal symptoms can last up to 12 months or longer. Symptoms can vary and are described as being of psychological, somatic, and/or neurological nature. A more significant severity of acute benzodiazepine withdrawal has been associated with specific risk factors. These include heavier dosing, multiple depressants used concurrently, oral versus injected use, increased duration of use, and use of short half-life benzodiazepines [5-8]. Table 1 summarizes these risk factors.

In our case, the individual presented with acute-onset delirium secondary to acute alcohol withdrawal which preceded with a 2-week prior termination of benzodiazepine use. Symptoms

persisted after treatment of AWS due to benzodiazepine withdrawal. We conclude that in cases of co-occurring substance use disorder of alcohol and Benzodiazepine use it is essential to get a detailed history and collateral information to prevent recurrence of withdrawal symptoms and complications like seizures and acute respiratory failure.

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