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Psychosis in the Context of Sodium Oxybate Therapy

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CASE REPORTS

Sodium oxybate (brand name Xyrem) is a sodium salt of gamma-hydroxybutyric acid (GHB), an endogenous CNS depressant, which is an effective treatment of narcolepsy. As a drug of abuse, GHB produces severe psychiatric side effects and withdrawal. However, there are no reports of these effects when using clinically recommended doses. This paper presents a case of a patient who developed altered mental status while taking the recommended dose of sodium oxybate and subsequently became psychotic upon abrupt discontinuation of the medication. It is important for prescribers of sodium oxybate to be aware of the possibility of significant psychiatric side effects of this medication, as well as withdrawal symptoms, even at clinical doses.

Keywords: Sodium oxybate, narcolepsy, psychoses - substance-induced, substance withdrawal syndrome

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Sodium oxybate (SO; brand name, Xyrem) is the sodium salt of γ-hydroxybutyric acid (GHB), an endogenous fatty acid that is the precursor of GABA and found throughout the CNS.[1] GHB is a rapidly acting CNS depressant, acting primarily on the GABA-B receptor,[2] and has previously been used as a drug of abuse for effects of euphoria and increased sexual desire.[3]

SO is a very effective, FDA-approved treatment available for symptoms of narcolepsy with cataplexy.[4,5] Several case reports describe significant side effects and withdrawal in cases of abuse (with estimated doses from 43 to 144 grams).[5] However, in randomized, double-blind, placebo controlled clinical trials, therapeutic doses of SO (4.5 to 9 grams) were well tolerated, and the main side effects noted were nausea, dizziness, vomiting, sleepiness, and nocturnal enuresis.[5] After abrupt discontinuation of SO, the most common withdrawal symptoms included anxiety, dizziness, insomnia, and somnolence.[4,5]

REPORT OF CASE

The current paper presents a patient with narcolepsy who experienced severe behavioral side effects while taking SO and withdrawal after its abrupt cessation. Ms. W is a 25-year-old female with a history of anxiety (taking scheduled buspirone), Hodgkin lymphoma (in remission), and chronic pain, for which she takes oxycodone 10 mg twice daily, as well as 5-10 mg every 4 hours as needed. She also takes diazepam 2 mg three times daily as needed for muscle spasms. Ms. W had no known history of psychotic behavior or previous psychiatric hospitalizations. One month prior to her admission, Ms. W was started on SO for narcolepsy. Over the course of the month, her SO was titrated up to 9 grams per day in two divided doses.

On the day prior to her hospital admission, she was brought to the Emergency Department (ED) by her family with complaints of "bizarre behavior." Her parents expressed concerns that she was becoming increasingly confused over the past several weeks. Family also noted that Ms. W seemed more concerned with religion and had become more "intense" in her Bible studies. As Ms. W's change in mental status correlated with an increase in her SO dose, the ED physician recommended that Ms. W discontinue SO.

That evening, Ms. W's behavior worsened. She was making illogical statements (e.g., "my aunt is my mother") and she locked herself in the bathroom, refusing to come out. When Ms. W's mother broke into the bathroom she found her lying on the floor with a knife in her hand and two scissors in her bra. The following morning, Ms. W brought a bottle of wine to her 10-year-old daughter to drink it since it was the "blood of Jesus." Later that day, Ms. W's parents brought her back to the ED and she was admitted to a medical team, who consulted the psychiatry service.

In the hospital, Ms. W was delusional and hyperreligous. She stated that SO had "opened the secrets of the Bible to me." She also stated that she was "being sacrificed for all mankind." She reported seeing ladybugs, which were "a sign of hope." Ms. W denied any thoughts of suicide or of hurting anyone else, replying "I have love for all mankind."

Ms. W's SO was not restarted during her stay in the hospital, while her home pain regimen was continued, which included her scheduled diazepam. She was monitored on the Clinical Institute Withdrawal Assessment (CIWA) protocol, and received a single 1 mg dose of oral lorazepam. Prior to starting on CIWA protocol, she already had received four 2 mg doses of her scheduled diazepam. She did not receive any additional oxycodone for breakthrough pain symptoms while in the hospital.

During her admission she was tachycardic (HR = 120 bpm maximum), but otherwise stable. Extensive laboratory workup and neuroimaging did not show any abnormalities. Over the next 2 days, Ms. W's mental status improved; she was discharged home 3 days after admission and returning to her baseline mental status.

One week after discharge, Ms. W presented to her outpatient pulmonologist requesting a retrial of SO. Ms. W was started

on 4.5 grams in divided doses with titration occurring every 2 weeks to a maximum total dose of 7.5 grams. One month later, Ms. W presented to the ED complaining of increased anxiety and "feeling pins and needles all over me." SO was tapered and Ms. W's symptoms resolved. Three weeks later she returned to her pulmonologist requesting a third trial of SO. This time SO was started at 3 grams in divided doses with slow titration up to a total dose of 5 grams. Ms. W was instructed to only take the medication Sunday through Wednesday. She is now taking 6 grams in divided doses nightly without any significant psychiatric side effects noted.

DISCUSSION

Several previous case reports have found depression, including suicidal ideation,[6] and anxiety as side effects while taking therapeutic SO.[7] Currently the only cases in the literature documenting severe withdrawal are associated with abuse. There are no previous cases reported where a patient withdrew after taking the clinically recommended dose of SO. Cases of severe GHB withdrawal from illicit use include tachycardia, confusion, and both auditory and visual hallucinations.[7] These symptoms peak within the first 24 hours after discontinuation of GHB and may continue for up to one week. As GHB is related to GABA, withdrawal should be treated similar to alcohol withdrawal, with benzodiazepines.[1]

The confusion, anxiety, and perceptual disturbances ("pins and needles") that this patient experienced on initial presentation to the ED is consistent with other case reports of psychiatric side effects while taking SO.[7] The more severe psychotic withdrawal symptoms, such as visual hallucinations and religious delusions, which emerged after abrupt discontinuation of SO are also consistent with previously described cases of GHB withdrawal.[1] Of note, concurrent use of sedative medications such as benzodiazepines and opiates is contraindicated with SO, and their concurrent use may have contributed to three deaths reported in the literature.[8] The patient's use of these drugs during this episode could have contributed significantly to the development of her psychiatric symptoms and make deriving strong conclusions from this information alone problematic. Although this case appears to be a rare occurrence, it is important for prescribers of SO to be aware of the possibility of psychiatric symptoms in patients taking SO and severe withdrawal symptoms if abruptly discontinued.

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