Isolated Sleep Paralysis Associated with Gabapentin for Alcohol Use Disorder: A Case Report

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Introduction

- Gabapentin has many applications including seizure disorders, neuropathic pain, and off-label use in alcohol use disorder.[1]
- Gabapentin, a GABA analog, has been shown to affect sleep architecture including increasing slow-wave sleep and reducing N1 sleep; however, reported effects on REM sleep vary.[2]
- Sleep paralysis is a REM parasomnia characterized by an inability to initiate voluntary movement of the trunk and limbs, as an extension of REM muscle atonia into the awake state.[3]
- No previously reported cases in literature of gabapentin use associated with sleep paralysis.

Case Presentation

- 30-year-old male patient with a history of alcohol use disorder, post-traumatic stress disorder, and bipolar disorder was voluntarily admitted for anxiety and active suicidal ideation in the setting discontinuation of alcohol 5 days prior.
- He denied a history of complicated withdrawal and denied hallucinations or illusions.
- **Exam at initial presentation notable for:**
  - Vitals within normal limits.
  - Mental status exam: Fair eye contact; moderately increased kinetics with fidgeting; normal rate, rhythm, volume-for-room, and prosody of speech; anxious mood with congruent affect; fair organization of thought process; no evidence of loosening associations; thought content positive for suicidal ideation with vague intent, but negative for auditory or visual hallucinations.
  - Clinical Institute Withdrawal Assessment (CIWA) score 13, with positive scoring for anxiety and agitation, but notably no psychosis or vital sign changes.

Timeline

Admission Day 1

- **Initiated on gabapentin 300mg TID and prazosin 1mg QHS** for PTSD-related nightmares
- Continued on **home dose disulfiram 250mg daily**
- 5 days since discontinuing alcohol use

Medications Administered

- Disulfiram 250mg daily
- Gabapentin 300mg TID
- *(Divalproex not yet initiated)*
- Prazosin 1mg QHS
- Melatonin 3mg QHS
- Trazodone 50mg QHS

Day 2

- **Divalproex sodium 500mg initiated** for mood symptoms. Selected by shared decision-making with patient given history of bipolar disorder and strong preference to avoid SSRI/SNRI, despite not currently meeting criteria for manic episode.

Medications Administered

- Disulfiram 250mg daily
- Gabapentin 300mg TID
- **Divalproex 500mg QHS**
- Prazosin 1mg QHS
- Melatonin 3mg QHS
- Trazodone 50mg QHS

Day 3

- To address ongoing anxiety, alcohol cravings, and insomnia, **gabapentin was increased to 400mg/ 400mg/600mg dosing.**
- **Divalproex sodium increased** from 500mg to 1000mg QHS towards therapeutic dosing range.

Medications Administered

- Disulfiram 250mg daily
- **Gabapentin 400/400/600mg**
- **Divalproex 1000mg QHS**
- Prazosin 1mg QHS
- Melatonin 3mg QHS
- ***(Trazodone PRN, not given)***

- Patient reported paralysis upon awakening, in which he felt fully awake and aware of surroundings, but unable to move any part of his body. He also noted a sensation of suffocation and felt like his feet were being lifted from the bed.
- No history of similar symptoms, increased daytime sleepiness, cataplexy, or hallucinations.

Day 4

- Engaged in shared decision-making with patient and **first trialed discontinuing prazosin**, given patient's concern about sleep paralysis symptoms.

Medications Administered

- Disulfiram 250mg daily
- Gabapentin 400/400/600mg
- Divalproex 1000mg QHS
- **Prazosin discontinued**
- Melatonin 3mg QHS
- **Trazodone 50mg QHS**

- Patient reported that sleep paralysis symptoms recurred upon awakening.

Day 5

- **Gabapentin was then decreased back to 300mg three times daily**, as per previous dosing.
- Prazosin was not restarted.

Medications Administered

- Disulfiram 250mg daily
- **Gabapentin 300mg TID**
- Divalproex 1000mg QHS
- Prazosin discontinued
- Melatonin 3mg QHS
- Trazodone 50mg QHS

- Patient reported resolution of the symptoms of sleep paralysis, with no further recurrence during the rest of the hospitalization.

Day 6

- Divalproex sodium increased to 1500mg nightly to reach therapeutic dosing range.

Medications Administered

- Disulfiram 250mg daily
- Gabapentin 300mg TID
- **Divalproex 1500mg QHS**
- Prazosin discontinued
- Melatonin 3mg QHS
- Trazodone 50mg QHS

Day 7-11

- No recurrence of sleep paralysis throughout rest of hospitalization; no further change in medications.
- Discharged home following resolution of suicidal ideation and improved anxiety, with follow-up in alcohol use disorder intensive outpatient program.

Medications Administered

- Disulfiram 250mg daily
- Gabapentin 300mg TID
- Divalproex 1500mg QHS
- Prazosin discontinued
- Melatonin 3mg QHS
- Trazodone 50mg QHS

Bold text indicates change in medication or dosing from previous day.

Discussion

- Patient had several concomitant conditions associated with isolated sleep paralysis (substance use, psychiatric illness); however, these influences were chronically present without previous occurrence.
- Timing for initiation, discontinuation, and titration of other sleep-modifying agents (divalproex, prazosin, melatonin, and trazodone) did not correlate with symptom timing. Therefore, we hypothesize that gabapentin is likely a driver of these symptoms.
- Mechanistically, gabapentin is believed to act on presynaptic voltage-gated ion channels, including calcium and sodium, to enhance GABAergic inhibitory signals.
- Animal studies have shown that simultaneous inhibition of $GABA_A$/$GABA_B$/glycine prevents REM atonia, suggesting that co-activation of these pathways are involved in generating atonia.[4]
- It may be postulated whether an up-regulation of GABA and associated inhibitory effects secondary to gabapentin use could be associated with the onset of isolated sleep paralysis, a REM parasomnia.
- Both alcohol use disorder and PTSD have been shown to decrease baseline levels of GABA.[5-6]
- Gabapentin-induced increases in GABA have notably been shown to be inversely proportional to an individual's baseline level of GABA.[7]
- Therefore, it follows that for this patient, the relative increase in GABA from dose escalation of gabapentin could have played a role in triggering sleep paralysis in an already susceptible person.

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