Case Report

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Acute Primidone-induced Suicidality: A Case Report Running Head: Acute Primidone-induced Suicidality

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Abstract

Antiepileptic drugs (AEDs) have been previously linked to suicidality. Primidone, an anticonvulsant commonly used to treat essential tremor (ET), has been associated with increased suicide risk in patients with seizures, which themselves increase suicide risk. However, an association with acute suicidality in subjects without any predisposition has not been documented. We present a case of acute suicidality following initiation of primidone for erroneously diagnosed ET in a patient with Parkinson's disease but no past psychiatric history or risk factors. Suicidal ideation quickly resolved after primidone was discontinued. Patients receiving primidone should, therefore, be carefully monitored after treatment initiation.

Keywords: Primidone; Suicidality; Suicidal ideation; Anticonvulsant; Antiepileptic; Essential tremor (ET); Parkinson's disease; GABA

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Introduction

Studies have suggested that antiepileptic drugs (AEDs) may increase the risk of suicidal behavior soon after treatment initiation [1]. Thus, valproate, lamotrigine, and phenobarbital are associated with rare acute suicidality [2]. Primidone is a drug structurally related to phenobarbital [3]. It is indicated for focal and generalized tonic-clonic seizures, and is also frequently used in the treatment of ET [4]. To our knowledge, no case reports of suicidality with primidone have been published. Here we present a case of SN, a 75-year-old female with tremors, who became acutely suicidal upon initiating treatment with primidone.

Case Presentation

SN is a 75-year-old Caucasian female who was brought to the emergency department after she became acutely suicidal. She reported a one-year history of progressively worsening bilateral hand tremors. Tremors were present at rest and disappeared when she reached out for objects. They significantly impaired her ability to perform activities of daily living. She also described gait instability, the onset of which coincided with that of tremors. Five days prior to hospitalization, SN consulted a general practitioner who prescribed primidone. She took 25 mg daily for two days. On day three she woke up feeling severely depressed, and started thinking of taking her life by jumping out of the window. She was in the process of moving her furniture away from the window when she realized that she needed help, and called a friend who took her to the emergency department. SN had no known past medical or psychiatric history. There was no family history of depression or suicidality. She was divorced, with four children; retired and residing alone in her apartment. She never smoked or used alcohol and illicit drugs. SN displayed masked facies, symmetrical cogwheel rigidity, and high-amplitude hand tremors. Her gait was somewhat unsteady, with regular speed. On mental status exam, speech was fluent and non-pressured. She described her mood as "depressed". Affect was mood-congruent. There was no evidence of psychosis. Her thought process was well-organized. There was no looseness of association or flight of ideas. SN denied auditory and visual hallucinations. She reported suicidal ideation with a plan to jump out of the window; and denied homicidal ideation. Memory and cognitive function were intact. All routine laboratory and imaging studies were within normal limits. She was admitted for safety, and primidone was discontinued. By the next morning, SN was no longer suicidal, described her mood as "happy",

and believed that her recent thoughts and actions were completely out of her character. She was diagnosed with Parkinson's disease, and started on carbidopa/levodopa 12.5/50 mg every eight hours, which significantly improved her tremors and rigidity. Weeks after discharge, SN remained free of any suicidal symptoms.

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Discussion

Primidone is an anticonvulsant that is widely used in the treatment of ET, as it reduces tremor amplitude by up to 60% [4-7]. To our knowledge, no reports of acute primidone-induced suicidal thoughts or behavior in subjects without predispositions or risk factors have been previously published. Herein we described a case of an otherwise healthy female with previously undiagnosed Parkinson's disease who developed suicidal ideation after she initiated treatment for ET with primidone. AEDs are believed to increase suicidality in the initiation phase of treatment [2]. Even though our patient did possess dopaminergic imbalance at baseline, this would not explain acute suicidality. Given the sequence of events, and considering that she had no risk factors, it is highly likely that primidone played a role in the genesis of suicidality. Patients with Parkinson's may develop depression and suicidality; however, the onset is usually more insidious in nature. In 2008, the FDA alerted physicians of an increased risk of suicidal behavior in patients receiving anticonvulsants based on the meta-analysis of 199 randomized clinical trials looking at 11 AEDs (primidone was not included) [8]. In subsequent investigations, no relationship between suicidality and primidone could be identified when primidone was used as an anticonvulsant [2,9-11]. In one study, primidone was found to be associated with a nearly two-fold increase in suicidal ideation and activity; however, increased risk disappeared when the data were corrected for psychiatric predisposition for mood disturbance [12]. Most of the research on primidone was conducted on patients with established diagnoses of epilepsy. The link between suicidality and use of primidone in the non-antiepileptic scenario has not been investigated. Therefore, there is a need for future work in this area; especially, given considerable prevalence of ET. A number of mechanisms underlying AED-associated suicidality have been proposed. Increased activity of GABA is perhaps the most applicable to our case, since primidone is known to act on GABA receptors, thus, potentiating synaptic inhibition [2,9,13]. The exact mechanism by which GABA-induced inhibitory neurotransmission triggers acute changes in the mood leading to suicidality is still beyond our understanding. Independent of mechanisms, it remains important to recognize that primidone can be associated with suicidal ideation and behavior as has been demonstrated with other anticonvulsants. Further investigation is necessary in order to confirm the association between primidone and acute suicidality and to elucidate the mechanisms behind it, given the widespread use of primidone in the treatment of ET. It is unclear at this point whether having affective disorder or a neurodegenerative disorder at baseline is a risk factor for acute suicidality as suggested by the evidence presented in this case report. This could potentially be one of the topics for future research. Healthcare providers have to be cautious when prescribing this agent. Perhaps, warning patients about suicidality as a potential side effect, and using questionnaires to assess for depression and suicidality immediately after treatment initiation could help ensure patient safety.

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