Manic Episode Following Ingestion of Caffeine Pills: A Case Report

To the Editor: Among stimulants, caffeine is the most prevalent, and there has been some research on its neuropsychiatric effects. Caffeine increases motor behaviors and has a wake-promoting effect through its inhibition of adenosine receptors. Caffeine can also directly and indirectly affect mood through several mechanisms. Although caffeine has been associated with triggering psychotic episodes,[1] case reports and the literature lack consideration of caffeine use and episodes of mania. A survey of patients with mood disorders showed an association of caffeine use with bipolar spectrum patients.[2]

We present a case of a patient with a history of bipolar disorder who consumed a significant amount of caffeine prior to an acute manic episode.

Case report. Mr A, a 57-year-old man, presented to the emergency department (ED) in 2014 complaining of chest pain. He had been driving from Montana to Virginia on the interstate to visit his daughter and had taken 800 mg of caffeine pills during the drive to stay awake. Shortly after consuming the pills, he began experiencing palpitations and moderate, nonradiating substernal pain, which led him to call the Emergency Medical Service.

On arrival at the ED, the patient's speech was pressured and disorganized, and he had flight of ideas. He reported having been awake for about 72 hours, but it was unclear if he had consumed other caffeine-containing foods, such as coffee or energy drinks. He exhibited significant grandiosity, stating that he had been a Navy SEAL, NASCAR driver, and pilot and that he "was born in the sun." Physical examination results were positive for sinus tachycardia, but otherwise normal. In the ED, laboratory testing revealed normal complete blood count, thyroid-stimulating hormone, and comprehensive metabolic panel findings, as well as a negative urine drug screen.

Shortly after arrival at the ED, Mr A was placed under a temporary detainment order and was transferred to our inpatient psychiatry unit. Records obtained from the Montana Veterans Affairs hospital where he had been treated indicated that Mr A was a Navy veteran and had been diagnosed with *DSM-IV-TR* schizoaffective disorder, bipolar type. His last documented history of a manic episode was in 2012, and he had been successfully treated with quetiapine 600 mg at bedtime. He had been noncompliant with treatment for several months, and his caffeine intake occurred in the setting of treatment noncompliance.

Initially, on our service, Mr A was treated with fluphenazine 5 mg BID and diphenhydramine 25 mg BID. During his first several days of admission, he continued to exhibit significant manic and psychotic symptoms. Mr A also continued to be significantly agitated; his speech remained pressured and loud, he refused to keep his clothes on, and he defecated in the shower. On day 3, he was placed on quetiapine 600 mg at bedtime. Over the next few days, his condition improved substantially, with a decrease in grandiosity, calming of speech, and resolution of delusions. He was determined to be stable for discharge, and follow-up plans were made with the local Veterans Affairs psychiatry department for outpatient treatment.

Discussion. Caffeine is readily and rapidly absorbed from the gastrointestinal tract, and its hydrophobic chemical structure allows it to pass easily through the blood-brain barrier.[3] Caffeine is a stimulant and functions primarily through inhibition of adenosine A_1 and A_2 receptors, which causes downstream release of excitatory neurotransmitters and at higher doses can cause blockade of $GABA_A$ receptors.[4,5] In low doses, caffeine has mood-elevation properties,[4] most likely due to the interaction between adenosine receptors and dopaminergic receptors.[6] In a study of mice, caffeine was also shown to increase brain levels of serotonin.[7] Caffeine was linked to an increase in suicidality in a case report of a patient who consumed a very large amount of caffeinated energy drinks.[8] Specifically implicating caffeine use in mania is a case series in which 3 bipolar patients who were also cocaine users were hospitalized, stabilized, and discharged from the hospital.[9] Upon discharge, the patients heavily consumed caffeinated energy drinks, contributing to a relapse in manic and depressive symptoms.

Caffeine use can also cause a relapse of mania by another, more indirect mode, through disruption of normal sleeping patterns. As mentioned before, caffeine is often used to reduce fatigue and has been shown to improve alertness and performance of specific tasks. While it can reduce fatigue, caffeine does disrupt normal sleep and can cause or worsen insomnia. Cases of obstructive sleep apnea and other sleep-depriving conditions have been reported to cause complications in treating mania and have even been reported to trigger mania. These links and reports led to a hypothesis by Wehr et al[10] that sleep deprivation causes mania relapse. There is also an abundance of evidence linking sleep disturbance with mood disturbance.[11]

Considering caffeine's mechanism of action, and the chronological relationship between its consumption by our patient and his manic episode, it appears likely that caffeine intake contributed to his acute exacerbation, in the context of lack of sleep and medication noncompliance. Considering the wide use of caffeinated supplements and beverages, there is an increased need for further research with regard to caffeine use and bipolar spectrum disorders.

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