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A Physician's Attempt to Self-Medicate Bipolar Depression with N, N-Dimethyltryptamine (DMT)

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ABSTRACT

N,N-dimethyltryptamine (DMT) is a psychoactive substance that has been gaining popularity in therapeutic and recreational use. This is a case of a physician who chronically took DMT augmented with phenelzine in an attempt to self-medicate refractory bipolar depression. His presentation of altered mental status, mania, and psychosis is examined in regards to his DMT use. This case discusses DMT, the possible uses of DMT, and the theorized mechanism of DMT in psychosis and treatment of depression, particularly involving its agonist activity at 5-HT1A, 5-HT2A, and 5-HT2C. It is also important to recognize the dangers of self-medication, particularly amongst physicians.

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Bipolar disorder; DMT, N, N-dimethyltryptamine; phenelzine

Introduction

N,N-dimethyltryptamine (DMT) is a chemical compound found in plants such as *Psychotria viridis* and is used by South American shamans to produce a psychedelic drink known as ayahuasca (de Lima Osório et al. 2011). In clinical studies, it has been used to treat depression (de Lima Osório et al. 2015; Palhano-Fontes et al. 2014) and addiction (Liester and Prickett 2012). Within the past 10 years, a resurgence of attention to the antidepressant effects of DMT has resulted in tourists venturing on spiritual retreats to experience its potential benefits. DMT has a larger proportion of new users compared to other substances (24%) and a lifetime prevalence of 8.9% from data collected from a global drug survey (Winstock, Kaar, and Borschmann 2014). The use of DMT in treatment of depression remains speculative and the neuropsychiatric effects of chronic DMT use are unclear. The following report details a case of one psychiatrist's treatment of his own bipolar depression with DMT and phenelzine, which resulted in mania and psychosis.

Case report

A 40-year-old retired male psychiatrist with bipolar I disorder and no past medical history presented to the hospital with altered mental status. On arrival, the patient was nonverbal, combative, and required six security guards to restrain him. When less restrictive measures failed, he was given propofol 1,000 mg IV, ketamine 500 mg IM, midazolam 5 mg IV, diazepam 20 mg IV, and fentanyl 4 mg IV with minimal effect. The patient subsequently seized and was intubated for one day. Labs were significant for elevated transaminases, which peaked at an ALT of 151 IU/L and an AST of 237 IU/L. Creatinine kinase was also elevated at 3,868 IU/L. Additional medical workup, including a head CT, blood cultures, a urinalysis, a serum vitamin B12 level, a serum folate level, a syphilis screen, an HIV screen, a hepatitis screen, a thyroid stimulating hormone level, and lumbar puncture, was unremarkable.

Psychiatry was consulted after the patient's delirium resolved and he was medically stabilized as he exhibited symptoms of mania and psychosis. He was pressured in his speech, hyperreligious, and delusional. He believed that demons were leeching into his soul and asked the medical staff for an exorcism. It was recommended that the patient be admitted to the behavioral health unit for mood stabilization.

After thorough history was obtained from his family, it was revealed that the patient was self-medicating in order to treat refractory depression with DMT and phenelzine. The patient had one prior episode of mania and otherwise remained depressed for the majority of his life. He failed previous trials of selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, mood stabilizers, first-

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and second-generation antipsychotics, ECT, and ketamine. The patient took up to 1 g of vaporized DMT daily for the past six months. After experiencing some improvement in his depression, the patient added phenelzine 60 mg daily to his regimen three weeks before hospitalization to achieve a greater anti-depressant effect. His only other current medication was clonazepam 4–6 mg daily as needed for sleep.

The patient obtained phenelzine and DMT through "the dark net," a collection of online websites for illegal activity. The family confirmed that the patient exhibited some hypomanic symptoms, such as decreased sleep, increased religiosity, and erratic spending in the past month. However, he did not become overtly manic or psychotic until DMT, phenelzine, and clonazepam were abruptly discontinued 2–3 days prior to hospitalization. The patient was flying out of state and did not want to travel with an illicit substance.

He was treated with lithium and clonazepam to target mania, and paliperidone was added for psychosis. On treatment day 7, the patient's psychotic symptoms resolved. However, he remained hypomanic and was discharged home against medical advice on lithium 600 mg twice a day (level of 0.8 mmol/L), paliperidone 6 mg/day, and clonazepam 3.5 mg as needed for sleep. Outpatient follow-up was arranged for the patient, but his condition after discharge is unknown.

Discussion

We considered several possible etiologies in the differential diagnosis, including DMT or phenelzine activation of mania, phenelzine withdrawal, serotonin syndrome, and the natural course of bipolar disorder. DMT appears to be most directly associated with this patient's psychotic presentation, given his pattern of chronic use of high doses of DMT and his lack of previous history of psychosis and overt manic symptoms prior to DMT use. This patient reported use of up to 1 g of vaporized DMT daily for six months, which is an extremely large amount compared to dosages commonly reported. In a comparative study of oral and smoked administration of DMT, 25 mg doses of smoked DMT were used on two separate sessions (Riba et al. 2015). According to a specialized website, threshold dosages for smoked/vaporized DMT begins at 2–5 mg and strong dosages range between 40–60 mg (Erowid 2015).

DMT is a chemical compound found in over 50 varieties of plants and is a psychoactive substance that produces distinct hallucinations (Domínguez-Clavé et al. 2016). The hallucinations commonly reported by users are brief and often involve religious figures and spiritual features (Straussman 2000). DMT has very limited oral psychoactive properties due to its rapid metabolism by monoamine oxidase. In South America, a religious brew known as ayahuasca is produced from a DMT-containing plant, *Psychotria viridis*, in combination with a naturally occurring reversible inhibitor of monoamine-oxidase-A, *Banisteriopsis caapi*, to produce spiritual experiences (Domínguez-Clavé et al. 2016). Utilizing this drug interaction, our patient augmented DMT with phenelzine to inhibit monoamine-oxidase aldehyde dehydrogenase. This inhibition led to an increase in the N-oxidation pathway and prolonged the psychoactive effects of DMT (Riba et al. 2012).

The mechanism by which DMT causes psychosis or improves depression is still under study. DMT is structurally similar to serotonin and shows agonist activity at 5-HT2A and 5-HT1A receptor sites (Domínguez-Clavé et al. 2016). One study suggests that visual hallucinations are caused by 5-HT2A agonism (Valle et al. 2016). Other psychedelic compounds, such as LSD, psilocybin, and mescaline, also exhibit agonist action on 5-HT2A receptors (Gonazalez-Maeso and Sealfon 2009). A similar psychoactive compound, 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), and its active metabolite, bufotenine, produces hallucinations by its effect on the serotonin receptors, particularly 5-HT1A, 5-HT2A, and 5-HT2C (Jiang et al. 2013). Supporting this theory is a study in 5-HT1A knockout mice which demonstrated decreased hallucinogenic activity of 5-MeO-DMT (Van den Buuse et al. 2011).

The agonist action of DMT on 5-HT1A, 5-HT2A, and 5-HT2C may also explain its antidepressant effects. Other psychoactive substances which are 5-HT1A, 5-HT2A, and 5-HT2C receptor agonists have also been associated with positive mood (Sanches et al. 2016). In one open-label trial, 93% of 15 participants given intramuscular DMT reported relaxation (dos Santos et al. 2016). Another study of six healthy volunteers found that inhaled DMT increased positive mood (Riba et al. 2015). Additionally, 17 volunteers with recurrent major depressive disorder were given one oral dose of ayahuasca and evaluated with the Hamilton Depression Rating Scale (HAM-D), Montgomery-Asberg Depression Rating Scale (MADRS), Young Mania Rating Scale (YMRS), and Brief Psychiatric Rating Scale (BPRS). There were statistically significant decreases in HAM-D, MADRS, and anxious-depression BPRS subscale scores from day 1 to 21 after the administration of ayahuasca. In this study, ayahuasca was well-tolerated. Nausea and vomiting were the only adverse reactions reported (Sanches et al. 2016). There have been no published studies in regards to DMT use in bipolar depression and only one case report of a man who became manic after use of ayahuasca (Szmulewicz, Valerio, and Smith 2015).

After learning about some of these preliminary studies, our patient, who failed numerous trials of

other conventional alternatives, self-medicated with DMT. The rate of self-medication amongst physicians may be higher than expected. A questionnaire sent to 567 psychiatrists in 2007 indicated that almost 43% of psychiatrists would consider self-medication for mild to moderate depression, 7% would consider self-medication for severe depression, and 15.7% had treated themselves for depression (Balon 2007).

This case report has several practical implications. As DMT gains popularity, it is important to recognize its presentation and its psychological and physiological impacts. A systematic review completed in 2017 discusses three case series and six case reports of ayahuasca or DMT use associated with psychosis. Through this analysis, the authors reported that there were no prolonged cases of psychosis when ayahuasca or DMT was used in a controlled study setting. Most cases of prolonged psychosis involved a personal or family history of psychiatric disorders, concurrent use of other substances such as cannabis, or multiple uses of ayahuasca or DMT (dos Santos, Bouso, and Hallak 2017). This case highlights that patients with vulnerabilities such as personal or family history of psychosis, non-psychotic mania, or concomitant use of other drugs should avoid hallucinogenic intake. Additionally, this patient serves as a good reminder of the potential consequences of self-medication, especially amongst physicians.

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