Case Report

Iron Supplementation in the Treatment of Cocaine Use Disorder

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Abstract: Many drastic actions are taken by cocaine users for the sake of experiencing high dopamine levels, which depends on iron for its synthesis. Dopamine depletion and iron deficiency are also involved in the symptoms of restless leg syndrome (RLS). The intersecting biochemical pathways of cocaine use, iron deficiency, and RLS have not been adequately investigated. This case report reveals the successful treatment of a patient with these conditions. A 63-year-old male with a history of cocaine use disorder, insomnia, and RLS sought emergency care for suicidality. Upon admission, he was also found to be iron-deficient. He revealed that his RLS worsened when he attempted to abstain from cocaine. He also used alcohol to sustain the effects of cocaine when the cost of cocaine was too high. During hospitalization, his mood, cravings, and RLS were resolved with adjunctive iron supplementation as well as 300 mg of Wellbutrin. If iron-deficient, replenishment of adequate dopaminergic receptor density and function via supplementation may play an essential role in the prevention of cocaine use and cessation of cocaine withdrawal. Further research is warranted to validate these findings and understand the implications of iron supplementation in addiction medicine.

Keywords: iron deficiency; cocaine; substance use disorder

Introduction

Iron is one of the many cofactors involved in synthesizing monoamine neurotransmitters, including dopamine [1]. Iron deficiency can cause many health issues, including depression, headache, fatigue, and restless leg syndrome (RLS) [2,3]. Iron deficiency is also implicated in the downregulation of dopaminergic receptors, a process observed in chronic cocaine use [3,4]. As documented in the literature, stimulant use interferes with iron homeostasis, leading to iron deficiency in the periphery and accumulation in the globus pallidus [5]. Our patient is a 63-year-old male who presented with suicidal ideation, RLS, and chronic cocaine use. He was found to be iron deficient upon admission. The relationship between cocaine use, iron deficiency, and RLS appears significant due to their intersecting biochemical pathways and this patient's worsening RLS when abstaining from cocaine. The significance of these relationships is exemplified by his symptom resolution after iron supplementation and Ropinirole administration. This case report assesses the relationship between these factors and points to the possibility that addressing iron deficiency may decrease the risk of cocaine use and addiction.

Case Presentation

A sixty-three-year-old male with a history of cocaine use disorder was admitted for suicidal ideation and paranoia. He had not slept for the last five days, using alcohol and cocaine before his admission, and had been paranoid with fleeting suicidal thoughts with no thoughts or intent. On his first day, the patient was very paranoid and minimally engaged in the conversation. The patient was closely monitored with CIWA score in the context of his alcohol use. The patient slept well after receiving Haldol 5mg and Ativan 2mg intramuscularly.

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On day two, the patient was tired but was less paranoid. He denied any suicidal or homicidal ideation but slept throughout the day, staying isolated. On day three a detailed interview was conducted, where the patient explained he began using cocaine at the age of 30. He was sober from cocaine for ten years but had a recurrence of use two years ago, with inpatient services being required, one year ago, due to paranoia and decreased sleep associated with cocaine use. He explained that in the past 10 days he had been increasing his cocaine use. He expressed a significant strain on his relationship with his family, financial difficulties, and several recent hospitalizations for cocaine use. He was smoking $200 worth of cocaine daily creating financial strain. He then discovered that using alcohol and cocaine simultaneously would prolong the stimulant's effects. He also endorsed that he has less motivation and had a depressed mood along with feeling hopelessness for a long time triggering his cocaine cravings. Various treatment options were discussed, and he decided to start Wellbutrin in the context of his motivation and cocaine use. He had used Wellbutrin in the past and felt that it was the most helpful with his motivation but never was useful in the context of cocaine cravings. The patient was informed that it is off-label for cocaine use, and he expressed understanding after the benefits and side effects of Wellbutrin were discussed.

During his course in the hospital, the patient explained that whenever he stopped using cocaine, his RLS worsened, contributing to using again. The patient tested positive for severe RLS symptoms on the RLS scale. He endorsed occasional cravings for cocaine use along with a depressed mood while he was in the inpatient unit. Wellbutrin was titrated to 300 mg daily in the context of his depression, along with the initiation of Requip 0.5 mg daily for his RLS, and eventually was increased to 2mg by the end of his hospital stay. The patient underwent Iron labs and CBC. His hemoglobin was 13.9g/dl, (14-18g/dl) His iron panel showed a ferritin level of 24 ug/dL (reference range 55-175 ug/dL) and an iron saturation of 9% (reference range of 15-50%). As the patient suffered from iron deficiency, a 325 mg ferrous sulfate tablet was prescribed daily. An iron infusion was suggested during his stay in the hospital, but the patient refused it. Over the next few days, the patient reported improvement in sleep quality and mood, along with a reduction in cravings for cocaine. Over the next several days, the patient's mood improved, and he became hopeful about his recovery. He also noticed a suppression in symptoms related to his RLS. He was discharged on day seven to a rehabilitation center for further stabilization of his cocaine use disorder. In follow-up, he reported that with the continuation of his regimen, he had a sustained reduction in his cocaine cravings and has been sober from substances.

Discussion

Dopamine synthesis requires several iron-binding enzymes, including tyrosine hydroxylase [2]. Dopamine is a neurotransmitter implicated in many physiological functions, including pleasure, memory, and addiction. Cocaine use and addiction are thought to be driven by the accumulation of dopamine in neuronal synapses, especially in the striatum, which is responsible for reward behavior and habit formation. This dopamine release is an exaggeration of the physiological response to pleasurable stimuli. Repeated cocaine use may lead to downregulated D2 dopaminergic receptors as well as presynaptic dopamine release from neurons. This disruption occurs primarily in the orbitofrontal cortex, cingulate gyrus, and dorsolateral prefrontal cortex, triggering behaviors such as impulsivity and impaired executive function. Thus, with repeated cocaine use, dopaminergic cells will release dopamine in expectation of the drug as well as stimulate motivation to seek the drug [3] One technique to prolong the release of dopamine, as described above, is polysubstance use with alcohol and cocaine. When consumed together, the cocaine undergoes transesterification with ethanol to produce cocaethylene, which has a prolonged half-life and greater psychoactive effects than cocaine in isolation. Furthermore, as reported by the patient, the use of alcohol and cocaine together created prolongation of the stimulant effects, reducing the financial strain of his addiction. Additionally, this phenomenon alleviated the impact of cocaine cessation, including the worsening of his RLS. Another reason that individuals use the two substances together is to alleviate the anxiety, depression, and pain that occur after the high [6]. This polysubstance use is not well-studied but warrants future research due to its high appeal and many risks.

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One study assessed 44 chronic cocaine users and iron distribution throughout the body, finding that iron levels decreased significantly in the periphery. [5] Another study demonstrated that iron deficiency has been associated with decreased dopamine receptors and DAT activity in rats, supporting the hypothesis that iron deficiency reduces the sensitivity of the dopamine receptors [7], stimulating cocaine-withdrawal symptoms and worsening RLS. Our patient likely experienced both conditions simultaneously, as his RLS was worse while attempting to stop using cocaine. This mechanism, along with the patient's worsening RLS during cocaine cessation, also raises a question of whether iron deficiency and, thus, a reduced number and sensitivity of dopamine receptors increases a drive towards dopamine-producing substance use.

One systematic review suggested that fetal or infantile iron deficiency may lead to learning and memory deficits as well as increased emotional reactivity and mental health disorders. These findings may be associated with and predispose individuals to substance use disorders [8]. Identifying and treating his iron deficiency may be one of many factors that reduced his risk of cocaine addiction. Iron supplementation during cocaine withdrawal may be a necessary adjunctive therapy to replenish dopaminergic stores. When a patient elects to discontinue cocaine use abruptly, withdrawal symptoms will likely ensue. Anxiety, irritability, paranoia, and fatigue are common symptoms seen after cocaine cessation [9]. As described above, repeated cocaine use may decrease dopamine sensitivity, leading to dopamine accumulation and prolonging addiction. Thus, many of the withdrawal symptoms of cocaine are associated with dopamine depletion. A study by the National Institute of Drug Abuse assessed the use of amantadine, an indirect dopamine agonist, for the treatment of cocaine withdrawal in a 61-participant trial. They found that the amantadine treatment improves abstinence in very severe cocaine withdrawal. Amantadine is an indirect dopamine agonist that may increase dopamine release; our patient experienced this as part of his treatment plan [9]. Theoretically, any process that increases dopamine should ameliorate cocaine withdrawal symptoms [9]. Ropinirole, a rapidly absorbed dopamine agonist, was also used in the treatment plan and likely contributed to some relief by fully activating D2 and D3 receptors [10]. The combined actions of ropinirole, amantadine, and iron on dopamine levels in our patient likely worked synergistically to relieve his RLS.

In this case, we also have confounding variables, like using Wellbutrin, which can potentiate decreased cravings. Our patient has used Wellbutrin in the past but did not have any reduced cravings from it. At the same time, the patient has been suffering from RLS for a long time and also had psychosocial stressors, which might have increased his use of cocaine use. It is also noted that the father suffered from RLS with cocaine use disorder, which might be a genetic component. Despite all the above, our patient has decreased cravings and has been sober for the last two years after his RLS was addressed with Requip and iron supplementation.

Conclusion

This case report demonstrates a case of iron deficiency, cocaine-use disorder, and RLS, three conditions with overlapping biochemical pathways that were successfully treated with adjunctive iron supplementation. If iron-deficient, replenishment of adequate dopaminergic receptor density and function via supplementation may play an essential role in the prevention of cocaine use and cessation of cocaine withdrawal. It is crucial to consider the potential of iron deficiency in patients who present symptoms of tiredness and motivation, even in the absence of anemia. This consideration can lead to a more effective identification of the underlying cause and effective treatment, which might also help in the cocaine cravings. Furthermore, iron deficiency may perpetuate cocaine use and increase the severity of the addiction. This may demonstrate a need for an increase in screening for RLS and warrant iron panels in needed cases as a primary preventative measure of substance use disorders.

Further research is warranted to validate these findings and understand the implications of iron supplementation in addiction medicine. It is crucial to explore the potential connection between iron deficiency, restless leg syndrome (RLS), and cocaine use disorder. Conducting additional case studies can provide valuable insights for better intervention and treatment of these conditions.

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