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Selective Serotonin Reuptake Inhibitor Discontinuation for Psilocybin Treatment and Contributions to Alcohol Addiction Relapse:

A Cautionary Tale

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There is an expanding clinical trial portfolio investigating psychedelics for psychiatric conditions.[1] This case report reviews a recommendation, based on early clinical observations,[2] to discontinue selective serotonin reuptake inhibitor (SSRI) therapy before psilocybin treatment and the possible association with subsequent addiction relapse.

Case Report

Mr A is a 31-year-old businessperson with major depressive disorder, generalized anxiety disorder, and alcohol use disorder (AUD), seen for consultation. Timeline follow back for alcohol use for the preceding month was 28/30 drinking days with 5–6 drinks per occasion. Aspartate transaminase and alanine transaminase were slightly increased to 63 U/L and 56 U/L, respectively. Assessment based on the American Society of Addiction Medicine placement criteria recommended residential-level treatment for severe AUD.

Despite encouragement from his spouse and parents, he declined this recommendation but was agreeable to cutting down on alcohol use, starting escitalopram 10 mg daily, and long-acting naltrexone 380 mg monthly. With this treatment, he achieved euthymia and sobriety, early remission not in a controlled environment. He did choose to pursue a psilocybin "ceremony" (ie, intentional consumption of psychedelic mushrooms) based on his web-based research. While there was interest in pursuing abstinence, there was a curiosity about the experimental intervention.

After 8 weeks of escitalopram treatment, the SSRI was stopped 1 week before psilocybin treatment. The ceremony was associated with psychosensory activation and perceptual disturbance that "trees were walking." The experience was "incredibly gratifying" coming to terms with his previous lack of awareness of how lucky he was in his life. He also described a heightened awareness of cravings after psilocybin. He did not restart his SSRI but continued with monthly naltrexone (3 months total treatment). He had a heavy relapse to drinking (several days 5 drinks per drinking day) after 3 months of sobriety and within 2 and 3 weeks after psilocybin and stopping escitalopram, respectively.

Discussion

Several factors contributed to relapse. There is an established efficacy of SSRI plus naltrexone for treating co-occurring depression and AUD, from the standpoints of both significantly higher rates of achieving abstinence and longer delays to relapse, in comparison to either drug as monotherapy or placebo.[3] In this case report, it is possible that the discontinuation of SSRI was associated with the return of symptoms of depression and anxiety, which directly contributed to relapse based on negative cravings and/or self-medicating emergent symptoms; perhaps a reduced relapse while still on maintenance naltrexone, but a relapse nonetheless. Choosing an unregulated psilocybin experience over comprehensive treatment for AUD with comorbid major depressive and generalized anxiety disorders placed the patient in a situation without support when the relapse occurred. While psilocybin may have provided him with an affirming experience that has been associated with positive psychiatric outcomes, it was insufficient alone or in combination with naltrexone to deter a return to heavy drinking. Monitoring of depression/anxiety and negative cravings in patients with dual diagnosis is often clinically employed[4]; it is unclear if greater awareness of cravings after psilocybin was related to the emergence of negative cravings with SSRI discontinuation or a therapeutic adaptation or adverse event from psilocybin.

There is evidence to suggest that 2 psilocybin sessions paired with 12 psychotherapy sessions are associated with a reduction in the percentage of heavy drinking days in participants with AUD *without* any comorbid major psychiatric or drug use disorders.[5] Future consideration should be given to the risk-benefit ratio of forgoing formal AUD treatment and discontinuing effective

serotonergic compounds for depression and anxiety when considering experimental serotonergic psychedelics.

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