The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

The antipsychotic potential of cannabidiol: clinical implications for patients with psychosis and comorbid cannabis use disorder

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A 22-year-old man is starting outpatient follow-up for a first episode of psychosis (FEP) that started in the context of a severe cannabis use disorder. The patient initially required 3 months of hospitalization and was stabilized with paliperidone. He accepted being switched to the long-acting injectable form and was discharged on paliperidone palmitate 150 mg, to be administered intramuscularly every 21 days.

During his follow-up at the FEP program, the patient reported that he had resumed cannabis consumption after his discharge and experienced a recrudescence of his positive psychotic symptoms and paranoia. He mentioned not having gone out in public for more than 2 weeks because he was under the impression that people were looking at him and reading his mind. The patient was referred to psychotherapy for motivational interviewing regarding his substance use, but he did not present to his appointment and lacked motivation to engage in this type of intervention.

The patient received psychoeducation concerning the different cannabinoids found in cannabis sativa, particularly the 2 most abundant: Δ-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).[1] The increased risks of psychotic symptoms and impaired cognition associated with cannabis with higher THC content were emphasized.[2] In the context of the patient's lack of motivation to discontinue use, harm reduction was undertaken. He was thus advised to select cannabis with higher ratios of CBD:THC.

At the next follow-up, the patient reported that he no longer bought his cannabis in the street, and had been going instead to a governmental source to purchase products with known THC ratios. He reported purchasing cannabis with a CBD:THC ratio of 13%:3%. He reported less anxiety, less paranoia, and being increasingly able to take outings from his supervised apartment.

About one-third of all patients with FEP are cannabis users.[3] There is now substantial evidence that patients with FEP who consume cannabis experience more relapses and greater positive psychotic symptoms, require more hospitalizations, are less compliant with psychiatric medications, and exhibit global functioning deficits compared with patients who abstain from cannabis.[4,5,6] In Canada, a cross-sectional survey done in 2016 collected information regarding current cannabis use treatment practices among Canadian English-speaking FEP programs. The study found that only 12% of FEP programs offer formal services targeting cannabis use, whereas the majority offer informal individual patient psychoeducation.[7]

Cannabis sativa produces more than 100 terpenophenolic compounds called cannabinoids, which are present in widely varying proportions.[8] THC, the main psychoactive compound, exerts its effect by binding to 2 G-protein-coupled cell membrane receptors: cannabinoid type 1 (CB1) and type 2 (CB2) receptors.[9] Unlike THC, CBD does not activate CB1 or CB2 receptors, interacting instead with many other non-endocannabinoid-signalling systems.[10] CBD may reduce the psychotropic activity of THC, enhancing its tolerability by counteracting some of the functional consequences of CB1 activation in the brain.[9,10] In healthy volunteers, predosing with CBD attenuates the experimental induction of psychotic symptoms by THC.[11]

CBD has antipsychotic properties and is active in both glutamate and dopamine-based laboratory models of schizophrenia symptoms.[9,10] It has been reported to reduce psychotic symptoms in patients with Parkinson disease.[12] There are 2 positive double-blind randomized controlled trials of CBD in schizophrenia. In one exploratory phase-2 trial, CBD was evaluated against amisulpride over a period of 4 weeks in 39 patients with acute exacerbations of schizophrenia.[13] Both groups showed similar, highly significant improvements in the primary outcome measure (Positive and Negative Syndrome Scale total score versus baseline scores), but CBD displayed a markedly superior adverse effect profile.[13] The second positive trial explored the safety and effectiveness of CBD as an adjunct to conventional antipsychotics in 88 patients with schizophrenia over a period of 6 weeks.[1] The results showed significant reductions in positive psychotic symptoms and higher clinician-rated global improvement scores.

Despite the need for larger randomized placebo-controlled trials to evaluate the therapeutic potential of CBD, these findings suggest that psychoeducation about the various ratios of CBD:THC found in cannabis strains, and their impact on neuropsychiatric symptoms, should be integrated into FEP programs.

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