patient with a depressive episode in the past. This conclusion can be speculative, as patient's symptoms could be explained by escitalopram-induced affective switch or primary bipolar disorder in our patient. However, the temporal association with Δ^8-THC use and the extant evidence on the association between cannabis (Δ^9-THC) and mood disorder cannot be ignored.[4] Cannabis has long been recognized as a risk factor for mania and subsequent bipolar disorder.[4] Cannabis use at baseline has been associated with an elevated risk of manic symptoms regardless of the prevalence and incidence of psychotic symptoms. The possible mechanism is dopaminergic receptor sensitization via cannabinoid receptors.[4] However, there is limited evidence for similar effects with Δ^8-THC.

The euphoric and psychoactive effects of Δ^8-THC are mediated by cannabinoid CB_1 and CB_2 receptors similar to Δ^9-THC, albeit with a weaker affinity at CB_1 receptors. Common adverse effects of Δ^8-THC are confusion, anxiety, drowsiness, and bradycardia.[2,3] There have been earlier reports of psychotic symptoms secondary to the use of Δ^8-THC.[5,6] The similarities between Δ^8-THC and Δ^9-THC have been implicated behind the psychotomimetic effects of the former.[6]

Various Δ^8-THC compounds are being increasing marketed on many online platforms without adequate regulation. A wide range of Δ^8-THC products (gummies, tinctures, oil, vaporizing pens) are available for use with no adequate caution or awareness. Even in India, there is an absence of legislation and restrictions for age limits for purchase. Healthcare professionals should be cautious about the potential adverse effects including the risk of psychosis and mood disorders with Δ^8-THC and the other legal THC derivatives.

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Use of Erythromycin in Clozapine Induced Constipation: A Case Report

To the editor,

Clozapine is the medication of choice for treatment-resistant schizophrenia. Clozapine has multiple serious side effects. This includes slowed gastrointestinal transit in up to 80% of patients due to its significant anticholinergic effect and serotonin receptor antagonism.[1] Clozapine-induced gastrointestinal hypomotility (CIGH) is a type of paralytic ileus due to impairment of muscle contraction in the digestive track.[1] The CIGH can result in severe constipation, paralytic ileus, and bowel obstruction, the latter being associated with a high mortality rate.[2] The usual management of CIGH is the administration of multiple laxatives, although there is little evidence of their efficacy.[2] Treatments that stimulate gut motility have been used recently with some success, including prucalopride.[3]

Oral erythromycin, an antibiotic, has also been used effectively as a prokinetic

at doses from 50 mg three times daily up to 500 mg four times daily. It acts as a motilin agonist through its interaction with motilin receptors in the stomach and upper gastrointestinal tract. Erythromycin accelerates gastric emptying through motilin receptors by increasing the frequency and amplitude of stomach and duodenal contractions.[4] We report a case where we successfully restarted clozapine in a patient at risk of CIGH using adjunctive erythromycin.

Patient A was a 48-year-old male with schizophrenia since 1996; his symptoms were managed on clozapine. Due to worsening of symptoms related to ongoing stressors, his clozapine was increased to 650 mg a day. With this dose, his psychotic symptoms got better however he developed severe CIGH leading to constipation after seven days. He was not able to pass stool for more than 10 days and developed severe cramps. He underwent USG and MRI of this abdomen which revealed a large volume of impacted materials indicating severe constipation. He was consulted with the surgical team for possible management plans. His bowel movement was extremely sluggish in physical examination. He did not respond to usual medicines for constipation such as laxatives (Lactulose, Metamucil, psyllium, PEG, Coloxyl Senna), bowel enema, prucalopride, and dietary changes. Because of severe cramps, we had to make a collaborative decision to reduce and stop his clozapine. Even while reducing his clozapine, his psychotic symptoms started worsening gradually. He was later tried on a combination of antipsychotics, but his mental state deteriorated, requiring ECT. Despite thrice-weekly ECT and multiple antipsychotics, he did not show any significant improvement. A decision was made to restart clozapine. We observed that his baseline bowel opening, without clozapine, was around every 2.5 days with the regular laxatives. We trialed him on erythromycin 50 mg TDS and regular laxatives, and his bowel opening improved to once a day after five days. The erythromycin was continued for five months with a maximum dose up to 500 mg four times a day. We restarted clozapine and titrated it to a therapeutic serum level of 569 IU (dose 650 mg). Patient A improved significantly in his mental state whilst maintaining a regular bowel habit.

The use of erythromycin may be an effective strategy for the management of CIGH and should be investigated in future clinical trials assessing its efficacy and tolerability. This will prevent the unnecessary need for stopping clozapine. The authors also suggest that clinicians need to be mindful of tachyphylaxis and strategies to manage it, including withholding erythromycin for a week or two.

Author Contributions

All ethical parameters are considered/all authors contributed and corrected the article.

Consent

The authors obtained a written informed consent from the patient for the publication of this case study.

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