The Potential Role of Fluvoxamine in Clozapine Associated Constipation: A Case Report*

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Introduction

Constipation is observed in up to 60% of patients receiving clozapine. Extreme cases can progress to ileus, which carries high mortality (Hayes, 1995). Several management strategies are used for treatment of clozapine-associated constipation; however, they may fail, thereby resulting in clozapine discontinuation. Our case describes the successful mitigation of clozapine-associated constipation with the addition of fluvoxamine and reduction of clozapine dose.

Case Report

47-year-old female with a history of schizoaffective disorder was admitted for worsening paranoia and poor self-care. She was started on clozapine and the dose was titrated to 50 mg daily and 75 mg nightly. Plasma clozapine level on this dose was 412 mcg/l and norclozapine level was 109 mcg/l. She developed problematic constipation and subsequent ileus. MRI of the abdomen showed possible ileus or obstruction. Several laxatives were unsuccessful, including senna, lactulose, and polyethylene glycol, used in combinations. The clozapine dose was reduced to 50 mg bid with no improvement of constipation.

Fluvoxamine was started and increased to 50 mg twice daily with the goal of reducing the clozapine dose while maintaining a therapeutic plasma level. The clozapine dose was further reduced to 25 mg daily and 50 mg nightly. Enema was added to clear the impacted stool. Constipation improved, ileus resolved, and bowel function returned. The clozapine level on this combination was 501 mcg/l and norclozapine level was 133 mcg/l. She remained stable without recurrence of catatonia, psychosis, or constipation.

Discussion

Multiple strategies have been implemented to address clozapine-associated constipation, including conventional laxatives, novel agents, and dietary modifications. If these measures fail, clinicians may discontinue or reduce the dose of clozapine to avoid serious complications, however, these strategies may lead to lower treatment efficacy (Patel, 2021). Clozapine is metabolized in the liver by the cytochrome P450 (CYP450) enzyme superfamily, mainly CYP1A2. Fluvoxamine, a potent CYP1A2 inhibitor SSRI, increases the efficacy of clozapine without raising the dose (Mong- Liang, 2018). In our patient, clozapine led to clinical improvement; however, clozapine use was compromised by gastrointestinal hypomotility resistant to various modalities. Improvement occurred despite the increase in clozapine level and the absence of change in the metabolic ratio of clozapine to norclozapine (3.7 on both doses). This suggests reduced motility might correlate more with oral clozapine dose than clozapine level.

Conclusions

Augmentation of clozapine with fluvoxamine may be an effective technique for the management of clozapine-associated constipation and hypomotility, especially in treatment-resistant cases when standard measures to treat constipation are not successful.

References

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