INTRODUCTION

-Clozapine is metabolized by the cytochrome P450 system (CYP), particularly CYP1A2 and to a lesser extent 2D6 and 3A4.
-Inflammation can impact the metabolism of Clozapine by impacting the CYP system and lead to toxicity.
-Cytokines such as IL-6 can reduce CYP activity.
-COVID-19 is a pro-inflammatory illness.
-Studies identify multiple cases of elevated Clozapine levels associated with infection, typically respiratory infections.
-This case illustrates how COVID-19 infection can significantly elevate Clozapine levels and cause toxicity.

BACKGROUND/LABS

- Norclozapine is a major metabolite of Clozapine.
- Measuring the ratio of Clozapine to Norclozapine is helpful for assessing drug metabolism, with a typical ratio of around 1:3:1. --Therapeutic Clozapine levels average around 350ng/ml, with toxicity possible above 750ng/ml.

CASE PRESENTATION

-A 66 year old male patient with history of schizophrenia is treated with Clozapine due to failing multiple other antipsychotics.
-In August, 2022 he was admitted to the Family Medicine Inpatient Medicine service for altered mental status after syncope at home.
-On exam, the patient was overly sedated – not at baseline per caretaker.
-No classic COVID-19 symptoms but was found to be COVID-19 positive.
-On admission, Clozapine and Norclozapine levels were 902 ng/ml and 287 respectively, significantly increased from baseline of 372 ng/ml Clozapine and 199 Norclozapine.
-Clozapine:Norclozapine ratio was elevated to ~3:1, suggesting reduced metabolism leading to toxicity.
-Clozapine dose was decreased to 200mg nightly from his prior dose of 100mg daily and 250mg nightly with resolution of over-sedation by day 3 after dose reduction.
-Two months later, Patient had recurrence of psychotic symptoms develop and levels were found to be subtherapeutic.

REFERENCES


de Leon J, Diaz FJ. Serious respiratory infections can increase clozapine levels and contribute to side effects: a case report. Prog Neuro-Psychopharmacol Biol Psychiatry 2003;27(6):1059-1063.
