

Letter

Do psychotropic drugs used during COVID-19 therapy have an effect on the treatment process?

People with mental disorders are more vulnerable to the novel coronavirus COVID-19 than the general population due to the risk of infection (including pneumonia), barriers to timely access to healthcare facilities due to their isolation in the psychiatric ward, and the fear, anxiety and depression accompanying the pandemic process.¹ Beyond that, though the psychological impact of COVID-19 remains unclear, infected patients may experience anxiety, depression, guilt, stigma and anger. The emotional problems thus may reduce immunity and compromise recovery; it may therefore be necessary to start a new drug treatment for COVID-19 patients who have not had previous mental disorders. In addition, the long-term side effects of psychotropic drugs (metabolic syndrome, extrapyramidal symptoms, electrolyte imbalance, etc), physical health problems (obesity, gynecomastia, sexual dysfunction, etc), substance use disorders (nicotine, alcohol, marijuana, etc), and medication non-adherence are other important problems in the fight against COVID-19.

Risky combinations and drug–drug interactions (DDIs) occur as a result of COVID-19 treatment accompanied by psychotropic drugs, which are indispensable in chronic mental disorders. For example, concurrent use of pimozide with atazanavir or lopinavir/ritonavir may increase the risk of raised serum pimozide levels, QTc prolongation, or torsade de pointes with high dependence on CYP3A or CYP2D6 enzymes. A similar situation exists for quetiapine and ziprasidone. If these drugs are used with atazanavir or lopinavir/ritonavir, the serum concentration of these psychotropic drugs may increase in COVID-19 patients. According to a case series, current dosing recommendations for the use of quetiapine—which is commonly prescribed in COVID-19 patients with a diagnosis of delirium—with lopinavir/ritonavir should be adjusted to a sixfold lower quetiapine dose.²

QTc prolongation has been highlighted in the latest cohort studies and in warnings from the European Medicines Agency

and the US Food and Drug Administration Adverse Event Reporting System. Therefore, the Tisdale Risk Score is strongly recommended to evaluate the risk of QTc prolongation in patients prescribed psychotropic drugs concomitantly with COVID-19 treatment. According to the risk score, the patients are categorised as ‘low’, ‘moderate’ and ‘high’ risk by evaluating age, gender, prescription of loop diuretics and QTc interval prolonging drugs, serum potassium concentration (≤ 3.5 mEq/L), QTc interval at admission (≥ 450 ms), number of QTc interval prolonging drugs (≥ 2), and presence of acute myocardial infarction, sepsis and heart failure.³

If clozapine, one of the most effective treatments of schizophrenia spectrum disorders, is used concomitantly with ribavirin, tocilizumab, interferon β or hydroxychloroquine, the risk of myelosuppression and potential haematological toxicity increases.⁴ Additionally, to minimise the risk of COVID-19 and pneumonia in patients treated with clozapine, smoking, sialorrhoea, absolute neutrophil count and serum clozapine levels should be closely monitored. According to a recent case report, in the patient diagnosed with COVID-19, clozapine toxicity has been shown to involve cytokine release down-regulating the metabolism of clozapine with CYP1A2 enzymes.⁵ Although it may have a different aetiopathogenesis, myocarditis induced by COVID-19 and triggered by clozapine should also be considered during this period.⁶

Finally, the serum concentration of midazolam, which is especially used in the intensive care unit as an anxiolytic, significantly increases in concomitant use with atazanavir or lopinavir/ritonavir. In a retrospective cohort study, in patients taking atazanavir or lopinavir/ritonavir concomitantly with intravenous midazolam, the incidence of severe prolonged sedation and length of hospital stay was significantly longer than in patients not taking any antiretroviral agents.⁷ Therefore, reduced bolus doses instead of continuous infusion should be considered during concurrent use of midazolam with these drugs.

The above mentioned information pertains to the high-risk DDIs that can be seen in COVID-19 treatments that accompany psychotropic drug prescription simultaneously. The clinical significance of potential DDIs other than these should be evaluated with patient-centred care using

current scientific databases with multidisciplinary teams, including consultation-liaison psychiatrists and infectious disease physicians.

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