The Another Side of COVID-19 in Alzheimer's Disease Patients: Drug-Drug Interactions

Fatma Balli[1], Emre Kara[1], and Salih Kutay Demirkan[1]

[1]Hacettepe University Faculty of Pharmacy

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Abstract

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Coronavirus Disease 2019 (COVID-19) outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a major public health problem. The elderly people are the most affected population by the COVID-19 outbreak in terms of mortality and morbidity. Delirium caused by hypoxia, a prominent clinical feature of COVID-19, may increase the need for treatment of Alzheimer's disease (AD) patients (1). Therefore, drug-drug interactions should be considered in AD patients while receiving COVID-19 treatment.

AD treatment consists of cholinesterase inhibitors (ChEIs) (donepezil, rivastigmine, galantamine) and memantine. In addition, antidepressants and antipsychotics are used to control for behavioral and psychiatric symptoms of patients (2). Despite ChEIs have few pharmacokinetic drug-drug interactions, donepezil and galantamine can be affected by specific substrates, inhibitors or inducers of the cytochrome P450 (CYP450) enzymes (such as CYP2D6, CYP3A4). Chloroquine (CQ) and hydroxychloroquine (HCQ) are metabolized by CYP2C8, CYP2D6, CYP3A4 and inhibits CYP2D6. Pharmacological effects of galantamine and donepezil may increase during CQ/HCQ treatment. Azithromycin has a low risk for CYP450 mediated drug interactions. Cardiac adverse effects (such as bradycardia, heart block, and QT interval prolongation) may appear related to both ChEIs and CQ/HCQ or azithromycin. Thus, more frequently electrocardiography monitoring should be considered when concomitant use. Lopinavir is primarily metabolized by CYP3A enzymes and ritonavir is a potent inhibitor for CYP3A and CYP2D6. Additionally, lopinavir-ritonavir are inhibitors of drug transporters such as p-glycoprotein, breast cancer resistance protein, and inducers of CYP1A2, CYP2B6, CYP2C19, CYP2C9, glucuronyl transferase enzymes. Lopinavir-ritonavir may increase plasma concentrations of galantamine and donepezil. Consequently, adverse reactions or toxicity risk of ChEIs may increase. In addition, caution should be advised in terms of bradycardia when using lopinavir-ritonavir and ChEIs together (2, 3).

Memantine undergoes limited hepatic metabolism and has a low risk for pharmacokinetic/pharmacodynamic drug-drug interaction. Therefore, memantine may be a safer alternative in COVID-19 treatment (2).

QT interval prolongation and ventricular arrhythmias (including Torsades de Pointes) should be monitor in the use of azithromycin, CQ, HCQ and lopinavir/ritonavir with antipsychotics, antidepressants. Caution may be required when using strong CYP2D6 inhibitors (such as paroxetine and fluoxetine) and CYP2D6 substrate CQ (2, 3). In addition, glycemic control should be monitored as selective serotonin reuptake inhibitors may increase the hypoglycemic effect of CQ and HCQ (4). Due to the effect of ritonavir on a large number of drug-metabolizing enzymes, the dose may need to be increased/decreased when used with antipsychotic and antidepressant drugs that may potentially affect their metabolism (3, 5).

No potential interaction is expected between tocilizumab, ribavirin, favipiravir and AD' treatments (3). Drug interactions should be evaluated in AD patient while receiving COVID-19 treatment. Principally, safer COVID-19 and AD treatments should be preferred, otherwise the patient should be closely monitored essential aspects.

References

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