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LETTER

PSYCHIATRY

Do we need to change our treatment approach to schizophrenia during the COVID-19 pandemic?

To the Editor,

According to the World Health Organization, coronavirus disease (COVID-19) has affected over 55 000 000 people worldwide and has resulted in approximately 1 300 000 deaths. It is still in progress at the time of writing this letter. Schizophrenia is a chronic mental disorder that affects 20 million people worldwide.[1,2] Patients with schizophrenia have high rates of comorbidities, including important predisposing factors for COVID-19, such as hypertension, diabetes mellitus and chronic obstructive pulmonary disease.[3] Therefore, more attention should be paid to the treatment of these patients during this pandemic.

The first step of viral infection is viral entry into host cells, which begins and maintains infection and triggers the host's immune response. Activation of the endocytic pathway and autophagy are critical processes for viral entry and replication. Therefore, these processes can be expected to play important roles in determining the efficacy of drugs developed to combat COVID-19.[4] Many drugs previously approved to treat various human diseases have been suggested as options for the treatment of COVID because of the rapid and global spread of this disease. Existing drugs with established antiviral efficacy can be directly and immediately used to treat COVID-19 because we have a significant understanding of their safety profiles.[5]

Chlorpromazine has a well-established lysosomotropic property that modulates autophagy and inhibits clathrin-mediated endocytosis. Clathrin-mediated endocytosis is an important potential mechanism of SARS-CoV cell invasion. Chlorpromazine blocks the assembly of clathrin adaptor protein 2 (AP2) at the cell surface and has been shown to significantly inhibit SARS-CoV entry into HepG2 cells.[6,7] Furthermore, previous studies have reported that chlorpromazine exerts immunomodulatory effects by increasing the levels of anti-inflammatory cytokines while decreasing those of inflammatory cytokines.[8] Additionally, chlorpromazine has been suggested to have antiviral properties for HCV, alphavirus and various coronaviruses, including human coronavirus 229E, SARS-CoV and MERS-CoV.[9]

Haloperidol has been reported to decrease the mortality rate of patients on mechanical ventilation, a finding attributed to the lowering of cytokine levels by the drug and the subsequent prevention of the cytokine storm.[10] Therefore, haloperidol may have a therapeutic effect on the progression and severity of COVID-19, which have been suggested to be related to the cytokine storm.[11] Furthermore, haloperidol can cause alkalinisation and inhibit autophagy; therefore, it may prevent SARS-CoV-2 entry into host cells because this process requires autophagy modulation and a low pH in intracytoplasmic vesicles.[12,13]

In the treatment of psychiatric patients during this global pandemic, it can be more appropriate to choose psychotropic drugs that have antiviral properties and possible therapeutic effects against the pathogenic mechanisms of the virus. The use of such drugs may contribute to the treatment of COVID-19 among infected patients and play a protective role against the transmission of SARS-CoV-2.[14] Haloperidol and chlorpromazine have been used for more than half a century for the treatment of schizophrenia. These two drugs, classified as first-generation antipsychotics (FGAs), are used less frequently now than in the past, although they are known to be effective and safe for the treatment of schizophrenia.[15]

Haloperidol may produce significant extrapyramidal side effects (EPS) which were often associated with its high doses.[16] However, PET studies have suggested that its low doses are preferable. Clinical response was associated with at least 65% occupancy of D2 receptors, while greater than 78% associated with EPS. Doses of haloperidol greater than 5 mg increased the risk of side effects without improving efficacy.[17] Therefore, we recommend that clinicians should use it in the lowest dose needed to avoid dose-related side effects including EPS during the current pandemic. Chlorpromazine has more anticholinergic side effects, and lower rates of EPS in contrast to haloperidol. However, there is a well-known risk of hepatotoxicity induced by chlorpromazine. Moreover, chlorpromazine was discontinued in chronic treatments because of its hepatotoxic effec [18,19] Nonetheless, clinicians may prescribe it in low doses and as a short-term treatment in patients with schizophrenia during COVID-19 pandemic.

The current pandemic has changed our views of and treatment approaches to many clinical conditions.[20] We must consider the side and therapeutic effects of drugs related to the immune system and infectious conditions when choosing treatment options for our patients.[21] In light of the possible antiviral and anticytokine properties of FGAs, including haloperidol and chlorpromazine, we recommend that clinicians reconsider these drugs for the treatment of patients with schizophrenia during the COVID-19 pandemic, weighing the potential benefits against the risk of adverse effects and drug interactions. At this time, however, the idea remains rather theoretical because there is no clinical data from COVID-19 patients with schizophrenia that have received SGAs or FGAs. Therefore, the effects of different antipsychotics on the prognosis and course of COVID-19 need to be studied in patients with schizophrenia.

DISCLOSURES

Authors have declared that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

Okan Ekinci
Aslı Erkan Ekinci

Psychiatry Department, Usak University Medical Faculty, Usak, Turkey

Correspondence
Okan Ekinci, Psychiatry Department, Usak University Medical Faculty, Usak, Turkey.
Email: drokanekinci@yahoo.com

Okan Ekinci and Aslı Erkan Ekinci contributed equally to this work.

ORCID

Okan Ekinci https://orcid.org/0000-0001-8059-9022
Aslı Erkan Ekinci https://orcid.org/0000-0001-6331-9412

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