Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Letter to the editor: Quetiapine safety in ICU delirium management among SARS-CoV-2-infected patients

This letter is about the paper by Hawkins et al. [1] entitled "A rapid review of the pathoetiology, presentation, and management of delirium in adults with the coronavirus disease 2019 (COVID-19)", which was published in the Journal of Psychosomatic Research (Volume 141) in February 2021. I eagerly studied the findings presented by the authors. Their results revealed that delirium (i.e., an abrupt, fluctuating, and generally reversible disturbance of mental function) is one of the most prevalent acute neuropsychiatric syndromes (ranging from 65% to 79.5%) among critically ill intensive care unit (ICU) patients with COVID-19, which can be a manifestation of both direct and indirect effects of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on the central nervous system. Since delirium might be accompanied by significant mortality and morbidity among patients with COVID-19 (particularly the elderly), delirium must be assumed as an alarming prognostic indicator for this group of patients [1,2]. Apart from the explanations about the pathoetiology and clinical manifestations of delirium, the authors described numerous pharmacological strategies (e.g., quetiapine) in the section "prevention and management of delirium in adults with COVID-19". Although quetiapine has been suggested as a treatment option for delirium management among the elderly and patients with neurological conditions due to its tolerability and wide therapeutic range [3], its use, like other antipsychotic medications, has been restricted for some reasons such as potential drug-drug interaction with anti-SARS-CoV-2 drugs [4], antipsychotic-related respiratory depression [4,5], and QTc interval prolongation [4].

A unique immunological property of quetiapine that has been disregarded by Hawkins et al. [1] is its potential effect on the neutrophil-derived extracellular traps (NETs) formation (or NETosis) during in vitro experiments— the complication that does not appear to be induced by clozapine [6,7]. NETs are networks of extracellular fibers composed of double-stranded DNA, histones, myeloperoxidase, and proteinase-3, which allow neutrophils to kill extracellular pathogens while minimizing damage to the host cells. Although NETosis had been firstly reported as neutrophil microbicidal mechanisms, extra evidence revealed that NETs have double-edged-sword activities. In this regard, observations suggest that NETs may play a key role in the pathogenesis of infectious, inflammatory, and thrombotic disorders (e.g., COVID-19). More to the point, SARS-CoV-2 can cause apoptosis of lung epithelial cells in mechanisms dependent on the angiotensin-converting enzyme (ACE2)–serine protease axis, virus replication, and PAD-4 signaling by stimulating NETosis in healthy neutrophils. These findings might emphasize the significant role of NETosis in the destruction of lung epithelial cells as a part of the severe COVID-19 infection pathophysiology [8]. Hence, NETosis stimulants (such as quetiapine) may intensify pulmonary epithelial cell damage among patients with COVID-19 [6,8]. Although these findings have been taken from the preliminary in vitro studies, clinicians should pay more attention to initiating or continuing the treatment of delirium with quetiapine in critically ill ICU patients with COVID-19 until reaching supplementary information in this field [9].

Declaration of Competing Interest

The author has no competing interests to report.

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