

COULD LITHIUM BE A NEW HOPE IN COVID-19 TREATMENT? A CASE REPORT

Doğancan Sönmez* & Çiçek Hocaoğlu

Recep Tayyip Erdogan University, Faculty of Medicine, Department of Psychiatry, Rize, Turkey, dogancansonmezz@gmail.com

* correspondence author

Dear Editor

The World Health Organization identified a new type of coronavirus (COVID-19) that was not previously detected in humans on January 5, 2020. It has been declared a pandemic by WHO as of March 12, 2020 (Liu et al. 2020). To date, more than 127 million cases of COVID-19 and more than 2.78 million deaths attributable to it have been reported worldwide. COVID-19 infection still continues its effects all over the world and in our country. There is no definitive cure yet and treatment algorithms change over time. Various pharmacological treatments are still being tried in the literature. When the literature was examined, it was found that one of them was lithium. Lithium, which is widely used in the treatment of bipolar disorder, also exhibits antiviral activity. There is evidence that it inhibits the reproduction of various types of viruses, including those belonging to some coronavirus family. In 1979, Julian Lieb observed that bipolar patients treated with lithium showed clinical remission of recurrent herpes simplex virus infection (Spuch et al. 2020).

We admitted a 38-year-old, primary school graduate, single mother of a child, unemployed female patient who was followed up in our clinic with the diagnosis of bipolar mood disorder for 13 years. For the last two weeks, he had symptoms of increased speech and purposeful activities, irritability, aggression and insomnia. According to the psychiatric examination and evaluation, a diagnosis of bipolar disorder manic episode was made. Lithium 600 mg/day and olanzapine 10 mg/day treatment, which the patient had previously used and benefited from, was resumed. COVID-19 symptoms were observed in all inpatients (9 patients) and some service workers as a result of the contamination of COVID-19 from outside while the patient was inpatient in the service. PCR tests of patients and service personnel were found to be positive. With the arrangement of the psychiatry service as a COVID-19 contaminated psychiatry service, the treatment and follow-up of the patients for COVID-19 infection were carried out by us under the control of the infectious diseases and clinical microbiology department. During this period, the only patient using lithium in the ward did not show any signs of infection and the PCR test repeated twice was negative. It was also observed that the patient could not comply with the isolation rules in the ward and was with patients with signs of infection despite all warnings. In the patient receiving lithium treatment, no symptoms and laboratory findings in favor of COVID-19 could be detected and COVID-PCR samples were negative, suggesting whether lithium has an antiviral effect against COVID-19.

Lithium, which is widely used in the treatment of bipolar disorder, is the first element in the periodic table group 1A

(Yung 1984). The use of lithium in psychiatry was in 1949, when John Cade tried on manic episode patients and got positive results (Rybakowski 2020). Lithium has also proven its antiviral and immunomodulatory effect. Lithium has demonstrated in vitro efficacy in inhibiting the replication of coronaviruses responsible for gastrointestinal and respiratory diseases in animals. The novel coronavirus has immunomodulatory properties that may provide additional benefit in attenuating the counter-host inflammatory response. The antiviral properties of lithium salts appear to be related to the activity of the lithium ion and its competition with magnesium ions. Magnesium acts as a cofactor for the enzymes necessary for the replication of viral proteins and nucleosides. When lithium replaces magnesium, it deactivates polymerase enzymes and prevents viral replication. Lithium inhibits glycogen synthase kinase 3-beta (GSK-3 β). Inhibition of GSK-3 β prevents the expression of longer viral subgenomic mRNAs and genomic RNA. Specifically, there is evidence to suggest that lithium can regulate both B and T lymphocytes. Lithium can increase the activity of B lymphocytes and reduce the ratio of circulation-suppressing T cells to cytotoxic T cells (Murru et al. 2020). The viral entry mechanism of the coronavirus into host cells has been shown to be dependent on angiotensin converting enzyme II (ACE-2) and a transmembrane serine protease enzyme called TMPRSS2. However, later and more severe manifestations of COVID-19 appear to be immunologically mediated by a pathway involving endocytosis of ACE-2 as well as SARS-CoV-2 followed by activation of angiotensin type 1 receptors (AT1R). Activation of AT1R; transcription factors cause a range of effects, including induction of inflammatory cytokines such as nuclear factor kappa B, STAT - 3, tumor necrosis factor-alpha, interleukin-6. The result of this process in vulnerable individuals is what is known as the "cytokine storm" or "inflammatory storm", which leads to lung damage and multi-organ dysfunction. Thus, the pathophysiology of COVID-19 is complex and involves both direct viral infection and immune / inflammatory mechanisms. The pharmacodynamics of lithium is complex and besides neural plasticity; It has also been documented that it attenuates the immune-inflammatory activation seen during mood disorders, including the normalization of cytokine levels (Rajkumar 2020).

The antiviral efficacy of lithium has been proven by studies in the literature. However, there are a limited number of studies in the literature on its effectiveness on COVID-19. The purpose of our letter is to contribute to the studies in the literature that lithium may be a new hope for the treatment of the COVID-19 pandemic, where our world is in difficult times.

Acknowledgements: None.

Conflict of interest: None to declare.

References

1. Liu YC, Kuo RL, Shih SR. COVID-19: The first documented coronavirus pandemic in history. *Biomed J* 2020; 43:328–33. <https://doi.org/10.1016/j.bj.2020.04.007>

2. Murru A, Manchia M, Hajek T, Nielsen RE, Rybakowski JK, Sani G, et al.: Lithium's antiviral effects: a potential drug for CoViD-19 disease? *Int J Bipolar Disord* 2020; 8. <https://doi.org/10.1186/s40345-020-00191-4>
3. Rajkumar RP: Lithium as a candidate treatment for COVID-19: Promises and pitfalls. *Drug Dev Res* 2020; 81:782–5. <https://doi.org/10.1002/ddr.21701>
4. Rybakowski JK: Lithium treatment in the era of personalized medicine. *Drug Development Research* 2020. <https://doi.org/10.1002/ddr.21660>
5. Spuch C, López-García M, Rivera-Baltanás T, Rodrigues-Amorim D, Olivares JM: Does Lithium Deserve a Place in the Treatment Against COVID-19? A Preliminary Observational Study in Six Patients, Case Report. *Front Pharmacol* 2020; 11. <https://doi.org/10.3389/fphar.2020.557629>
6. Yung CY: Neuropsychiatric manifestations of alkali metal deficiency and excess. *Pharmacol Biochem Behav* 1984; 21:71–5. [https://doi.org/10.1016/0091-3057\(84\)90166-7](https://doi.org/10.1016/0091-3057(84)90166-7)