Post-COVID-19 Hyperglycemia: A Concern in Selection of Therapeutic Regimens

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an RNA betacoronavirus responsible for coronavirus disease 2019 (COVID-19),[1] has already caused nearly four million deaths around the world according to the WHO data.

Some comorbidities that increase the risk of severe illness for COVID-19 have been reported, including hypertension, cardiovascular diseases, diabetes mellitus (DM), and obesity. While DM and uncontrolled glycemia have been identified as a risk factor for increased COVID-19 severity and associated mortality, the virus has also been reported to predispose the patients to hyperglycemia. The pathophysiological mechanisms are not completely understood, but inflammation, impaired immune condition, and induction of the renin–angiotensin–aldosterone system (RAAS) are suggested to be some of the potentially involved processes.[2] Increased pulmonary ACE2 (angiotensin converting enzyme 2) as the main SARS-CoV-2 entry receptor in diabetic patients may also play a part. High levels of blood sugar during the disease course may further contribute to the complexity of the disease through affecting the immune and inflammatory responses. Moreover, cases of hyperglycemia and even DM following COVID-19 recovery are observed in previously healthy patients. Although the viral infection is believed to be a contributing factor thereof, the probable role of administered drug regimens should not be ignored. While the etiology is still unclear, selection of appropriate therapeutic protocols with considering the risk of increased blood sugar in COVID-19 patients is of high importance.

During the one-and-half-year-long exhausting global struggle with SARS-CoV-2, different therapeutic approaches have been proposed, many of which were abandoned in a short time. Remdesivir, an adenosine analog prodrug, is the first and the only broad-spectrum antiviral drug approved by the US Food and Drug Administration (FDA) to treat hospitalized patients with COVID-19 infection. NIH COVID-19 treatment guidelines recommend its usage in hospitalized patients who require supplemental oxygen. It is also suggested in some other therapeutic guidelines. Thus, remdesivir is currently being broadly indicated in COVID-19 patients. Dexamethasone is also widely used in advanced stages of the disease based on its proven survival benefit in critically ill patients infected with SARS-CoV-2.[3] Given the widespread incidence of the disease all over the world, remdesivir plus a corticosteroid (dexamethasone or prednisolone) regimens are administered broadly in many countries. While high dose corticosteroids are found to be correlated with the onset of diabetes, hyperglycemia is not included in the list of remdesivir side effects. However, concerns regarding the probable role of remdesivir in increasing blood sugar levels have been recently raised. Apparently, such associations are needed to be clarified through further investigations. Meanwhile, more caution in prescription of this drug especially in combination with a corticosteroid could be helpful, considering several serious side effects of this drug as well as the controversies in the results of remdesivir trials in COVID-19 patients. In this regard, a meta-analysis evaluating the efficacy and safety of remdesivir in randomized clinical trials of COVID-19 found no significant decrease in mortality or mean time to clinical improvement despite higher rates of hospital discharge and recovery reported upon remdesivir usage.[4] In another meta-analysis, no mortality benefit was reported upon remdesivir indication in COVID-19 patients.[5]

Therefore, bearing in mind the side effects of remdesivir and performing a risk-benefit analysis seems essential to avoid probable serious complications in COVID-19 patients. Future trials and investigations on this subject could help physicians to make better decisions in choosing optimum therapeutic approaches for COVID-19 patients.

Conflict of Interest: None declared.

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