Can beta-adrenergic blockers be used in the treatment of COVID-19?

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At present, there is no effective drug against the present coronavirus disease 2019 (COVID-19) pandemic. It is known that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein binds to human angiotensin-converting enzyme 2 (ACE2), which acts as a receptor, and binding to ACE2 is crucial for the cellular entry of SARS-CoV-2 [1]. Any drug that interrupts the binding of spike protein with the ACE2 receptor will be useful in the treatment of COVID-19.

Renin-Angiotensin-Aldosterone System (RAAS) plays a crucial role in the regulation of blood pressure, sodium level, extracellular fluid volume, etc. Along with the classic pathway which produces effects like vasoconstriction and inflammation, one more pathway with opposing actions to classic pathway exist which produces effects like vasorelaxation and it is anti-inflammatory. Unlike the classic RAAS pathway which uses ACE, the vasorelaxation arm uses ACE2 [1].

It is known that COVID-19 patients exhibit pneumonia, and severe cases had complications like acute respiratory distress syndrome (ARDS), respiratory failure and septic shock which carries a high mortality rate [2]. Recent studies showed that beta-adrenergic blockers reduced the mortality in septic shock patients [3]. Beta-adrenergic blockers also showed beneficial effects in ARDS and respiratory failure patients [4,5]. Beta-adrenergic blockers by its inhibitory action on the sympathetic system negatively regulate renin release by Juxtaglomerular (JG) cells in the kidney. A decrease in renin may reduce the activity in both arms of RAAS and may decrease ACE2, which may decrease the SARS-CoV-2 virus entry into the host cell.

Considering the potential role of beta-adrenergic blockers in decreasing the SARS-CoV-2 entry into the cells by downregulating ACE2 receptors, and its role in reducing the mortality in respiratory failure, ARDS and septic shock conditions, it may be a good candidate drug for treating COVID-19 patients (Figure 1). I propose that beta-adrenergic blockers may be beneficial in COVID-19 patients with hypertension comorbidity, by regulation of blood pressure and decreasing SARS-CoV-2 cellular entry. In low doses, beta-adrenergic blockers may be beneficial in COVID-19 patients with normal blood pressure, as it may decrease the SARS-CoV-2 entry into the cell. I suggest doing a retrospective study on the COVID-19 patients, who were already on beta-adrenergic blockers for their previous cardiovascular illness and its effect on mortality. The proposed retrospective study will test the validity of the hypothesis and clarify the role of beta-adrenergic blockers in COVID-19 patients.

<Insert Figure 1 here>

Keywords: SARS-CoV-2, COVID-19, ACE2, Beta-adrenergic blockers, Septic Shock, ARDS.

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Figure Legends

Figure 1: Beta-adrenergic blockers effect on RAAS and COVID-19.

A) Beta-adrenergic blockers by its inhibitory action on the sympathetic system decrease the renin release by Juxtaglomerular (JG) cells in the Kidney. A decrease in renin may reduce the activity in both arms and may decrease ACE2 receptors. B) Decreased ACE2 receptors will affect the SARS-CoV-2 cellular entry and thereby reduce the viral infectivity. Beta-adrenergic blockers have been shown to reduce the mortality rate in ARDS, septic shock and respiratory failure. Beta-adrenergic blockers will be beneficial in COVID-19 patients in two ways, by reducing the SARS-CoV-2 virus cellular entry and by reducing the complications like ARDS, Septic shock and respiratory failure in severe cases.