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Corticosteroids Administration Following COVID-19-induced Acute Respiratory Distress Syndrome. Is it harmful or Life-saving?

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Until now, April 22, 2020, Covid-19 has been confirmed in 2471136 patients and 203 countries and territories with mortality rate over 169000 patients [1]. Right now, there is no definite cure for it and developing treatments including vaccines and antiviral compounds are under evaluations for efficacy. COVID-19 infection can be mild, severe, or even critical. The symptoms may range from fever (the most common symptom), chills, fatigue and cough to decreased arterial oxygen saturation, changes in respiratory rate and dyspnea. The dyspnea in critically patients is more severe. In severe cases, respiratory failure, acute respiratory distress syndrome (ARDS) and septic shock have been reported. Septic shock is also associated with hypoxia and acidosis [2-4].

ARDS is the most important cause of death in this group of patients. This feature of the disease may be caused by various factors, including inflammatory mediators and cytokine storm [5]. The computed tomography (CT) imaging findings have shown that the lung with ARDS has a ground-glass appearance, in which white fluid-filled patches are seen inside the lung. The fluid inside these patches has a jelly state [6, 7]. Pathological samples obtained from lung tissue also indicate pulmonary damage, obvious destruction of pneumocytes and formation of a hyaluronan membrane, which more emphasized on ARDS occurrence [8].

Cytokine storm caused by Covid-19 infection is a severe immune response. The occurrence of cytokine storm can lead to severe tissue damages. Pre-inflammatory factors are involved in this process and one of them is interleukin 6 (IL-6) which affects different cells. IL-6 performs various functions such as regulating body temperature, increasing the production of acute phase protein and differentiation of B cells [9]. On the other hand, the production of interleukin 1 (IL-1) as an inflammatory mediator will be increased during cytokine storm, as well. IL-1 can cause fever and stimulating the production of hyaluronan which has been seen in fibrosis [10]. Based on studies on SARS-CoV, rapid spread and proliferation of the virus as a result of delayed interferon-1 production and subsequent rapid accumulation of macrophages and monocytes may also be involved in tissue destructions and a similar mechanism might be seen in COVID-19 infection [11].

When there is no proper immune system response, the virus causes extensive tissue damages, especially to organs where ACE2 is most commonly seen, such as the lungs [7]. Therefore, since the lungs are damaged, efforts should be focused on suppressing the inflammation, managing the symptoms and theoretically any compounds that may help this inflammation subside could play an important role in reducing the incidence of ARDS and consequently the mortality rate.

The use of corticosteroids in different phases of ARDS has been inconsistent with conflicting results. Corticosteroids exert their anti-inflammatory effects by regulating the signaling pathways on the membrane and inside the cells, stopping pre-inflammatory gene-related processes (genes responsible for producing pre-inflammatory factors). Furthermore, they are able to increase the production of anti-inflammatory mediators such as interleukin 10 (IL-10) [12].

Corticosteroids have been investigated in some clinical protocols for evaluation of their effectiveness in reducing inflammatory responses and cytokine storm. According to the guideline of World Health Organization (WHO), systemic corticosteroids should not be routinely used in viral pneumonia except in clinical trials. However, WHO has recommended that these compounds can be used in exacerbations of asthma and COPD,

and septic shock, considering each patient's condition and assessing the benefits and risks. This guideline further states that the use of corticosteroids in similar conditions such as influenza may lead to secondary super infections and increase mortality rate [13]. But in another study on SARS-CoV, the use of corticosteroids was associated with improvement in time to survival in severe patients and decrease in mortality rate [14]. Delayed viral clearance is another concern. In a study on patients with MERS-CoV, the use of corticosteroids did not make a significant difference in mortality rate. However, its association with a delay in viral clearance from the lungs of patients was reported [15].

Side effects are another limiting factors for use of corticosteroids in patients with Covid-19. A similar study in patients with SARS-CoV showed that use of higher doses of corticosteroids in such conditions could cause a corticosteroid-induced diabetes, with 36.3% of patients experiencing such complication [16].

The guideline of Surviving Sepsis Campaign for the management of patients with Covid-19 has recommended the use of corticosteroids under the following conditions: 1) in patients with Covid-19 who are suffering from septic shock, the use of corticosteroids (low-dose) are preferred over not using it. The guideline notes that there is no difference in mortality rate and side effects. However, there is weak recommendation that using corticosteroids in these conditions can reduce the time of resolution of shock and ICU and hospital length of staying; 2) In cytokine storm, if the patient has not yet developed ARDS, corticosteroids are recommended in ways other than routine procedures, and if ARDS occurred, the use of these compounds is recommended over not using them. Lesser need of oxygen, improved radiographic findings and reduced length of staying in ICU and hospital are some of the advantages that this guideline has referred to. However, there is just a week recommendation over the use of these compounds in this guideline [17].

Based on what has been discussed, it could be concluded that the use of corticosteroids in the current situation should be limited, since there are no significant benefits over their effectiveness. On the other hand, there is a risk in prolongation of viral clearance and secondary infections and mortality rate. The use of these compounds should be limited to clinical trials to further evaluate their effectiveness in this new found disease. The clinical conditions of patients should be carefully evaluated throughout the studies and close monitoring should be performed while discontinuing these drugs.

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AUTHOR CONTRIBUTION

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CONFLICT OF INTEREST

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