

Effectiveness of Glucocorticoid Therapy in COVID-19 Patients

(Brief Review)

Ratiani Levan¹, Gabunia Luiza², Khetsuriani Shorena², Gamkrelidze Natia², Sulashvili Nodar²

¹First University Clinic, Tbilisi State Medical University, Tbilisi, Georgia

²Scientific Research-Skills Center, Tbilisi State Medical University, Tbilisi, Georgia



Abstract – Glucocorticoid therapy is widely used among patients with different severe pulmonary inflammatory diseases. The novel study results recommend the use of corticosteroids for treatment of severe form of COVID-19 infection. Study results also indicate the importance of monitoring of these patients due to the possible adverse reactions of glucocorticoid therapy.

Keywords – COVID-19 Infection, glucocorticoids, corticosteroids, adverse reactions, dexamethasone.

An infection caused by a novel coronavirus – COVID-19 emerged at the end of December 2019 and has caused a major challenge to the public health worldwide. On March 11, 2020, the WHO declared COVID-19 as a global threat [1].

Specific drugs are not available so far for the prevention and treatment of COVID-19, therefore symptomatic supportive treatment is still the most effective in management of COVID-19 infection [2].

The patients having mild symptoms and rapidly progressed to severe condition are correlated with an increased risk of mortality [3].

The control the inflammatory response is a big concern in order to prevent the worsening of the disease in mild patients [4].

The clinical manifestation is diverse: from asymptomatic or mild disease to severe pneumonia in where the disease progressed into acute respiratory distress syndrome (ARDS) requiring long lasting mechanical ventilation, sometimes extracorporeal membrane oxygenation (ECMO) [5,6].

In the pathogenesis of severe COVID-19, the host immune response plays a major role and it is apparent that COVID-19 pneumonia is linked with both hyper inflammation and immunoparalysis [7].

Massive vascular inflammation, disseminated coagulation, shock and ARDS is frequently provoked [7,8].

As full-genome sequencing analyses shows SARS-CoV-2 is a representative of beta-coronaviruses, related to the Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV. Therefore, treatment of COVID-19 can be based on the experience from the SARS and MERS epidemics [9].

Glucocorticoids are commonly used in the treatment of several pulmonary inflammatory diseases.

COVID-19 patients with systemic inflammatory response develop multiorgan failure including the lungs and other organs. The novel study results recommend the use of corticosteroids (glucocorticoids) due to their potent anti-inflammatory effects, reducing the damaging effects on tissues and organs.

Glucocorticoids are broadly used among critical patients with other coronavirus infection such as SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) [10,11].

Several therapies target for limitation of the inflammatory response, though strong evidences of benefit are lack. Corticosteroids might be beneficial in defeating both hyperinflammation and ARDS [12,13].

There are contradictory opinions about the use of glucocorticoids for COVID-19 treatment. Some current clinical studies do not support the use of glucocorticoids, due to their several side effects[14,15].

Usage of glucocorticoids may often associate with significant adverse reactions, such as delayed viral elimination, opportunistic infections and also inhibition of the hypothalamic-pituitary-adrenal axis [16,17].

Studies included strict monitoring of patients taking dexamethasone, special attention was paid to the development of side effects (hyperglycemia, secondary infections, psychiatric effects, aseptic necrosis, etc.). Long lasting use of glucocorticoids may cause development of latent infections (e.g., hepatitis B, herpes virus, tuberculosis, strongyloidiasis).

Some clinicians suggest that short-term glucocorticoid therapy with small or medium dose scould be beneficial for patients with severe conditions in COVID-19 infection[18]. The modern guidelines on COVID-19 are also changeful about the use of glucocorticoids. Some guidelines suggested short-term therapy with medium or small doses of glucocorticoids for patients with rapid or severe disease progression, but according to the WHO guidelines glucocorticoids should only be used under clinical trials [19,20].

The RECOVERY trial reported that the use of dexamethasone as in contrast with common care reduced 28-day mortality in patients requiring oxygen therapy or mechanical ventilation [21].

Prospective meta-analysis of seven randomized clinical trials revealed that administration of corticosteroids was associated with lower 28-day all-cause mortality [22,23].

The Surviving Sepsis Guideline on management of COVID-19 recommends use of steroids in COVID-19 patients on mechanical ventilation with ARDS and refractory shock [24].

Hospitalized patients with COVID-19 infection were involved in randomized, multicenter studies. According to the results, the mortality rate was notably decreased in patients receiving dexamethasone compared with patients taking standard treatment[23].

Advantages of glucocorticoids were marked in patients who were on mechanical ventilation, while the assets of dexamethasone were not observed in patients who did not require mechanical ventilation [25].

Guideline panel recommends the use of 6 mg dexamethasone daily for 10 days before the hospital discharge in patients on mechanical ventilation or needing extra oxygen supply. Also, glucocorticoids are not used in patients who do not require additional oxygen supply and are not on mechanical ventilation. Despite dexamethasone prednisone, methylprednisolone, hydrocortisone may be also used. Both the immediate benefits as well as the late positive clinical results reveal that the use of corticosteroids (predominantly, prednisone and methylprednisolone) is also recommended in COVID-19 patients who also have other pulmonary infections. In patients with pneumocystic pneumonia and hypoxia, prednisone therapy remarkably reduces the risk of lethality, but clearance and elimination of the virus from the body is delayed. Glucocorticoids were used in patients with acute respiratory distress syndrome and they notably reduced mortality and duration of hospital stay in patients on mechanical ventilation.

Dexamethasone mildly induces cytochrome-P450 (CYP) 3A4 enzyme in the liver, which on its turn increases the elimination of drugs that are metabolized in the liver by the this enzyme (e.g., antidepressants, calcium channel blockers, antifungal azoles, probiotics, benzodiazepines, estrogens, erythromycin, inhibitors of viral proteases, proton pump Inhibitors, etc.), decreasing their therapeutic concentration in the blood which should be taken into account while combining dexamethasone with the above drugs.

Conclusion: based on above, studies show positive effect of corticosteroids on short-term mortality and decreased need for mechanical ventilation. So far, obtained data is scanty for reasoning, prolonged viral elimination and secondary infections related

to corticosteroid use should be considered as unfavorable adverse reactions. The best timing regimens, safe dosing and duration of treatment with corticosteroids requires further examination. The fact that administration of glucocorticoids is frequently accompanied by remarkable adverse reactions should be always considered, therefore strict monitoring of patients undergoing this therapy is crucial as well.

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