Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Corticosteroids for COVID-19: the search for an optimum duration of therapy

Michael A Matthay and B Taylor Thompson[1] have very nicely summarised the evidence-based role of dexamethasone in hospitalised patients with COVID-19. Their pertinent analysis is based on the background of the RECOVERY trial,[2] which concluded that therapy with dexamethasone at a dose of 6 mg once daily for up to 10 days decreased 28-day mortality in patients with COVID-19 on respiratory support. Patients not requiring oxygen showed no benefit but had a possibility of harm with corticosteroid therapy.[2]

One crucial feature of corticosteroid therapy is its duration, particularly in patients with COVID-19 with sustained persistence of ground-glass opacities. Currently, an extended course of corticosteroids beyond 10 days is considered only in select cases of severe COVID-19.[3] One rationale for prolonged treatment is the prevention of post-disease fibrosis in patients with COVID-19 for whom risk factors for pulmonary fibrosis might be established.

However, in COVID-19, such a long-lasting course of corticosteroids can inadvertently lead to poor treatment outcomes. The possible effect of steroids in the procoagulant environment of patients with COVID-19, in which even anticoagulant treatment does not sufficiently shield from the thrombotic complications found in deceased patients, should be considered. A hypercoagulable state with profound endothelial injury following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has an essential role in thrombosis. In autopsy studies of patients with COVID-19, diffuse alveolar disruption with large vessel thrombi and microthrombi were seen.[4] Dexamethasone (6 mg per day) tends to increase clotting factor and fibrinogen concentrations. Thus, it is plausible for exogenous glucocorticoids to precipitate clinical thrombosis.[5] In addition, protracted corticosteroid therapy might contribute to the so-called long COVID syndrome that manifests with fatigue and psychological symptoms, in which steroid-related adverse drug reactions such as myopathy, neuromuscular weakness, and psychiatric symptoms might have a part to play.[6,7]

Late in the disease course, corticosteroids do not appear to have a role in managing acute respiratory distress syndrome (ARDS). Routine use of methylprednisolone for persistent ARDS is not recommended despite improving cardiopulmonary physiology. Even initiating methylprednisolone therapy more than 2 weeks after the onset of ARDS might increase the risk of death.[7]

A meta-analysis of 21 350 patients with COVID-19 concluded that overall mortality was greater among patients with the disease who were receiving corticosteroids than among patients who were not treated with corticosteroids. The duration of steroid therapy ranged from 3 to 12 days.[8] The prothrombotic influence of steroids, coupled with their adverse drug reactions, might have contributed to increased mortality.

Corticosteroids thus seem to be a double-edged sword in the fight against COVID-19 and need to be used judiciously, considering the risk–benefit ratio, as a short-course (eg, up to 10 days) therapeutic agent in a select group of patients with COVID-19 for whom survival benefit has been reported. There is no evidence supporting long-term use of steroids in patients with COVID-19 to prevent potential adverse sequelae such as pulmonary fibrosis. On the contrary, such an extended course of steroids could be detrimental.

We declare no competing interests.

*Gyanshankar P Mishra, Jasmin Mulani
gpmishra81@gmail.com

Department of Respiratory Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra 440018, India (GPM) and Department of Biochemistry, Government Medical College, Nagpur, Maharashtra, India (JM)

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Published Online
November 26, 2020
https://doi.org/10.1016/S2213-2600(20)30530-0

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