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High-dose steroids for the treatment of severe COVID-19 pneumonia: the need of the hour?

To the Editor

Ever since the results of the RECOVERY trial [1] were made public, steroids became the mainstay of the treatment of patients with moderate to severe COVID-19 pneumonia needing oxygen support. As the pandemic progressed and patients with moderate to severe disease requiring oxygen were treated with 6 mg dexamethasone for 10 days, it soon came to light that the recommended dose did not show a significant mortality benefit. In clinical practice, high-dose steroids are used in disease processes involving high inflammatory activity such as auto-immune diseases, septic shock unresponsive to fluid resuscitation and vasopressors, chronic obstructive pulmonary disease (COPD) exacerbation, severe asthma, and allergy. Therefore, to consider high-dose steroids for the management of severe COVID-19 pneumonia is not a novel concept.

Edara *et al.* [2] published a case series where they treated two patients who were deteriorating on conventional regimen of steroid therapy with high doses of methylprednisolone reaching up to 500–750 mg/day and reported a positive outcome. So *et al.* [3] treated seven patients with COVID-19 intubated secondary to acute respiratory distress syndrome with high-dose methylprednisolone 500–1000 mg/day and reported a positive recovery in all seven patients. A study from Iran [4] randomised sixty-eight hospitalised patients with confirmed severe COVID-19 into two groups with a ratio of 1:1, with one group receiving standard care with the addition of methylprednisolone pulse (intravenous injection,

250 mg/day⁻¹ for 3 days) and the second group receiving standard care alone (which included the conventional dose of the steroid). The number of patients with a clinical improvement was higher in the group receiving methylprednisolone pulse therapy as compared to the group receiving standard care (94.1% vs 57.1%), and the mortality rate was lower in the methylprednisolone group (5.9% vs 42.9%; $p < 0.001$). These studies, though not adequately powered, do raise a possibility of benefit to patients with severe disease when treated with high doses of steroid.

A question now arises on defining the subset of patients who would qualify for the high-dose steroid therapy. This query was answered by a recent study published by Spanish authors [5] to test whether high-dose corticosteroid pulse therapy (1.5 mg/kg/24h of methylprednisolone or dexamethasone equivalent) was associated with increased survival in Covid-19 patients at risk of hyper-inflammatory response. The group provided with the initial criteria using laboratory markers to stratify these patients. The parameters proposed were (IL-6 ≥ 40 pg/mL, and/or two of the following: C-reactive protein ≥ 100 mg/L, D-dimer ≥ 1000 ng/mL, ferritin ≥ 500 ng/mL and lactate dehydrogenase ≥ 300 U/L) and a positive outcome was noted in the subjects receiving the higher doses.

These are times where the scientific knowledge is being updated on a daily basis and guidelines are changing every day in the light of new evidence. Under such circumstances the sound data available showing a benefit of high-dose steroids in severe COVID-19 pneumonia and the

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criteria where they should be instituted warrants further investigation in the form of adequately powered randomised control trials to answer this new but pressing question — is this the need of the hour?

Conflict of interest

None declared.

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