



Is high-dose glucocorticoid beneficial in COVID-19?

To the Editor:

We read with interest the article by EDALATIFARD *et al.* [1], and we congratulate them for performing a randomised controlled trial amidst the ongoing pandemic. We have a few concerns regarding the methods and interpretation of the current study. While the intervention group's mortality is low, the mortality in the control group is disproportionately high for the severity of illness (acute respiratory distress syndrome (ARDS) not present, patients not intubated). The mortality in ARDS due to coronavirus disease 2019 (COVID-19) among mechanically ventilated patients is 50% or less, and it has improved over time from 42% to 25% [2, 3]. The mortality in the current study's control arm (43%) was worse than the mortality in the control arm of the RECOVERY trial (26%) [4]. The survival difference between the two study groups may be due to the better supportive care provided to the intervention arm due to the trial's unblinded nature. Also, the justification provided for the sample size is inadequate. The authors have cited studies using methylprednisolone in asthma, COPD and pre-operative patients as references for the sample size calculation.

The primary outcome chosen was clinical improvement, defined as "Borg score >3, improved dyspnoea, no fever for 72 h, $S_{pO_2} >93\%$, tolerated oral regime, normal urinary output, and reduced CRP level without any treatment side-effects". Most of these are subjective parameters. The quick defervescence and a sense of well-being intuitively explain the improvement in the subjective parameters observed in the study group. The choice of Borg scale and subjective sensation of dyspnoea for acute respiratory failure, instead of more reliable and objective scores, such as arterial oxygen tension/inspiratory oxygen fraction ratio, APACHE-II or the SOFA score, raises concerns regarding the interpretation of the trial.

Finally, diabetes mellitus was the most common comorbidity in the study. However, more patients in the control group had diabetes mellitus, which spuriously decreased the observed adverse events in the intervention arm. Such high doses of glucocorticoids can predispose the patients to devastating complications such as COVID-19-associated pulmonary aspergillosis and COVID-19-associated mucormycosis. We believe that more extensive research is required before high-dose glucocorticoids can be recommended for treating severe COVID-19 patients.

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High-dose glucocorticoids are not currently recommended for treating severe COVID-19 pneumonia
<https://bit.ly/39VQ3O8>

Cite this article as: Muthu V, Sehgal IS, Prasad KT, *et al.* Is high-dose glucocorticoid beneficial in COVID-19? *Eur Respir J* 2021; 57: 2100065 [<https://doi.org/10.1183/13993003.00065-2021>].

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Received: 9 Jan 2021 | Accepted: 17 Jan 2021

Conflict of interest: None declared.

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- 3 Lim ZJ, Subramaniam A, Ponnappa Reddy M, *et al.* Case fatality rates for patients with COVID-19 requiring invasive mechanical ventilation. A meta-analysis. *Am J Respir Crit Care Med* 2021; 203: 54–66.

- 4 RECOVERY Collaborative Group, Horby P, Lim WS, *et al.* Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021; 384: 693–704.

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