



LETTER TO THE EDITOR

Corticosteroids in COVID-19: A double-edged sword – a retrospective study



Corticoides en el tratamiento de la COVID-19: un arma de doble filo

Dear Editor,

Corticosteroids have received increasing focus as an emerging therapy in COVID-19, particularly in patients receiving respiratory support as demonstrated by the RECOVERY trial.¹ Previous evidence already supported the use of steroid treatment in patients with acute respiratory distress syndrome (ARDS) undergoing mechanical ventilation.^{2,3} However, there is no current consensus regarding the ideal dose and treatment duration in this population.

Furthermore, the focus of the discussion on corticosteroid use in COVID-19 has been on the timing of treatment initiation according to disease stage, and concerns about steroid-related delay in viral clearance.⁴ However, it is likely that benefits are dependent on the cumulative dose and duration of corticosteroid therapy, but these questions remain unaddressed in high quality randomized trials.⁵

To contextualize this problem, we reviewed a retrospective cohort of 65 patients admitted to a secondary referral intensive care unit (ICU) with SARS-CoV-2 pneumonia and ARDS undergoing mechanical ventilation in a 5-month period. This cohort is composed of predominantly male patients (75.4%), with a mean age of 65.1 years [57–74], with a median duration of ventilation of 10 days [5–16] and an ICU mortality rate of 13.9%.

Patients were treated with different doses of corticosteroids according to the evolution of the scientific evidence during the pandemic and the patients' clinical course. Patients at the beginning of the pandemic did not receive corticosteroids. Patients admitted later during the year received corticosteroids according to the protocol proposed by the Critical Illness-Related Corticosteroid Insufficiency

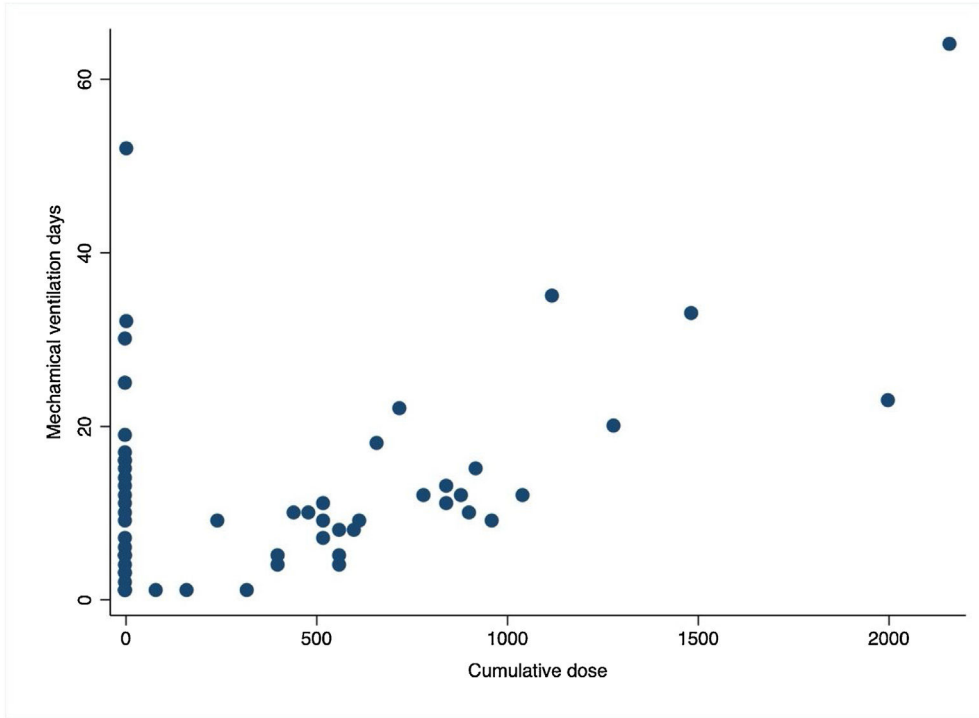
in Critically Ill (CIRCI) Patients Guideline³ or the RECOVERY trial protocol.¹

We plotted the duration of mechanical ventilation and cumulative corticosteroid dose (expressed as methylprednisolone equivalent dose) and invasive mechanical ventilation duration (Fig. 1A). We used a cubic spline regression model to plot the relationship between the two variables, using three knots at the 25th, 50th and 75th percentile – namely 160 mg, 520 mg and 960 mg (Fig. 1B). There was a strong correlation between total corticosteroid dose and ventilation days ($p < 0.001$), following a U-shaped pattern. The shortest ventilation time associated with a cumulative dose of 560 mg, while higher doses were associated with longer duration of mechanical ventilation. In order to correct for possible longer duration of treatment with corticosteroids due to inertia we looked at the relation between total duration of mechanical ventilation and methylprednisolone-free ventilation days. After controlling for methylprednisolone-free ventilation days the correlation remained significant ($p < 0.001$). There was no correlation with increased infection rates or mortality, but we found a strong correlation between higher cumulative doses of corticosteroids and ICU-acquired myopathy ($p = 0.03$).

This study has some limitations. Given the retrospective nature of the cohort and the change in evidence regarding the efficacy of treatments in COVID-19, treatment was not standardized for all patients. Similarly, the dose and duration of corticosteroid varied among patients and tapering was done based on individual patient condition, as per the CIRCI Guideline. The mean dose of methylprednisolone used in our cohort was 653 mg. Despite this heterogeneity, the mortality rate was distributed evenly throughout the 5-month period.

In sum, our analysis suggests that corticosteroid therapy in COVID-19 needs to be carefully titrated and readily tampered when clinical improvement occurs, given the lack of evidence for benefit of higher doses. Considering current evidence, we suggest that prolonged treatment with corticosteroids in COVID-19 should be avoided.

A – Scatterplot of cumulative methylprednisolone dose and ventilation days



B – Cubic spline curve model

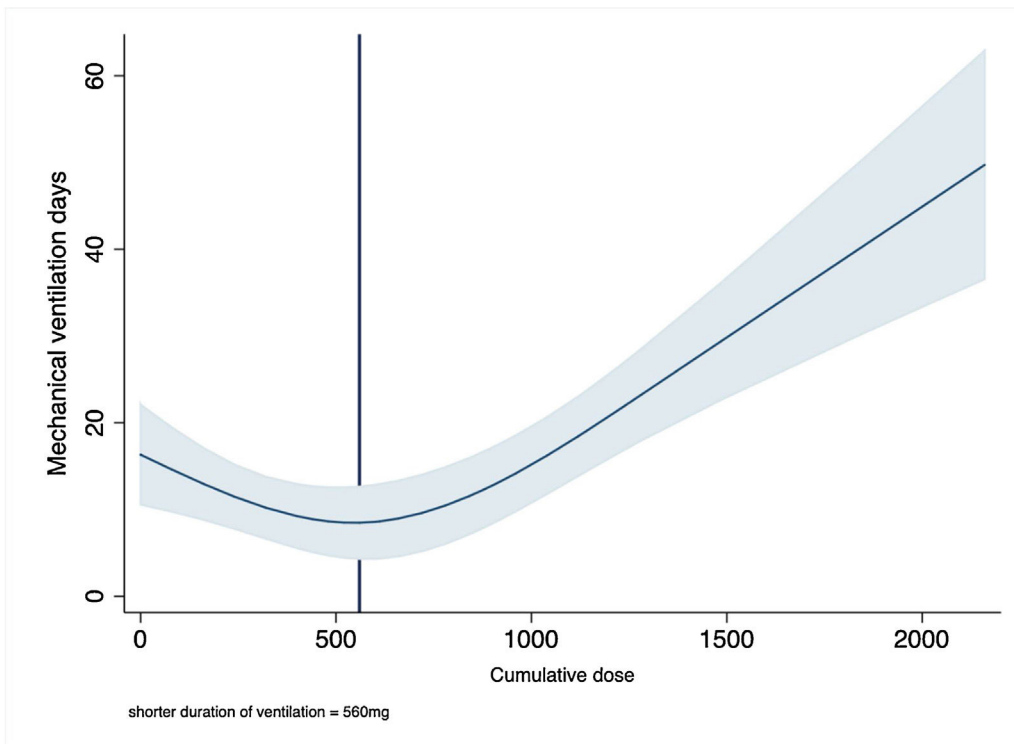


Figure 1 (A) Scatterplot of cumulative methylprednisolone dose and ventilation days. (B) Cubic spline curve model.

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Authors' contributions

RM, LM, JJM and PTF were responsible for the study conception and manuscript draft. RM and LM collected data. All authors read and approved the final manuscript.

Conflicts of interest

None declared.

References

1. The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 – preliminary report. *N Engl J Med.* 2020, <http://dx.doi.org/10.1056/NEJMoa2021436>.
2. Meduri GU, Golden E, Freire AX, Taylor E, Zaman M, Carson SJ. Methylprednisolone infusion in early severe ARDS: results of a randomized controlled trial. *Chest.* 2007;131:954–63.
3. Annane D, Sebille V, Bellissant E. Effect of low doses of corticosteroids in septic shock patients with or without early acute respiratory distress syndrome. *Crit Care Med.* 2006;34:22–30.
4. Xu K, Chen Y, Yhan J. Factors associated with prolonged viral RNA shedding in patients with COVID-19. *Clin Infect Dis.* 2020: ciaa351.
5. The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA.* 2020;324:1330, <http://dx.doi.org/10.1001/jama.2020.17023>.

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Strategies to maintain high-quality education and communication among the paediatric and neonatal intensive care community during the COVID-19 pandemic



Estrategias educativas y de comunicación de alta calidad en cuidados intensivos pediátricos y neonatales durante la pandemia de COVID-19

Dear Editor,

The coronavirus 2019 (COVID-19) pandemic represents a real challenge for the medical community. Considering these circumstances, the European Society of Paediatric and Neonatal Intensive Care (ESPNIC) analyzed how to efficiently reach its members, how to easily share updated content on the new disease, and how to implement new education and communication strategies.

A discussion on the impact of the pandemic on medical education has already been started within the medical community.¹ The transition to online classes and the cancellation of clinical practice sessions, rotations and medical conferences, result in less collaborative experiences and networking, which are known to impact on the career development of young investigators.² As a first step in the process of filling this gap, starting in 2020 spring, ESPNIC offered a series of webinars (promoted via social media as #ESPNIC-COVID19 webinars) focusing on the management of COVID-19 in children and neonates (webinar topic list is uploaded as

Electronic Supplementary Materials Table 1). Each webinar included 60 min of free-to-access expert teaching followed by a 20-min discussion on the topic and the possibility of true networking with the speakers during and after the sessions. Almost 3000 people attended the ESPNIC webinars from 97 different countries (distribution displayed in ESM – Fig. 1). Interestingly, 15% were multidisciplinary health-care providers not regularly working in the intensive care field. Besides the webinars, ESPNIC provided online tutorials focused on non-invasive and invasive ventilatory support, which was felt as most relevant topics for the audience in the given circumstances.

The “virtual wave” during the pandemic is confirmed by increased social media engagement in our field.³ In order to increase its educational impact, ESPNIC nominated a “Social Media board”, consisting of intensive care physicians, trainees, and communication experts. Scientific papers, literature contents, as well as qualified educational materials for young trainees, have been regularly shared, reaching over 3500 followers in the first few months. A recent analysis of the use of social media for sharing high-quality content during the pandemic identified ESPNIC as a point of reference in the networking pattern of the paediatric intensive care community.³

In conclusion, the COVID-19 pandemic represented a true accelerator of the teaching evolution into remote learning. These virtual formats have been proposed and applied by academic institutions and scientific societies as the “new normal” for postgraduate and continuing medical education. However, the complete shift of standard educational activities into their online version can lead to online networking tiredness, anxiety or worry secondary to the