CE-COMMENTARY

High-dose steroids for the treatment of severe COVID-19: a new therapeutic tool?

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The interesting Research Letter by Piccica et al. focuses on a hot topic of the last 2 years, since the SARS-CoV-2 pandemic caused an unprecedented crisis of national health systems all over the world. Few therapeutic approaches have so far been approved for the management of COVID-19 and only steroids have been demonstrated to reduce mortality in patients with acute respiratory failure [2]. This evidence comes from the large multicentre RECOVERY trial, in which intravenous dexamethasone (6 mg once daily for up to 10 days) caused a significant reduction in the incidence of death. These findings, in combination with the substantial lack of efficacy of antivirals and immunomodulatory drugs [3–5], has led to a change in paradigm in the clinical management of COVID-19, dexamethasone marking a milestone in pharmacological treatment.

However, some uncertain aspects still remain. First, since the rationale of dexamethasone in COVID-19 is to modulate and mitigate inflammation-mediated lung injury, a weight-based dosing of steroid therapy could be more appropriate. Second, most patients hospitalized for COVID-19 with need for oxygen therapy and/or respiratory support take more than 10 days to recover [6]: it seems reasonable that dexamethasone could be given for more than 10 days, but no solid supporting evidence is yet available. Third, a significant proportion of patients who recover from COVID-19 complain of persistent respiratory symptoms associated with parenchymal fibrotic strands and persisting CT evidence of ground-glass opacities, even 3 or 6 months after hospital discharge [7, 8]: a higher dose of steroid therapy may help tackle the inflammatory burden in an early phase of disease, hopefully lowering the probability of developing chronic lung damage.

Piccica et al. described their experience with a high dose of intravenous methylprednisolone (≥ 2 mg/kg/day) in a small cohort of hospitalized COVID-19 patients [1]. All patients showed radiography and/or high resolution computed tomography evidence of lung infiltration and needed respiratory support with oxygen and/or mechanical ventilation. Despite significant deterioration in clinical status at baseline (in terms of PaO2/FiO2 ratio and prevalence of ARDS) in the high-dose group, the authors did not observe a statistically significant difference in mortality between the low- and high-dose steroid cohort. Significantly, the latter group showed a longer latency of therapy from onset of symptoms, suggesting that a higher dose of methylprednisolone may also be helpful in advanced COVID-19 pneumonia. Finally, no evidence of severe or unexpected adverse events was reported.

The results of Piccica et al. [1] are intriguing as they suggest that a higher dose of steroids may be beneficial in terms of early mortality, especially in patients with advanced disease and/or "do not resuscitate" status, for whom it could be a potential therapeutic option.

High-dose intravenous steroids are a promising tool for the management of severe cases of COVID-19 also by virtue of wide drug availability in all care settings and its well-known safety profile. However, more and larger studies are needed to better understand the effectiveness of this approach compared with fixed-dose dexamethasone, currently the gold standard treatment for this severe condition.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights This comment does not contain any studies with human or animal participants performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

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