Clinical Infectious Diseases

CORRESPONDENCE

The Right Time for Steroids in COVID-19

To the Editor—We have read with interest the work by Fadel et al [1] who describe a beneficial effect of early steroid treatment in patients with moderate to severe coronavirus disease 2019 (COVID-19), in terms of a composite endpoint of progression to intensive care unit admission, need for mechanical ventilation, or death.

Recommendations for steroid treatment in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been cautious [2], based on prior experience with other similar respiratory viruses. Nevertheless, the lack of effective therapy has forced the use of different anti-inflammatory drugs in patients showing deterioration in the course of the disease [3], with the hope to counteract the hyperinflammatory state that lies beneath respiratory insufficiency in COVID-19. Our own experience (unpublished preprint data, https://doi.org/10.1101/2020.05.22.20110544) [4] is in line with that from Fadel and co-authors.

However, we would like to make a point on what we consider "early" treatment. From a physiopathological standpoint, we assume that during the first days after the infection by SARS-CoV-2, clinical manifestations are due to direct viral damage, whereas in a second phase, lung damage is driven by a hyperinflammatory response. With the limitations of current knowledge, it could be considered that anti-inflammatory therapy administered too early in the course of the disease could be deleterious, whereas given at the right time it would hamper inflammation, with a positive effect in oxygenation and therefore in survival.

But when is it too early? Which is the right time? In their article, Fadel et al take as a reference the moment of hospitalization. We disagree with this approach. The moment a patient is admitted to the hospital is variable, and depends on a wide array of circumstances. Nonetheless, the moment of symptom onset in COVID-19 is typically distinct: the vast majority of the patients can recall the exact day of the beginning of fever, cough, or dyspnea.

Considering the day of onset of symptoms as a reference for the time of initiation of steroid treatment, we found a beneficial effect on mortality in patients treated with steroids in a median of 10 days from symptom onset (Fernández-Cruz et al, unpublished preprint data, https://doi.org/10.1101/2020.05.22.20110544) [4]. Patients with >8 days of symptoms will presumably be in the inflammatory phase of the disease and benefit from anti-inflammatory therapies such as steroids. In the work by Fadel et al, it is difficult to ascertain which was the time from the onset of symptoms to initiation of steroid treatment. The fact that a large proportion of patients in the standard of care group also received steroids makes it more difficult to interpret.

Based on these considerations, we suggest that in future studies evaluating the effect of immunomodulatory drugs in COVID-19, the moment of the onset of symptoms should be considered the reference time for the start of the study drug.

Note

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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