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Letter to the Editor

The proper use of corticosteroids for 2019-nCov pneumonia: Towards promising results?

Dear Editor,

The debate about the role of the use of corticosteroids (CS) as treatment support in patients with pneumonia due to novel coronavirus (2019-nCoV) is currently ongoing with several different opinion and a substantial lack of evidence. About this, we read with great interest the letter by Fang et al. recently published in this journal.[1] Generalising available data about other viral or bacterial pneumonia is not entirely applicable to nCoV infection and a detailed examination is requested. A previous reported summary of clinical evidence about the role of CS in SARS-CoV, MERS-CoV and Influenza virus showed all negative effects related to CS administration: delayed clearance of viral RNA from respiratory tract or blood, onset of psychosis, diabetes, avascular necrosis, increased mortality.[2] However, the report by Stockman et al. is not a meta-analysis but only a systematic review with a qualitative inclusion criteria of the studies and does not provide a quantitative effect size of reported factors. On the other side, a meta-analysis reported a reduction of mortality and rate of mechanical ventilation in patients with severe community-acquired pneumonia (SCAP)[3] but in this analysis the higher heterogeneity was observed and in the subgroup evaluation of other pathogen identified only 31 (9.4%) were influenza virus A or B, while 45 (13.6%) were Legionella species. The low number of viral pathogens and the subgroup analysis with other bacterial pathogens (in particular Legionella, with some evidences of harm from CS use) does not provide in our opinion a solid evidence of benefit from CS use. A 2019 meta-analysis about the effect of CS in influenza pneumonia described the negative impact on mortality, days of hospitalization, days in intensive care unit (ICU) and secondary bacterial and fungal infections; in all these outcomes, however, the reported heterogeneity was higher (except for the days in ICU, but with only two studies included) and the only subgroup analysis performed was between H1N1 vs other viral infection; is likely that other subgroup analysis should be assessed such as according age, comorbidities, severity

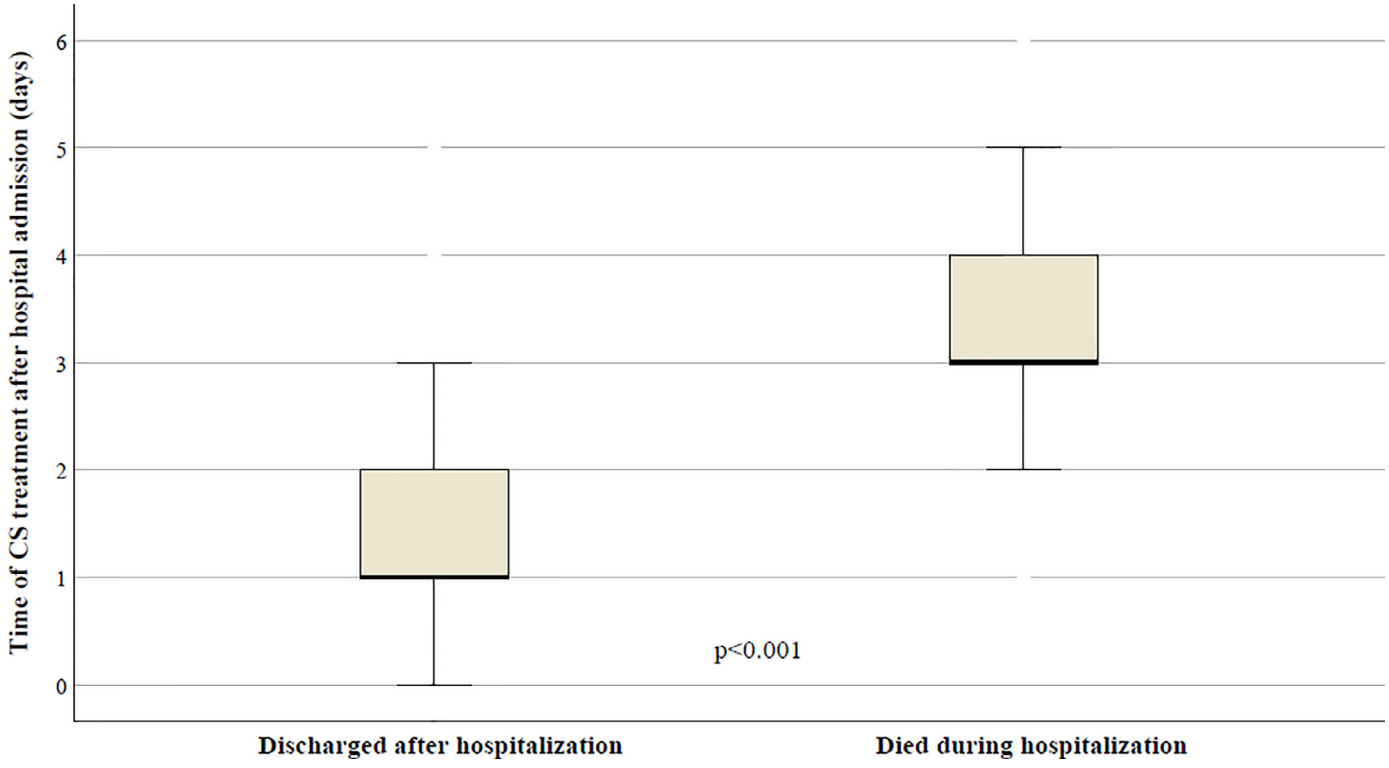

Fig. 1. Relationship between timing of CS administration and mortality in patients with 2019-nCoV pneumonia.

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of pneumonia, need of non-invasive ventilation and others. Despite some data supporting the benefit of the use of CS in viral pneumonia,[4] a recent expert consensus statement focused the attention on the caution of this therapeutic support in the 2019-nCoV pneumonia, especially in critically ill patients with underliyng diseases and major risk of other bacterial or fungal infection.[5] Two major issues, in our opinion, should be deepened in the approach of this discussion: first, the dose and the type of CS used can play a decisive role on the outcome in 2019-nCoV pneumonia: low or moderate dose of methylprednisolone were considered useful in influenza viral pneumonia, while in acute lung injury, acute respiratory distress syndrome (ARDS) or septic shock higher doses of both methylprednisolone and dexamethasone were employed with conflicting results.[6] Second, the timing of the CS use maybe a pivotal role in this topic because an early administration in patients without severe hypoxaemic respiratory failure before the ARDS development could prevent the onset of cytokine-related lung injury, while a late use of CS in subjects with advanced lung damage and critical condition can lead to bacterial infections, delayed clearance of virus and other unfavorable outcomes. Unfortunately, the timing data was not reported in the majority of the available studies and consequently the results may be affected by an important bias. In the study by Wu et al. [7] a reduction of the risk of death was observed in patients with ARDS treated with methylprednisolone (HR = 0.38, p = 0.003): 50 of 84 patients with ARDS received CS treatment (59.5%) but no informations on the dose and duration of this treatment were reported; the Authors conclude that this finding should be evaluated with caution due to low size of patients and a possible risk of bias.

In a recent paper by Horby et al.[8] an encouraging evidence of effectiveness of the use of dexamethasone (at the dose of 6 mg/daily for up to 10 days) was reported in a large randomized study; a lower mortality rate was observed in patients receiving dexamethasone than in other subjects without glucocorticoids treatment; in particular, this result was more evident in patients with mechanical ventilation or respiratory support, while no clear benefit were observed in patients without need of oxygen.

In this context, we reported our experience on the CS use in the first 149 patients admitted in our unit of infectious diseases affected by SARS-CoV-2 infection. Despite the use of CS does not seem related to a reduction of mortality rate (OR = 0.857; 95%CI = 0.377–1.947; p = 0.703), we found a significant lower mortality in patients without ARDS who received an early CS administration (median 1.0 days after hospital admission) in comparison to late CS treatment (median 3.1 days) (OR = 0.224; 95%CI = 0.127–3.449; p = 0.018) (Fig. 1). This finding could mean a positive effect of the CS supportive timing therapy before the ARDS development, but the low number and higher heterogeneity of these patients require further confirmations.

In conclusion, at this time we have some evidence about a positive effect of CS support; further studies are required to better understand the proper use, dose and timing of this treatment during 2019-nCoV pneumonia.

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Lucio Boglione*
University of Eastern Piedmont, Department of Translational Medicine, Novara, Italy

Roberto Rostagno, Federica Poletti, Roberta Moglia, Bianca Bianchi, Maria Esposito, Stefano Biffi, Silvio Borrè
Saint Andrea Hospital, Unit of Infectious Diseases, Vercelli, Italy

*Corresponding author.
E-mail address: lucio.boglione@uniupo.it (L. Boglione)