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Contrasting evidence for corticosteroid treatment for coronavirus-induced cytokine storm

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To the Editor—Two recent articles concerning corticosteroid usage in the coronavirus disease 2019 (COVID-19) pandemic provide opposing evidence and run the risk of muddying the waters on this controversial yet important topic.[1,2] On the one hand, Russell et al[1] tabulated a number of mainly observational clinical studies cautioning more harm than benefit with corticosteroid usage. On the other hand, Shang et al,[2] acknowledging that existing evidence is inconclusive at best, referenced recommendations by Chinese physicians with frontline clinical experiences of COVID-19 who advocate short courses of corticosteroids at low-to-moderate doses for more severe disease.

In clinical settings, physicians tend to use corticosteroids only for treating critically ill patients. Therefore, selection bias and confounders in observational studies might contribute to any observed increased mortality in patient groups treated with corticosteroids. The papers cited by Russell et al[1] omit to address coronavirus mortality, and the strength of the evidence presented does not support the certainty of the authors' conclusions (Table).

Similar to respiratory viral diseases such as the seasonal influenza, two categories of people seem susceptible to die from COVID-19: older adults, especially those with chronic disease or other co-morbidities, and seemingly healthy adults with exacerbated autoinflammatory syndrome termed the cytokine storm syndromes.[3-5] On the contrary, children and infants seem to survive epidemics of

TABLE. Adapted from cases reported by Russell et al[1] with counter comments

Virus	Outcomes of corticosteroid therapy	Counter comments
MERS-CoV	Delayed clearance of viral RNA from respiratory tract	Not significantly associated to 90-day mortality
		Not about SARS-CoV-2
SARS-CoV	Delayed clearance of viral RNA from blood	No relevant mortality and morbidity data
		Small sample size: 9 patients received early hydrocortisone vs 7 patients received placebo
		Not about SARS-CoV-2
SARS-CoV	Complication: psychosis	No relevant mortality and morbidity data
		Small sample size: only 15 patients with SARS-related psychosis
		Not about SARS-CoV-2
SARS-CoV	Complication: diabetes	No relevant mortality data
		Study was comparing SARS patients receiving different dosages of methylprednisolone
		Not about SARS-CoV-2
SARS-CoV	Complication: avascular necrosis in survivors	No relevant mortality data
		Not about SARS-CoV-2
Influenza virus	Increased mortality	No relevant mortality and morbidity data
		Significant statistical heterogeneity in the analysis of the effect of corticosteroids on mortality
		Not about SARS-CoV-2
RSV	No clinical benefit in children	No relevant data on mortality and morbidity
		Study was on children with bronchiolitis, a disease of a different pathophysiology
		Not about SARS-CoV-2

Abbreviations: MERS-CoV = Middle East respiratory syndrome–related coronavirus; RSV = respiratory syncytial virus; SARS-CoV = severe acute respiratory syndrome coronavirus

coronavirus infections with very mild disease.[6]

We acknowledge the potential risks associated with high-dose corticosteroids in treating COVID-19 pneumonia, and agree that corticosteroid usage should be avoided if there are other efficacious anti-inflammatory immunomodulating medications against the cytokine storm, such as intravenous immunoglobulin, interleukin-1 inhibitors, interleukin-6 inhibitors, and Janus kinase inhibitors.[4] However, on the basis of recommendations by frontline Chinese physicians and local clinical experience during the severe acute respiratory syndrome epidemic, a short course of corticosteroids at low-to-moderate dose is probably justifiable for critically ill patients with hyperinflammation.[7,8] Chinese researchers are running a prospective randomised controlled trial to review the efficacy and safety of corticosteroids.[9] Until further evidence becomes available, whether to use corticosteroids or not remains controversial.

Author contributions

All authors contributed to the concept of the study, acquisition and analysis of the data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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