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LETTER TO EDITOR Re: Steroids in mild COVID-19—reading between the lines!

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Dear Editor,

We would like to thank Dr Kounis and his colleagues for taking interest in our paper and providing their valuable opinion.¹ In his letter, Dr Kounis highlights the possible use of corticosteroids in mild COVID-19. While we agree that inhaled corticosteroids have been the mainstay of treatment in patients with obstructive airway disease, their use outside this cohort of patients is still being studied. Existing evidence and standard practices on management of COVID-19 do not support the blanket use of steroids in mild COVID-19.² The recently published STOIC trial asserted that inhaled budesonide reduced the likelihood of needing urgent medical care and the time to recovery in mild COVID-19 infection.³ However, a subsequent larger trial (PRINCIPLE) failed to replicate these results completely. Only a reduced time to clinical recovery (12 vs. 15 days) was observed in their study, with no overall effects on hospitalization rates or mortality.⁴ While the STOIC trial was not placebo-controlled, the PRINCIPLE trial had several limitations, namely- subjective self-reported outcome, inclusion of patients with presumed COVID-19, and enrollment of usual care group over a longer period of time than the inhaled steroids group. As of now, no clinical trial has shown any benefit of using corticosteroids in mild COVID-19, with a recently conducted meta-analysis suggesting possible harm.⁵ Interestingly, our commentary¹ alluded to the practice of using systemic steroids (oral or parenteral) as an extrapolation to their use in severe COVID-19, which did not have and still has no scientific basis besides being potentially harmful.^{6,7} While use of systemic steroids, for the said indication, cannot be justified in the wake of available evidence, we feel that the jury is still out on the role of inhaled steroids in mild COVID-19 and would require further trials before a definitive verdict.

Looking at alternative therapeutic options, monoclonal antibodies like casirivimab-imdevimab have been reported effective in reducing hospitalization and mortality when administered to mild-moderate COVID-19 patients.⁸ Interim results of a new oral antiviral agent, molnupiravir also show a 50% reduction in risk of hospitalization or death in this cohort, when administered within 5 days of symptom onset.⁹ Another oral agent is being studied in the EPIC-HR trial, interim results of which show reduction in hospitalization and death by 89%.¹⁰ Although a number of studies have shown encouraging results, a critical review of the complete trial results would be needed before their routine use.

With the advent of newer promising agents, lack of unequivocal benefit with inhaled steroids and possible harm associated with steroids (systemic > inhaled), it is both logical and imperative that their use be not 'generalized' in patients with mild COVID-19.

Conflict of interest. None declared.

References

- Ray A, Goel A, Wig N. Corticosteroids for treating mild COVID-19: opening the floodgates of therapeutic misadventure. QJM 2021; 114:541–42.
- Kumar S, Mehta S, Sarangdhar N, Ray A, Sinha S, Wig N. Management of COVID-19 from the pulmonologist's perspective: a narrative review. Expert Rev Respir Med 2021; 15:519–35.
- Ramakrishnan S, Nicolau DV, Langford B, Mahdi M, Jeffers H, Mwasuku C, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. *Lancet Respir Med* 2021; 9:763–72.
- 4. Yu L-M, Bafadhel M, Dorward J, Hayward G, Saville BR, Gbinigie O, et al.. Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. The Lancet 2021; 398:843–55. 10.1016/S0140-6736(21)01744-X

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- Sahu AK, Mathew R, Bhat R, Malhotra C, Nayer J, Aggarwal P, et al. Steroids use in non-oxygen requiring COVID-19 patients: a systematic review and meta-analysis. QJM 2021; 114:455–63.
- Sarda R, Swain S, Ray A, Wig N. COVID-19 associated mucormycosis and evolving evidence. QJM 2021; hcab191.
- Swain, S, Ray, A, Sarda, R, et al. COVID-19-associated subacute invasive pulmonary aspergillosis. Mycoses. 2021; 00: 1–8.
- Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, et al. REGEN-COV antibody combination and outcomes in outpatients with Covid-19. N Engl J Med 2021; 384:238–51.
- Merck Sharp & Dohme Corp. Merck and Ridgeback's Investigational Oral Antiviral Molnupiravir Reduced the Risk of Hospitalization or

Death by Approximately 50 Percent Compared to Placebo for Patients with Mild or Moderate COVID-19 in Positive Interim Analysis of Phase 3 Study. Merck.com. https://www.merck.com/news/merck-andridgebacks-investigational-oral-antiviral-molnupiravirreduced-the-risk-of-hospitalization-or-death-by-approxi mately-50-percent-compared-to-placebo-for-patientswith-mild-or-moderat/ (28 November 2021, date last accessed).

10. Pfizer. Pfizer's Novel COVID-19 Oral Antiviral Treatment Candidate Reduced Risk of Hospitalization or Death by 89% in Interim Analysis of Phase 2/3 EPIC-HR Study. https://www.pfizer. com/news/press-release/press-release-detail/pfizers-novelcovid-19-oral-antiviral-treatment-candidate (28 November 2021, date last accessed).