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McKean D, Chung SL, Fairhead R, et al. Corticosteroid injections during the COVID-19 pandemic: experience from a UK centre. *Bone Joint Open*. 2020;1(9):605-611.

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Authors' reply:

Sir,

The authors would like to thank Mr Dean for his letter in response to our article.[1] His calculations are correct based on the assumptions he makes and, as we acknowledge in our paper, this small observational study is not adequately powered to calculate definitively the relative risk of corticosteroid injections (CSI).

It is clear that future studies will be needed to understand fully the risk of CSI with COVID-19. However, we hope our article may provide a useful starting point.[1]

Research in other fields may also help us to understand the potential risk of steroids during the SARS-CoV-2 pandemic. Since our article was published, a nationwide population-based study in South Korea of 44,968 individuals reported that inhaled corticosteroids (ICS) did not increase the risk of SARS-CoV-2 infection. Furthermore, different doses or types of ICS did not appear to affect the risk of SARS-CoV-2 infection.[2]

Peters et al analyzed gene expression of ACE2 in sputum cells from 330 participants in the Severe Asthma Research Program-3 and 79 healthy controls: they reported that the use of ICS was associated with a decreased expression of the angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2).[3] Cell entry of coronaviruses depends on binding of the viral spike proteins to cellular receptors and on S-protein priming by host cell proteases. SARS-CoV-2 uses ACE2 for entry and TMPRSS2 for S-protein priming. As such, decreased expression in lung cells may reduce susceptibility to SARS-CoV-2 infection or lead to a less severe COVID-19 disease. Of note, Peters et al reported that intramuscular injection of triamcinolone acetonide did not lower the expression of either gene.[3] The reason for this is uncertain but may be related to the assessment of sputum cell gene expression at different timepoints after exposure to corticosteroid as samples were taken two to four weeks after CSI.

Schultze et al analyzed the association between ICS and COVID-19-related death among 148,557 people with chronic obstructive pulmonary disease (COPD) and 818,490 people with asthma using linked electronic health records (EHRs) in England, UK. Their study suggested there is neither a

demonstrable benefit nor clear evidence of harm from ICS against COVID-19-related mortality among people with COPD and asthma.[4]

The authors believe that further studies into the systemic effects of CSI, expression of ACE2 and TMPRSS2, and longer-term susceptibility to SARS-CoV-2 infection are required. In the meantime, clinicians are faced with the challenge of balancing the undefined theoretical risks of CSI with the known therapeutic benefits of CSI when treating patients who may have significant pain and disability.[5] The authors hope that our study, and these letters, may help inform the discussion about the likely low risk of CSI during the ongoing pandemic.

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1. **McKean D, Chung SL, Fairhead R, et al.** Corticosteroid injections during the COVID-19 pandemic: experience from a UK centre. *Bone Joint Open*. 2020;1(9):605-611.
2. **Lee SC, Son KJ, Han CH, Jung JY, Park SC.** Association Between Inhaled Corticosteroid Use and the Severe Acute Respiratory Syndrome Coronavirus 2 Infection: A Nationwide Population-based Study in South Korea. In Review; 2020 Sep [cited 2020 Oct 14]. Available from: https://www.researchsquare.com/article/rs-72221/v1 (date last accessed 23 October 2020).
3. **Peters MC, Sajuthi S, Deford P, et al.** COVID-19–related Genes in Sputum Cells in Asthma. Relationship to Demographic Features and Corticosteroids. *Am J Respir Crit Care Med*. 2020;202(1):83–90.
4. **Schultze A, Walker AJ, MacKenna B, et al.** Risk of COVID-19-related death among patients with chronic obstructive pulmonary disease or asthma prescribed inhaled corticosteroids: an observational cohort study using the OpenSAFELY platform. *Lancet Respir Med*. 2020;S2213-2600(20)30415-X.
5. **Little CP, Birks ME, Horwitz MD, Ng CY, Warwick D.** COVID-19: A rethink of corticosteroid injection? *Bone Joint Open*. 2020 Jun;1(6):253–256.

Conflict of Interest: None