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Letter to the Editor

Pain Management Best Practices from Multispecialty Organizations During the COVID-19 Pandemic and Public Health Crises—Evaluating the Risk of Infection Associated with Corticosteroid Injections

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Dear Editor,

We are writing in response to "Pain Management Best Practices from Multispecialty Organizations During the COVID-19 Pandemic and Public Health Crises" specifically to address the issue of increased risk of infection with single-dose administration and therapeutic steroid injections [1]. As noted in the guidelines, and in multiple other studies, there is clear evidence that systemic steroids cause immunosuppression, leading to increased risk of infection. Few studies have, however, evaluated the effects of single-dose steroids and steroid injections on the risk of infection.

A careful subanalysis of ENIGMA-II clinical trial data found that single-dose steroids given perioperatively did not increase the risk of postoperative wound infections [2]. On the other hand, in a claims-based analysis of patients who underwent knee arthroplasty, those who received intraarticular steroid injections within three months of the procedure had significantly greater adjusted risk of periprosthetic joint infection compared with those without any injections [3]; however, this study also found that patients who received hyaluronic acid injections had the highest risk. The authors postulated that direct inoculation and seeding of the joint during previous access, as well as both agents being immunosuppressive, were causes of increased risk.

Evidence for the effects of corticosteroid (CS) injection on risk of viral infection is even more limited. A large retrospective study from 2018 reported an increased risk of influenza among flu-vaccinated patients who had a CS injection compared with those without [4]. The authors reported a single unadjusted relative risk (RR) corresponding to a 52% higher risk of influenza associated with CS injections. However, influenza was rarely reported in either group (<2%), and the absolute risk difference of 0.56% suggests that the risk difference may be a more clinically meaningful measure of association. Regardless, any crude estimate of risk based on the study's data is problematic, as the CS and non-CS groups differed on a number of confounding baseline variables, including age, gender, and prevalence of rheumatoid arthritis. As the data presented in the article allow calculation of the RR stratified by age group (<65 years, ≥65 years), we performed this additional analysis, which found a significantly increased risk of influenza associated with CS injections only in the younger group (<65 years: RR = 1.92, 95% confidence interval [CI] = 1.40–2.63; ≥65 years: RR= 1.19, 95% CI = 0.83–1.70). Understanding the increased risk in the younger age group of CS patients, but not in the older group, merits further study and may be related to their receipt of a lower-dose vaccine.

This study also relied on medical chart review to ascertain both vaccination status and subsequent infection, and it is not clear how reliably these data were captured in the medical records. As the CDC estimates that about 12% of US adults aged 50–64 years and 4% of those aged 65 years and above experience symptomatic influenza each season [5], the study's observed incidence of <2% suggests that a large majority of cases were not captured in their cohort. The increased risk in the CS group may at least party be explained by information bias, for example, if CS patients were more engaged in clinical care and therefore more likely to have flu symptoms recorded in their charts.

Steroids have been used in the treatment of patients with COVID-19 infection, and there is little evidence to

date that they provide any benefit. Observational studies have reported worse outcomes for COVID patients treated with steroids, but these studies did not account for differences in severity of illness that might have prompted the use of steroids. As anyone newly exposed to the virus is likely to become infected, a critical question is whether those receiving single-dose steroids before exposure will have a more severe course of COVID disease. A recent study that divided 78 COVID-19 patients into having either "general" or "severe" disease found that low-dose CS therapy was not associated with slower viral clearance in either group [6].

The reluctance to administer single steroid-based injections when the risks associated with developing severe COVID disease are unknown is understandable, as steroid injections have systemic absorption and systemic steroids decrease immunity and increase the risk of infection. As systemic steroids do show a dose-response curve, it is not clear if there is a safe low dose at which their effects on immune function may be avoided when using injection low-dose or soluble steroids. In this communication, we want to emphasize that avoiding steroids, or using low-dose and soluble steroids when possible, is a reasonable strategy, but that evidence for the increased risk of viral infection associated with CS injections is unclear. Patients should be counseled that data on steroid usage and viral clearance in COVID are early and evolving. Prospective studies to evaluate the impact of CS injections on the clinical course of COVID-19 illness will help guide decision-making.

References

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