

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.

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Letter to the Editor

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Pain Management During COVID-19 and Steroids: Striking a Balance

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Dear Editor,

The authors would like to thank Gill and Breeze for their astute comments regarding our paper, “Pain Management Best Practices from Multispecialty Organizations During the COVID-19 Pandemic and Public Health Crises” [1]. Ironically, an influx of requests to the American Society of Anesthesiologists about the use of steroids was the triggering event for the development of these guidelines.

The authors point out the conflicting evidence for an increased risk of infection with steroid injections, which is likely a result of a very small effect size and the importance of context. To make their case for a (possible) lack of association between steroids and infection, they cite an unplanned post hoc analysis from data obtained during the 2014 ENIGMA-II study, which sought to determine the effect of nitrous oxide on cardiac mortality in individuals with coronary artery disease after noncardiac surgery [2]. This study found no association between intraoperative intravenous dexamethasone and postoperative wound infection. However, neither the steroid, the route of administration, nor the population being studied is appropriate for generalization to a chronic pain population receiving mostly depo-steroid injections. A more relevant comparison would be to examine the effect of a recent epidural steroid injection (ESI) on the postoperative infection rate after spine surgery, as the route and steroid used more closely reflect practices in a pain treatment center. When this scenario is examined, there is fairly consistent evidence that preoperative ESIs, which are the most commonly performed procedure in pain centers across the United States [3], are associated with an increased risk of surgical site infections in patients undergoing spine surgery [4–6].

Although randomized studies such as ENIGMA-II are often cited as the reference standard for evidence, it must be emphasized that the most common definition of “SPIN,” commonly defined in medicine as “the use of specific reporting strategies, for whatever motive, to highlight that an experimental treatment is beneficial despite a statistically nonsignificant difference, or to distract the reader from statistically non-significant results” includes the overstatement of safety when a clinical study is not designed or powered to evaluate safety events [7]. For this reason, large-scale registries or database reviews are perhaps the most sensitive means to determine the relative risk for a rare event. This is evident from the multispecialty working group recommendation for practitioners to use a nonparticulate steroid for the initial lumbar transforaminal ESI despite no clinical trials demonstrating improved safety (i.e., the parachute analogy) [8]. The effect of a single-shot steroid injection on the risk of developing COVID-19 is perhaps best illustrated by the large 2018 retrospective study out of the Mayo Clinic, which found a 52% higher risk for influenza in individuals who underwent intra-articular steroid injections [9]. Gill and Breeze correctly point out that baseline

differences between groups, which are unavoidable in retrospective studies with this design, and the low absolute risk of viral infection (< 1%) are reasons to interpret these results with caution.

Triamcinolone acetonide is commonly used as an inhalation agent for asthma, while its variant, triamcinolone acetate, is frequently used for ESI. Whereas inhalational delivery of corticosteroid is different than epidural administration, a pharmacokinetic study found that blood lymphocyte concentration was reduced by 60% four hours after inhaled triamcinolone acetonide, with peak serum levels occurring two hours after administration [10]. In this study, the terminal half-life of inhaled triamcinolone was 3.6 hours [10]. In contrast, Hooten et al. found that serum triamcinolone did not peak until 22 hours following epidural injection and had a terminal elimination half-life of 219–523 hours (cervical vs lumbar ESI); however, the authors did not measure the effect on lymphocytes [11, 12]. Following lumbar facet joint injections, the same group reported that serum cortisol levels were suppressed for an average of 4.4 days, with the maximum effect of triamcinolone on cortisol suppression observed at serum levels >1.9 ng/mL [13]. Collectively, these data suggest that standard doses of epidurally administered triamcinolone lead to concentrations twice as high as those seen following inhalation administration (4.1–5.4 ng/mL vs 2 ng/mL) [11, 12] and that neuraxially administered steroids can have measurable systematic effects [13]. Finally, inhaled corticosteroids carry a relative risk of 1.56 for pneumonia compared with placebo and other inhaled treatments, which warrants further examination [14].

Gill and Breeze conclude their letter by stating that reducing the dose of steroids, when possible, is a reasonable strategy, which is a point we wholeheartedly concur with. Regarding the use of nonparticulate steroids, based on pharmacokinetics, it is likely that the peak immunosuppressant effect for an equianalgesic dose would be greater, but the duration of immunosuppression would be less than with depo-steroids. Whether the benefits outweigh the risks of any procedure is a question that can only be answered based on a shared decision model, taking into consideration the specific issues that affect each patient (i.e., personalized medicine). This is true regardless of whether the procedure is being considered during a pandemic.

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Letter to the Editor

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Pain Management Best Practices During the COVID-19 Pandemic: The Well-being Perspectives of Chronic Pain Fellows

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