Systemic Corticosteroids, Chronic Inflammatory Skin Disease, and COVID-19: What Do We Know?

An assessment of the risk of COVID-19 infection imposed by systemic corticosteroid use in the setting of chronic inflammatory skin disease.

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>> Corticosteroids (CS) describe a group of versatile pharmacological agents, as 1.2 percent of the adult US population received an oral CS during the period from 1999-2008.[1] The short- and long-term effects of systemic CS (SCS) have been established in almost every organ system. Dr. Anthony Fauci, now NIAID director and lead member of the White House Coronavirus Task Force, detailed CS's immunologic mechanisms and implications in 1976. CSs provide therapeutic benefit in many inflammatory and immune-mediated conditions, but also result in increased risk of infection. A 1989 meta-analysis of 71 controlled clinical trials found a significantly increased infectious complication rate in patients receiving SCS across multiple medical specialties. The authors provided two additional takeaways. First, a qualitative deficiency exists in the reporting of infectious complications; in the meta-analysis less than eight percent of trials reported infectious etiology. Second, underlying disease influences infection risk. When stratified by underlying disease, the relative risk of infectious complications was highest in those receiving SCS for neurologic diseases.

To date, the FDA has approved remdesivir and issued early-use authorization for bamlanivimab for COVID-19 treatment. SCS's role in treatment is under active investigation. Although found to delay viral clearance during previous novel coronavirus outbreaks, low-dose CS therapy may not delay SARS-CoV-2 clearance, initial data suggests.[2] Further, there is preliminary evidence of dexamethasone's benefit in a subset of infected patients.[3] While SCS as a therapeutic option is being studied, little is known regarding risk of COVID-19 infection in dermatologic patients on long-term SCS. In light of this, we consulted the literature for published safety data to assess infection risk in patients receiving SCS for chronic inflammatory skin diseases.

One randomized clinical trial (RCT) investigating efficacy of prednisolone versus cyclosporine for atopic dermatitis (AD) reported no infections among the prednisolone group (n=21) and four common colds in the cyclosporine group (n=17).[4] (Table 1) Despite this, authors ulti-

Amid the ongoing COVID-19 pandemic, there is concern for increased risk of viral infection among individuals on immunosuppressive or immunomodulatory therapy. The theoretical risk of a patient on long-term systemic corticosteroid therapy for chronic inflammatory cutaneous disease has not been established. In the absence of high-risk comorbidities identified by the CDC, there is no adequate evidence suggesting that dermatologic patients on long-term systemic corticosteroids are at an increased risk of COVID-19 respiratory viral infection.

the**bottom**line

TABLE 1. SUMMARY OF INCLUDED STUDIES WITH PRIMARY SAFETY DATA ON SYSTEMIC CORTICOSTEROIDS (CS) IN CUTANEOUS INFLAMMATORY DISEASES.

Reference	Study Type	Primary Disease	Interventions (n)	Reported Adverse Events	Study Conclusion
Schmitt et al., 2009	Multicenter, double-blind, randomized clinical trial	Atopic Dermatitis (Eczema)	Prenisolone[1] (21) Cyclosporine[2] (17)	Adverse Event (prednisolone/cyclosporine) -Exacerbation/rebound (17/11) -Common cold (0/4) -Reversible hypertension (3/4)	Advised against the routine clinical use of prednisolone due to a high likelihood of disease rebound after short-term therapy.
Bakhtiar et al., 2018	Single-center, randomized clinical trial	Generalized Lichen Planus	Oral CS[3] (79) Methotrexate[4] (79)	None	Concluded that compared to systemic CS, methotrexate is not significantly efficacious in the treatment of generalized LP, but it is a good steroid-sparing alternative.

[1]Prednisolone initial dose: 0.5-0.8mg/kg daily for 2 weeks; followed by placebo for 4 weeks. Follow-up period: 12 weeks.
[2]Cyclosporine dose: 2.7-4.0mg/kg daily for 6 weeks. Follow-up period: 12 weeks.
[3]Oral CS: 40mg oral corticosteroids (unspecified) daily for 8 weeks; followed by taper according to protocol.
[4]Methotrexate: 10mg oral methotrexate once weekly for 8 weeks.

mately argued against prednisolone use in AD due to high rebound rates following discontinuation after short-term therapy. Another RCT investigating oral CS vs. methotrexate for generalized lichen planus (LP) reported no remarkable adverse events with either agent.[5] (Table 1) Methotrexate was not found to be significantly more efficacious over oral CS, however authors concluded methotrexate is a "good steroid-sparing alternative" for LP. Two limitations of these RCTs include small sample size and short duration of SCS therapy. Therefore, we are cautious to suggest generalizability to dermatologic patients receiving long-term SCS.

Overall, there is a paucity of primary safety data for long-term SCS use in inflammatory cutaneous disease. There are multiple explanations for this, such as RCTs being designed to primarily evaluate efficacy rather than safety, a shift in focus to steroid-sparing agents for chronic inflammatory conditions, due to the multiple adverse effects seen with CSs, and the advent of immunomodulators/biologics. In the absence of high-risk comorbidities identified by the CDC, there is no adequate evidence suggesting that dermatologic patients on long-term SCS are at an increased risk of COVID-19 respiratory viral infection. Per AAD recommendations, discontinuation of systemic immunosuppressants may be warranted in COVID-19-infected patients upon an individual case basis. ■

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