

# Cyclosporine in SJS/TEN Management: A Brief Review

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*Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered to be among the most severe dermatologic emergencies with high risk for morbidity and mortality if managed poorly. These disease processes usually are the result of a reaction to antipsychotic or antibiotic medications, though the complete list of potential causative drugs is extensive. Despite the life-threatening nature of these conditions, studies evaluating systemic immunomodulating agents that would be effective in halting the poor overall outcome are limited. Over the last several years, reports advocating the benefits of cyclosporine, corticosteroids, and intravenous immunoglobulin (IVIG) have shown variable responses in their treatment of SJS/TEN. In this article, cyclosporine and its potential as an emerging therapeutic option for SJS/TEN patients is discussed.*

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As dermatology residents, the telephone calls we get at 2 AM usually are the toughest for 2 reasons: (1) we rarely get calls at 2 AM, and (2) it usually means there is a case to rule out Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Stevens-Johnson syndrome and TEN are severe mucocutaneous eruptions that usually develop due to drug reactions and involve a continuum of conjunctivitis, mucocutaneous sloughing, keratinocyte death, and bullae development. Body surface area (BSA) coverage determines the distinction between SJS and TEN; less than

10% BSA affected indicates SJS, 10% to 30% BSA affected indicates overlap between SJS and TEN, and greater than 30% BSA affected indicates TEN.<sup>1</sup> The mortality rates for these conditions range from 1% to 5% in SJS versus 25% to 30% in TEN.<sup>2</sup>

Being driven and dedicated residents, we rise to the challenge by arranging appropriate consultations, obtaining frozen section biopsies, providing recommendations to remove unnecessary medications, and offering skin care management. However, what comes next? Intravenous immunoglobulin (IVIG)? Cyclosporine? Or is it appropriate to allow the reaction to continue its course? Dermatology programs have a varying standard of care due to the limited number of studies conducted on SJS/TEN patients. Few studies have relayed the efficacy of cyclosporine; however, published results have shown that cyclosporine can decrease the overall mortality risk and minimize disease progression.<sup>2-5</sup> In this article, I will review some of the key studies conducted in the last 5 years regarding the use of cyclosporine in the therapeutic plan for SJS/TEN.

In one retrospective analysis conducted by Kirchof et al<sup>1</sup> in 2014, 35 patients with SJS/TEN who were treated with IVIG and 15 who were treated with cyclosporine were evaluated for mortality benefit. Two patients were treated with both cyclosporine and IVIG and were included in both arms of the study. Overall, the evaluation indicated that cyclosporine can potentially have a better overall advantage in treatment of SJS/TEN over IVIG.<sup>1</sup> Although this study had an uneven number of patients treated with IVIG versus cyclosporine, a nonstandardized way of comparing patients with early SJS to TEN patients, and no double-blind randomized trial, cyclosporine may still show benefit over IVIG.

Singh et al<sup>6</sup> conducted an uncontrolled open study in a tertiary care center (July 2011–June 2012)

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that showed a similar result of benefit with cyclosporine in SJS, SJS/TEN, and TEN patients. Eleven participants were included in the study based on SCORTEN (Score of Toxic Epidermal Necrosis) criteria (age, >40 years; heart rate, >120 BPM; serum blood urea nitrogen level, >28 mg/dL; body surface area affected, >10%; serum bicarbonate, >20 mEq/L; serum glucose, >252 mg/dL). They were treated with cyclosporine 3 mg/kg for 7 days and then tapered over another 7 days. Six participants were treated with corticosteroids. Participants treated with cyclosporine reepithelialized in 16.7 days compared to 23 days with corticosteroids. The hospital stay was 18.09 days in participants treated with cyclosporine versus 26 days in those treated with corticosteroids. Lastly, 2 participants who were treated with corticosteroids died as opposed to none with cyclosporine.<sup>6</sup> Although the power of this study also was limited and it was not a randomized, double-blind, controlled trial, it provides more evidence that cyclosporine can be efficacious in SJS/TEN patients.

A phase 2 open trial conducted by Valeyrie-Allanore et al<sup>7</sup> evaluated the benefit and efficacy of cyclosporine in SJS/TEN patients. There were 29 participants at the start of the study (SJS, n=10; SJS/TEN, n=12; TEN, n=7) and 26 completed treatment. Cyclosporine was administered orally at 3 mg/kg for 10 days and tapered over the following month. This study noted 3 basic principles: First, patients tolerated cyclosporine well; second, limited disease progression was noted in 62% (18/29) of participants around day 3 and in only about 35% (11/29) of IVIG patients; and third, no deaths were noted in all participants.<sup>7</sup>

## Final Thoughts

Case reports have indicated that cyclosporine may be effective in limiting progression of SJS/TEN; however, a double-blind study has not validated this finding. Hence, patients should be evaluated on a case-by-case basis to determine if they should be treated with cyclosporine or IVIG or simply complete the course of the disease process with supportive care.

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