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CORTICOSTEROIDS IN STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS: A REVIEW OF RECENT CLINICAL EVIDENCE

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ABSTRACT

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, life-threatening mucocutaneous reactions with high mortality. The role of systemic corticosteroids remains controversial. This review summarizes recent clinical evidence on their use in SJS and TEN.

Methods: PubMed was searched for English-language clinical studies published between 1 January 2015 and 31 December 2025 using the terms "Stevens–Johnson syndrome" or "toxic epidermal necrolysis" combined with "corticosteroids" or "systemic corticosteroid therapy." Eight relevant studies (one systematic review and meta-analysis and seven retrospective studies) were included. Study design, corticosteroid regimens, outcomes, and adverse events were extracted and summarized descriptively.

Results: The meta-analysis of 96 studies (3,248 patients) found a survival benefit with corticosteroids in all analyses, significant in only one. Several single-center cohorts from China reported mortality significantly lower than that predicted by the SCORTEN severity score. In contrast, a Japanese nationwide cohort of 1,846 patients found no significant association between early corticosteroid therapy and lower in-hospital mortality, and a US multicenter cohort showed lower-than-predicted mortality in all groups, including supportive care alone. Adding intravenous immunoglobulin showed a favorable but non-significant trend. Corticosteroid-related complications were mostly mild where reported.

Conclusion: Evidence on corticosteroids in SJS/TEN is inconclusive, limited by retrospective designs, small samples, and heterogeneous dosing. Corticosteroids may be reasonable in selected patients but are not a proven standard treatment. Prospective multicenter studies and randomized trials are needed.

Keywords: Stevens-Johnson Syndrome; Toxic Epidermal Necrolysis; Corticosteroids; Mortality; SCORTEN; Literature Review

1 INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, severe mucocutaneous reactions characterized by blistering and erosion of the skin and mucous membranes. They are classified by the proportion of body surface area (BSA) with epidermal detachment: less than 10% for SJS, 10% to 30% for SJS/TEN overlap, and more than 30% for TEN [1,2]. The estimated incidence is 2 to 13 per million people per year, and published mortality is around 20% to 25%, based mainly on European cohorts [2]. Medications are the most frequent trigger, accounting for nearly 90% of cases in a large US cohort, and survivors may suffer long-term sequelae [2]. The disease is thought to result from keratinocyte death mediated by cytotoxic T cells and cytokines, including granulysin [3,4].

Management begins with prompt withdrawal of the causative drug and transfer to a specialized unit for supportive care, both of which have been linked to better outcomes [2,5]. Prognosis is commonly estimated with the SCORTEN severity score, which is also widely used as the benchmark for judging whether a treatment lowers mortality [2,6]. Because of the immune-mediated mechanism, various systemic immunomodulating therapies have been proposed, including corticosteroids, intravenous immunoglobulin (IVIG), cyclosporine, and, more recently, TNF inhibitors [4]. Yet no evidence-based standard treatment exists. The rarity and severity of the disease make randomized trials difficult, and the only randomized trial identified in a major systematic review tested thalidomide and found a harmful effect [4,7].

Systemic corticosteroids are among the most commonly used agents, but their role remains controversial. In a US multicenter cohort, corticosteroids were the most frequent pharmacologic therapy, given alone or with IVIG [2]. Early reports from burn centers argued that corticosteroids were harmful, citing a higher risk of sepsis and other infectious complications [8]. More recent studies and a meta-analysis point to a possible survival benefit, whereas other studies show no benefit or even harm [2,4]. The literature is further complicated by wide variation in drug, dose, timing, and use of corticosteroids in combination with other agents such as IVIG [4].

Given these conflicting findings, a structured summary of the available clinical evidence is useful to clinicians who must make treatment decisions without firm guidelines. This literature review therefore summarizes and compares eight studies, comprising a systematic review and meta-analysis and several retrospective cohorts, that examined the use of corticosteroids in SJS and TEN [2,4,9–14].

2 MATERIALS AND METHODS

Given the ongoing debate regarding the efficacy and safety of systemic corticosteroids in the management of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), recent studies may provide further insight into their therapeutic outcomes. Therefore, we identified studies published in PubMed from 1 January 2015 to 31 December 2025. This literature review included clinical studies published in English that evaluated the use of systemic corticosteroids in patients with SJS and TEN. The search parameters included the terms “Stevens–Johnson syndrome” or “toxic epidermal necrolysis” combined with “corticosteroids” or “systemic corticosteroid therapy.” Relevant studies were selected based on their relevance to the review topic. Data regarding study design, corticosteroid regimens, treatment outcomes, and adverse events were extracted and summarized descriptively.

3 RESULTS AND DISCUSSION

Table 1: Literature Review Results

No.	Author (Year)	Study Design and Sample	Summary of Key Findings	Verdict on Corticosteroids
1.	Choonhakarn et al. (2015)	Retrospective study; TEN in Thai patients treated with dexamethasone pulse therapy	Two of 18 patients receiving corticosteroids died (11%), both with SCORTEN 5–6. No patient died if SCORTEN was below 4. This is a small study with no control group.	Cautiously supportive, mainly in lower-risk patients
2.	Liu et al. (2016)	Retrospective study; 70 patients treated with steroids, Shandong, China	Actual mortality was significantly lower than SCORTEN-expected (SMR 0.30, p = 0.0168), and also in the low-dose group (SMR 0.20, p = 0.0145). A later review describes this study as showing benefit regardless of regimen, low-dose (≤2 mg/kg/day) or high-dose (>2 mg/kg/day).	Supportive

3.	Zimmermann et al. (2017)	Systematic review & meta-analysis; 96 studies, 3,248 patients	Corticosteroids were linked to a survival benefit in all three analyses, but it was statistically significant in only one: aggregated data OR 0.5 (95% CI 0.3–1.01), unstratified IPD OR 0.7 (0.5–0.97), stratified IPD OR 0.8 (0.4–1.3). Cyclosporine looked promising and IVIG showed no benefit.	Promising but not conclusive
4.	Micheletti et al. (2018)	Multicenter retrospective cohort; 377 adults, 18 US centers	Observed mortality (14.7%) was lower than the 21% predicted by SCORTEN (SMR 0.70). The SMR was lowest with steroids plus IVIG (0.52). By group, the SMRs were: steroids only 0.72, IVIG only 0.79, supportive care only 0.70. Every group did better than predicted, including supportive care alone, so the authors say no firm conclusion on the best treatment can be drawn.	Inconclusive; combination with IVIG deserves further study
5.	Chateau et al. (2019)	Retrospective cohort; 36 HIV-infected SJS/TEN patients, South Africa	Patients treated with skin care plus systemic corticosteroids and IVIG had a survival rate of 97%. There was no control group, so the result cannot show that the drugs caused the good outcome.	Supportive (steroid + IVIG in HIV population), but low-level evidence
6.	Morita et al. (2019)	Retrospective cohort, Japanese national claims database; 1,846 patients	Early steroids (started within 2 days of admission) were not significantly associated with lower in-hospital mortality. By propensity matching, RR was 0.83 (0.37–1.85) for >2 mg/kg/day and 0.61 (0.28–1.36) for ≤2 mg/kg/day.	Not supported (no significant benefit)
7.	Yang et al. (2022)	Propensity-matched retrospective study; 224 patients before matching, China	Compared steroids + IVIG against steroids alone. After matching (93 vs 52 patients), mortality was 45% lower with combination therapy, but this was not statistically significant (p = 0.555). The infection rate was lower with combination therapy (OR 0.33, p = 0.047).	Steroids were used in both arms; IVIG may add benefit
8.	Ye et al. (2022)	Retrospective study; 56 patients, all treated with steroids, Beijing	Actual mortality was 1.8% (1/56), significantly lower than the expected 15.0% (SMR 0.13). About 73% of patients had possibly steroid-related complications, and 97.6% of those were mild. Initial doses were roughly 0.4–2.6 mg/kg/day, and 57% also received IVIG.	Supportive (early, short-course, moderate-to-high dose)

4 EFFECTIVENESS OF SYSTEMIC CORTICOSTEROIDS

The effectiveness of systemic corticosteroids in Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) remains controversial. Although several studies have reported favorable survival outcomes, others have found no significant association between corticosteroid treatment and reduced mortality. Overall, the available evidence remains inconclusive and is insufficient to establish systemic corticosteroids as a standard treatment for SJS/TEN.

Zimmermann et al. (2017) conducted a comprehensive meta-analysis involving 96 studies and 3,248 patients. Corticosteroid treatment was associated with lower mortality across three analytical approaches, although statistical significance was achieved only in the unstratified individual patient data analysis (OR 0.7). These findings suggested a potential survival benefit but did not provide sufficient evidence to establish corticosteroids as an effective standard therapy.

Several single-center studies have also reported favorable outcomes. Liu et al. (2016) observed lower mortality than predicted by SCORTEN, with a standardized mortality ratio (SMR) of 0.30. Similarly, Ye et al. (2022) reported an observed mortality rate of 1.8%, compared with a predicted rate of 15.0% (SMR 0.13), following early administration of moderate-to-high-dose corticosteroids for a short duration. Choonhakarn et al. (2015) and Chateau et al. (2019) also

reported favorable survival outcomes in Thailand and South Africa, respectively. However, the absence of appropriate control groups in these studies limits the ability to attribute the observed outcomes directly to corticosteroid treatment.

In contrast, Morita et al. (2019), in a nationwide observational study involving 1,846 patients, found no statistically significant association between early systemic corticosteroid administration and reduced in-hospital mortality. This finding remained consistent across both lower-dose (≤2 mg/kg/day) and higher-dose (>2 mg/kg/day) treatment groups.

Micheletti et al. (2018) further highlighted the limitations of using SCORTEN-predicted mortality to evaluate treatment effectiveness. In their US cohort, observed mortality was lower than predicted across all treatment groups, including patients receiving supportive care alone (SMR 0.70). This finding suggests that improvements in supportive care, differences in patient characteristics, and limitations in mortality prediction may partly explain the favorable outcomes reported in uncontrolled studies.

5 DOSAGE, TIMING, AND COMBINATION THERAPY

Variations in corticosteroid dosage, treatment initiation, and duration complicate comparisons across studies. Zimmermann et al. (2017) reported considerable heterogeneity in corticosteroid regimens, ranging from low to high doses. Liu et al. (2016) reported favorable outcomes with low-dose treatment, whereas Ye et al. (2022) investigated early administration of moderate-to-high doses for a short duration. Choonhakarn et al. (2015) employed dexamethasone pulse therapy.

Although these findings suggest that different regimens may be associated with favorable outcomes, none of these studies was specifically designed to determine the optimal corticosteroid dose, timing, or duration. Consequently, the most appropriate treatment regimen remains uncertain.

The potential benefit of combining corticosteroids with intravenous immunoglobulin (IVIG) is also unclear. Micheletti et al. (2018) reported the lowest SMR among patients receiving combined corticosteroids and IVIG (0.52). Similarly, Yang et al. (2022) observed a 45% reduction in mortality with combination therapy compared with corticosteroids alone, although the difference was not statistically significant ($p = 0.555$). Yang et al. also reported a lower incidence of infection in the combination group (OR 0.33), suggesting a potentially relevant finding that warrants further investigation.

Nevertheless, the available evidence does not establish whether adding IVIG provides a significant advantage over corticosteroid monotherapy. Zimmermann et al. (2017) also found no clear survival benefit associated with IVIG monotherapy, further emphasizing the uncertainty surrounding immunomodulatory treatment strategies in SJS/TEN.

6 SAFETY AND RISK OF INFECTION

The safety of systemic corticosteroids is an important consideration in SJS/TEN because their immunosuppressive effects may increase susceptibility to infection. Patients with SJS/TEN are already vulnerable to infectious complications due to extensive epidermal damage, mucosal involvement, and potential systemic dysfunction.

Ye et al. (2022) reported that complications potentially associated with corticosteroid treatment occurred in 73.2% of patients, although most were mild. The only death occurred in a patient with pre-existing severe renal failure. While these findings provide some information regarding the observed safety profile, the absence of a control group prevents reliable assessment of whether corticosteroids increase complication rates compared with supportive care alone.

Therefore, the available evidence remains insufficient to establish the overall safety of systemic corticosteroids in SJS/TEN, particularly regarding infection and sepsis. Further comparative studies are needed to distinguish treatment-related adverse effects from complications attributable to the underlying disease and other clinical factors.

Limitations of the Available Evidence

Several methodological limitations restrict the interpretation of current evidence. Most studies investigating corticosteroid treatment in SJS/TEN are retrospective and observational. Zimmermann et al. (2017) noted that the randomized controlled trial identified in the broader SJS/TEN literature evaluated thalidomide rather than corticosteroids. Consequently, high-quality randomized evidence specifically assessing corticosteroid efficacy remains lacking.

In observational studies, treatment allocation is not randomized, and patients receiving more intensive treatment may have more severe disease. This confounding by indication can distort estimates of treatment effectiveness. Differences in baseline disease severity, treatment initiation, and supportive care may also contribute to variations in clinical outcomes.

Furthermore, several studies relied on SCORTEN-predicted mortality as a reference rather than using a concurrent control group. Although SCORTEN is useful for estimating mortality risk, discrepancies between observed and predicted mortality do not establish a causal treatment effect. Small sample sizes in some studies further limit statistical precision, while differences in patient characteristics, HIV status, causative medications, geographic location, and healthcare settings restrict the generalizability of the findings. Publication bias also cannot be excluded.

The frequent use of corticosteroids alongside relatively low mortality in some Asian cohorts warrants further investigation. However, this observation should be interpreted cautiously because differences in genetic background, drug exposure, patient characteristics, and healthcare systems may also influence outcomes. These findings alone cannot establish that corticosteroids are more effective in particular populations.

7 CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

Systemic corticosteroids remain a treatment option in clinical practice for SJS/TEN, although their effectiveness in reducing mortality has not been conclusively demonstrated. Treatment decisions should consider disease severity, patient comorbidities, potential complications, and the availability of appropriate supportive care and clinical expertise. Prompt withdrawal of the suspected causative drug and specialized supportive care remain essential components of management.

Future research should prioritize prospective, multicenter studies with clearly defined treatment protocols and clinical outcomes. Randomized controlled trials, where feasible, comparing corticosteroids with appropriate control groups or alternative treatment strategies could help clarify their effects on mortality and complications. Further studies should also investigate the optimal corticosteroid dose, timing, and duration, as well as the potential benefits and risks of combination therapy with IVIG.

8 CONCLUSION

The available evidence regarding systemic corticosteroids in SJS and TEN remains inconclusive. A comprehensive meta-analysis and several single-center studies suggest a potential survival benefit, particularly in cohorts reporting favorable outcomes following early treatment. However, the largest nationwide observational study found no significant association between early corticosteroid administration and reduced in-hospital mortality. Furthermore, mortality was lower than SCORTEN-predicted estimates across all treatment groups, including patients receiving supportive care alone, highlighting the limitations of attributing favorable outcomes to corticosteroids.

The predominantly retrospective and observational nature of the evidence, together with differences in treatment regimens, patient characteristics, and supportive care, prevents definitive conclusions regarding efficacy and safety. Although combination therapy with corticosteroids and IVIG appears promising, a statistically significant mortality benefit has not been established. Systemic corticosteroids may therefore be considered in selected patients based on individual clinical circumstances, but they cannot currently be regarded as a definitively proven standard treatment. Further prospective multicenter studies and well-designed clinical trials are needed to clarify their role in SJS/TEN management.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

The authors declare that they have no conflicts of interest related to this work.

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