short & snappy
-A CLINICAL OVERVIEW

Burning Through the Evidence for Cyclosporine in Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis

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Clinical question: In adults with Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), does cyclosporine (CSA) compared to other adjuvant and supportive therapies reduce mortality?

Background: SJS and TEN are life-threatening mucocutaneous reactions typically caused by medications. SJS affects <10% body surface area (BSA), whereas TEN involves >30% BSA. Severity of illness can be calculated using SCORTEN - a validated predictor of mortality based on 7 risk factors. [1,2,3] Supportive care is currently the mainstay intervention, and involves discontinuing offending medication(s), airway support, transfer to an ICU/burn unit, wound care, and fluid/electrolyte monitoring. Some evidence suggests adjunctive therapies, such as CSA, corticosteroids, IVIG, anti-TNF-alpha antibodies, and plasmapheresis, may hasten recovery and reduce mortality. [1,2]

Review of Relevant Literature:

- Two guidelines: U.K. guidelines - evidence for CSA is inconclusive. Indian Association suggests CSA may be used alone or in combination with corticosteroids, based on limited, inconsistent evidence. [4,5]
- Four meta-analyses: [6,7,8,9]
  - Ng QX et al 2018 (n=256, 9 case series, 1 phase II trial) mean SCORTEN 1.65-4.3, compared CSA + supportive care to adjuvant therapies (such as cyclophosphamide +/- corticosteroids, IVIG +/- CSA, corticosteroids +/- CSA, or supportive care alone). [6]
    - Standardized mortality ratio (SMR = observed/predicted using SCORTEN) favored CSA + supportive care (0.32, p=0.002). Publication bias and heterogeneity among studies.
  - 3 earlier meta-analyses showed trend towards reduced mortality + morbidity with CSA vs other therapies, including IVIG, corticosteroids, and supportive care. Significant variability in baseline characteristics between patients. [7,8,9]
- Two prospective studies: [10,11]
  - Phase II trial included in 2018 meta-analysis studied CSA + supportive care (n=29) vs IVIG (n=34 from historical cohort). Mean SCORTEN 1.27. Mean age 34.
  - CSA cohort: ~3 predicted deaths per SCORTEN, none occurred. IVIG: 8 predicted deaths, 11 occurred. CSA – epidermal detachment stabilized in 62%, 38% had disease progression vs 35% stabilized in IVIG group and 65% had progression. All results non-statistically significant (NSS). [10]
- Four retrospective cohort studies: [12,13,14,15]
  - 2018 single center study (n=174) showed no reduction in mortality, progression of skin detachment or re-epithelialization with CSA + supportive care vs supportive care alone. [12]
  - Two small studies showed NSS mortality benefit. One study compared CSA (SMR 0.42, 95% CI 0.09-1.22) vs supportive care only (SMR 1.02, 95% CI 0.37-2.21), and the other compared CSA (SMR 0.43) vs IVIG (SMR 1.43). Latter study included patients treated with both therapies; significantly more patients on CSA had SJS vs TEN (58.8% vs 29.7%). [13,14]
  - 2019 single center study comparing CSA (n=13) vs corticosteroids (n=35) found complete re-epithelialization occurred sooner in CSA group (mean 9.6 vs 14.1 days). Duration of hospitalization ~ 7 days shorter (NSS) in patients on CSA. [15]

Bottom Line: Among the adjunctive therapies for SJS/TEN, CSA has the most evidence for improved outcomes. Limited data from cohort studies and case reports show delayed disease progression, shorter time to re-epithelialization and NSS reduction in mortality. Side-effects, such as neutropenia, nephropathy, and pneumonia, must be weighed against potential benefits.

Google Drive Link to References