

IVIG Use in the Treatment of Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome: A 10-year Retrospective Analysis of a Single Burn Center

Cooper, R; Pressman, M. PhD.; Foster, K. MD

Abstract

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis syndrome (TENS) are immune-mediated medical conditions characterized by fever and mucocutaneous lesions, treated with supportive care and removal of causative agents. Adjunctive agents are sometimes used with treatment protocols but have been incompletely evaluated: one such adjunctive treatment is intravenous immunoglobulin (IVIG), a blood product containing IgG antibodies from blood plasma donors.

The use of IVIG in the treatment of SJS/TENS remains controversial due to mixed results demonstrated in the literature, and at present is not considered a component of the standard of care. This study seeks to provide additional data on the efficacy of IVIG treatment on mortality in a small cohort of patients presenting with these syndromes at a regional burn center over a 10-year period. Data from 86 patients presenting with SJS/TENS was retrospectively collected from patient medical records.

IVIG use showed a potential, but not significant improvement on mortality in comparison to the non-treatment group. Mortality in the IVIG treatment group was 30.6% versus 35.1% in the non-IVIG treatment group. In the treatment group receiving IVIG, the odds ratio for mortality was 0.81 (95% CI 0.3-2.0) versus 1.22 in the non-IVIG treatment group.

The risk of death was moderately correlated with age and strongly correlated with severity of the disease process. Of those patients diagnosed with SJS/TENS, the majority were between ages 35-70 (odds ratio 2.26), although mortality was slightly higher for ages >70 (41.7% versus 40.4%). Of the 86 patients, the highest mortality percentage and odds ratio was for those diagnosed with TENS (55.2% and 4.62 respectively).

There is ultimately no new evidence that the benefit of IVIG in the treatment of SJS/TENS is anything more than potential. Further exploration should include a rigorous analysis and comparison of different dosing regimens.

Introduction

SJS and TENS are related conditions characterized by fever and mucocutaneous lesions which can result in necrosis and sloughing of the epidermis lasting several weeks. The etiology of these conditions are incompletely understood, although are suspected to be immunologic in nature. Medications are by far the

leading trigger of SJS/TENS, followed by infection. SJS/TENS differ based on a continuum of severity: SJS is a less severe condition in which epidermal sloughing is limited to less than 10% of the body surface area (BSA) with reported mortality ranging from 1-5%, while TENS involves sloughing >30% of the BSA with reported mortality ranging from 25-35%. The two conditions overlap between 10-30% of BSA. SJS/TENS can occur in all age groups, although TENS typically affects older individuals; women (60%) are more often affected than men.

Standard of care in the treatment of SJS/TENS includes the prompt withdrawal of any suspected causative medications or agents and supportive care. Adjunctive medical treatments include glucocorticoids and IVIG, all of which suffer from limited evidence given a paucity of research and a lack of controlled trials. This study is designed to assess IVIG by retrospectively considering mortality of SJS/TENS patients in the context of IVIG treatment during hospitalization at a regional burn center.

Methods

Data collection was performed by retrospectively reviewing patient electronic and paper medical records for 86 subjects diagnosed and treated for SJS/TENS over a 10-year period at the Arizona Burn Center. Although not burn victims, the presentation of SJS/TENS warrants similar treatment protocols; thus a burn center provided an excellent data pool from which to analyze a relatively rare disorder. Collected demographic data included age, ethnicity, gender, physical exam

and laboratory findings, suspected diagnosis, possible offending agents, estimated extent of body surface and mucous membrane involvement, IVIG use, mortality, and length of hospital stay. Total body surface area (TBSA) affected was determined via chart reporting, applying specifically to the estimated amount of surface area to experience sloughing.

On analysis, IVIG use was compared to non-use as specific treatment for SJS/TENS. The outcome measure was patient mortality during the course of hospital admission and treatment for SJS/TENS.

Results

A total of 86 Patients with documented diagnoses of SJS/TENS were identified at the Maricopa County over a 10-year period. Of the 86, 27 (31.4%) were male while 59 (68.6% were female). The average age at diagnosis was 47. Overall mortality was 28/86 (32.6%). 48 patients were able to be assigned a specific diagnosis based on TBSA involvement: 7 (14.6%) were diagnosed with SJS, 12 (25%) were diagnosed with SJS/TENS overlap, and 29 (60.4%) were diagnosed with TENS.

Of those patients diagnosed with SJS/TENS, 37 (43%) did not receive treatment with IVIG; of those not treated, 13 died yielding a mortality rate of 35.1%. Of those patients diagnosed with

SJS/TENS, 49 (57%) received treatment with IVIG; of those treated with IVIG, 15 died yielding a mortality rate of 30.6%. The odds ratio of mortality for the IVIG treatment group was 0.81 versus 1.22

The risk of death was moderately correlated with age and strongly correlated with severity of the disease process. Of those patients diagnosed with SJS/TENS, the majority were between ages 35-70 with the highest odds ratio (2.26), although mortality was slightly higher for ages >70 (41.7% versus 40.4%). Of the 86 patients, the highest mortality percentage and odds ratio was in the TENS group based on TBSA severity (55.2% and 4.62 respectively).

Discussion and Conclusions

From these 86 patients, we observed that there may be a trend of some benefit from the use of IVIG in the treatment of SJS/TENS. Mortality (percentage and odds ratio) was lower with the IVIG treatment group when compared with the non-IVIG treatment group; however confounding variables are possibly present and no clear statistical significance is evident. Demographically, severity of the disease process in the form of TENS was significantly associated with increased mortality regardless of treatment.

This was an observational study with some inherent limitations; notably results are based on a small sample size of subjects included from one region of the United States, and the treatment regimen did not factor in the diverse array of treatment protocols including dosing. While this study can't be used to definitively determine the efficacy of IVIG as a treatment, it does provide insight into how treatments are administered, inform clinical practice, and provide data to support the design of future studies.

The only clear way to delineate to effectiveness of IVIG in the treatment of SJS/TENS is to design a controlled, prospective trial, investigating and summarizing patterns of use of IVIG in the treatment of SJS/TENS as done in this study may offer a stepping stone toward achieving that goal in the long-term, and help establish consensus treatment protocol in the short-term.

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Table 1: IVIG treatment of patients diagnosed with SJS/TENS. *p<0.05

	Mortality		OR	(95% CI)
Treatment				
IVIG	15/49	30.6%	0.81	(0.3-2.0)
No IVIG	13/37	35.1%	1.22	(0.5-3.0)
Age				
<35	4/27	14.8%	0.25	(0.1-0.8)
35-70	19/47	40.4%	2.26	(0.9-5.8)
>70	5/12	41.7%	1.58	(0.5-5.5)
Severity				
SJS (<10% TBSA)	0/7	0.0%	undefined	undefined
SJS/TENS overlap (10-30% TBSA)	4/12	33.3%	0.625	(0.2-2.4)
TENS (>30% TBSA)	16/29	55.2%	4.62	(1.2-17.2) *