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Original Article

Role of systemic steroids in the outcome of Stevens-Johnson syndrome and toxic epidermal necrolysis

Nadia Ali Azfar, Muhammad Ali Zia, Lamees Mahmood Malik, Abdur Rahim Khan, Muhammad Jahangir

Department of Dermatology, Jinnah Hospital Lahore

Abstract

Background Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are cutaneous adverse reactions which usually develop as a result of drug therapy. The role of systemic steroids in the treatment of SJS and TEN is debatable.

Objective To see the clinical outcome of patients suffering from SJS or TEN, treated with or without steroids.

Patients and methods Forty patients of SJS and TEN were enrolled from the inpatient department of Jinnah Hospital Lahore. Clinical data were recorded on a pro forma. Clinical outcome of patients treated with or without steroids was recorded and analyzed.

Results A total of forty patients were enrolled in the study. Twenty nine patients were suffering from SJS and 11 were suffering from TEN. Twenty three patients of SJS (79.31%) were treated without steroids. Two patients died (8.7%) and twenty one (91.30%) recovered. Six patients were given steroids (20.68%), out of these 2 (33.3%) died and 4 (66.76%) recovered. There were eleven patients of TEN, four (36.37%) were managed without steroids, one expired (25%) and rest of the three (75%) patients recovered. Seven (63.63%) patients were given steroids, three (43.86%) patients expired while four (57.14%) recovered.

Key words
Stevens-Johnson syndrome, toxic epidermal necrolysis, steroids, drug reaction.

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis are cutaneous adverse reactions having an incidence of 0.4-1.2 and 1.2 to 6 million persons per year according to the available data.[1] Though studies regarding incidence are unavailable in our setup, we come across these patients in our daily practice. The mortality from these life threatening problems is 5-15% in case of SJS and 30-35% in case of TEN.[2] SJS-TEN begins as painful erythematous, morbiliform eruption over the trunk, extremities and face. Gradually, there is development of erosions and blisters along with extensive epidermal detachment. SJS is labeled when there is less than 10% of the body surface area and two or more mucosae are involved, while in TEN more than 30% of the epidermis is lost in sheet like erosions with prominent mucosal involvement. Both the conditions are part of the same disease spectrum.[3] The skin failure is similar to burns giving rise to sepsis, thermodysregulation, fluid and electrolyte imbalance as well as internal organ

Address for correspondence
Dr. Nadia Ali Azfar,
Senior Registrar,
Department of Dermatology,
Jinnah Hospital, Lahore.
E mail: nadiaazfar@hotmail.com

involvement.[4,5] Drugs have been found to be the leading causative factor in both the conditions. Both SJS and TEN are considered T cell-mediated disorders in which activation of CD8 T lymphocytes results in apoptosis and necrosis of keratinocytes.[6] Drugs act as haptens or prohaptens or may cause a direct pharmacological interaction between major histocompatibility complex and T cell receptors.[7] Anticonvulsants are the most common culprit agents implicated.[8] They can bind with MHC and T cell receptor and cause activation of T cells. Patients are mostly treated conservatively with immediate withdrawal of the culprit drug. Use of corticosteroids in the treatment of such patients is still controversial. Review of literature has revealed studies in favour of steroids[9] while others have shown no beneficial effect, while still others have shown increased mortality with the use of steroids.[10] In our study we aimed to compare the clinical outcome of patients who were not given steroids with those in whom steroids were given at anytime during or before their stay in the hospital.

Patients and methods

This observational study was conducted in the inpatient dermatology department of Jinnah Hospital, Lahore from December 2006 to December 2009. 40 patients of both sexes and all ages, clinically diagnosed as having SJS or TEN, were enrolled. Their detailed history was taken and physical examination was performed. Patients were divided into 2 groups, those who did not receive steroids at all and those who received steroids for one day or more. Clinical outcome was assessed in terms of recovery and demise. The data were recorded on a comprehensive pro forma and later subjected to descriptive statistical analysis.

Results

A total of 40 patients, SJS (n=29) and TEN (n=11), were enrolled for the study. Out of these, 24 patients were females and 16 were males. The male: female ratio for patients of SJS was 4:3.3, while all patients of TEN (100 %) were females.

The age range for both SJS and TEN patients was from 3-72 years. The mean age was 29.07±15.82 years. The mean age for patients of SJS was 28.29±14.54 years, while that for patients of TEN was 31.18±18.56. The detailed demographic data is shown in (**Table 1**).

Table 1 shows the causative drugs in both groups In patients of SJS, Fansidar® (sulfadoxine + pirimethamine) was found to be the most common culprit drug in 10.34% followed by carbamazepine in 6.9% while in patients of TEN Fansidar® and carbamazepine had an equal frequency of 18.18 %.

Out of 29 patients of SJS, 23 (79.31%) did not receive steroids before or during their hospital stay. Twenty one (91.30%) patients recovered while 2 (8.7%) expired. Out of 6 who received steroids, 4 (66.6%) recovered while 2 (33.3%) expired (**Table 2**).

The patients of TEN were also assessed according to the steroid intake. Out of 11 patients, 4 (36.37%) did not receive steroids, 3 (75%) recovered and one (25%) expired. Seven patients were given steroids, 4 (57.14%) recovered while 3 (43.86%) expired (**Table 3**).

Discussion

Cases of SJS and TEN have been reported worldwide and the condition is common in all age groups and both genders.[3] Various studies

Table 1 Demographic data and causative drugs in SJS and TEN (n=40).

	SJS (n=29)	*TEN (n=11)*
Age (years)	28.27±14.54	31.18±18.56
Male	16	0
Female	13	11
Causative drugs		
Fansidar®	3	2
Carbamazepine	2	2
Ciprofloxacin	0	2
Allopurinol	2	1
Metronidazole	2	0
Unknown	19	4

SJS=Stevens-Johnson syndrome, TEN=Toxic epidermal necrolysis

Table 2 Clinical outcome of 29 patients with Stevens-Johnson syndrome.

	Received steroids (n=6)	*Did not receive steroids (n=23)*
Recovered	4 (66.6%)	21(91.30%)
Expired	2(33.3%)	2(8.7%)

Table 3 Clinical outcome of 11 patients with toxic epidermal necrolysis.

	Received steroids (n=7)	*Did not receive steroids (n=4)*
Recovered	4 (57.14%)	3 (75%)
Expired	3 (43.86%)	1 (25%)

have shown a different gender distribution for cases of SJS and TEN. In a study conducted in Malaysia, Yapp *et al.* noted a male preponderance.[11] In our study, male: female ratio of cases of SJS did not show much difference. A review article by Saha mentioned that cases of TEN are mostly females.[12] All patients of TEN in our study were females.

The mean age of our patients was 28 years in cases of SJS. Our SJS patients were of a younger age group as compared to previous studies reporting a mean age of 40 years.[11] In a study in France, the patients of TEN had a mean age of 46.8 years,[13] our patients were comparatively younger with a mean age of 31 years.

Drugs are the most common etiological agent. In our study sulpha drugs were the most common culprit followed by carbamazepine. Similar drugs have been reported in previous studies.[11]

The mainstay of treatment in SJS and TEN is supportive care which includes fluid and electrolyte replacement, environmental temperature control, control of infection, nutrition, pain and topical skin care. The use of corticosteroids has been controversial for many years. Steroids have been accepted as a treatment option as they suppress the necrolytic process in the skin as well as internal organs. In a study conducted by Yamane *et al.*[14] the effect of treatment was analyzed on 46 patients and it was concluded that early treatment with corticosteroids reduced morbidity and improved survival in patients of SJS and TEN. Studies have also reported better outcome in patients treated with methyl prednisolone and dexamethasone pulse therapy.[15,16] Tripathi *et al.*[17] have reported almost 99% recovery in patients of SJS treated with steroids. Literature search has also revealed that corticosteroids may prove beneficial in cases of TEN due to their antiapoptotic effect on keratinocytes.[18] On the other hand steroids have also shown to decrease host resistance, increase morbidity, complications, prolong recovery and decrease survival.[9,10] This is in accordance to our results. We found a much better outcome in patients of SJS treated without steroids. The percentage of recovery was more than 90% in patients treated without steroids while it was only 67% in patients treated with steroids. Our patients of TEN managed without steroids showed a recovery of 75 % which was significantly more than in patients treated without steroids showing 57% recovery. The mortality percentage in SJS and TEN was significantly high in patients treated with steroids, 33% and 44%, respectively. Van et al have suggested that steroids increase apoptosis in the presence of

tumour necrosis factor (TNF) released in cases of SJS and TEN resulting in increased necrolysis and morbidity.[19] A study conducted by Halebian *et al*.[20] on two similar groups of patients treated with and without steroids, showed a 66% mortality in the patients treated with steroids again highlighting lack of any beneficial effect of steroids on outcome. A retrospective study by Kelmen *et al.*[21] showed that corticosteroid therapy was an independent factor for increasing the mortality. Another study by Kim *et al*.[22] showed similar results.

We conclude that the use of systemic corticosteroids in SJS and TEN is associated with increased mortality. Hence, the use of corticosteroids in patients should be avoided.

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