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Original Research

Assessment of severe cutaneous adverse reactions (SCAR's) like Steven–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)

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ABSTRACT:

Background: Adverse drug reactions (ADRs) are a necessary side effect of medication use. One of the most common adverse medication reactions is cutaneous symptoms. The present study was conducted to assess severe cutaneous adverse reactions (SCAR's) like Steven–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). **Materials & Methods:** 55 patients who had severe cutaneous adverse reactions of both genders were selected. The SCAR's were evaluated for their characteristics, causality, severity and prognosis. Causality assessment was done by using a validated ADR probability scale of Naranjo. **Results:** Out of 55 patients, males were 34 and females were 21. Type of SCARs was SJS in 35 and TEN in 20 patients. Associated drugs were carbamazepine in 26, phenytoin in 12, lamotrigine in 10, levofloxacin in 4 and Ibuprofen in 3 cases. Causality was possible in 38, probable in 14 and definite in 3 cases. The difference was significant (P< 0.05). **Conclusion:** Associated drugs were carbamazepine, phenytoin, lamotrigine, levofloxacin and Ibuprofen. To get outcome-based results, patients should be taught to refrain from re-exposure to the suspected substance or drugs.

Keywords: Adverse drug reactions, Steven–Johnson syndrome, toxic epidermal necrolysis

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INTRODUCTION

Adverse drug reactions (ADRs) are a necessary side effect of medication use. One of the most common adverse medication reactions is cutaneous symptoms.[1] Numerous multicentric pathways have demonstrated that the acute cutaneous response to the medications impacted 3% of inpatients at hospitals. Usually, reactions take place a few days after four weeks following the start of treatment.[2] TEN and SJS are two uncommon acute, potentially fatal SCARs with mucocutaneous discomfort, erythema, and a significant exfoliation and separation of skin layer. Less than 10% of the body's surface area has SJS. epidermal separation, 10–30% overlap between SJS and TEN, and TEN by over 30%.[3,4]

The yearly incidences of TEN and SJS are 0.4-1.2 and 1.2-6 per million persons, respectively. With a ratio of 1.5:1, both affect women more often than males, and the prevalence rises with age. For SJS, the average death rate is 1-5%, but for TEN, it is 25–35%. The elderly, immunocompromised individuals, and radiation patients are more vulnerable.[5,6] Approximately one hundred medications have been linked to SJS/TEN. Sulphonamides, antibiotics, oxicam NSAIDs, quinolones, AEDs, and allopurinol are the medications most commonly implicated.[7,8]The present study was conducted to assess severe cutaneous adverse reactions (SCAR's) like Steven–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

MATERIALS & METHODS

The present study was conducted on55 patients who had severe cutaneous adverse reactions of both genders.All were informed regarding the study and their written consent was obtained.

Data such as name, age, gender etc. was recorded. The SCAR's were reported in a structured questionnaire based on adverse drug reaction (ADR) reporting form provided by the Central Drug Standard Control Organization (CDSCO) Ministry of Health and Family welfare, Government of India. The SCAR's were evaluated for their characteristics, causality, severity and prognosis. Causality assessment was done by using a validated ADR probability scale of Naranjo as well as WHO Uppsala Monitoring Center

(WHO-UMC) system for standardized case causality assessment. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 55		
Gender	**Male**	**Female**
Number	34	21

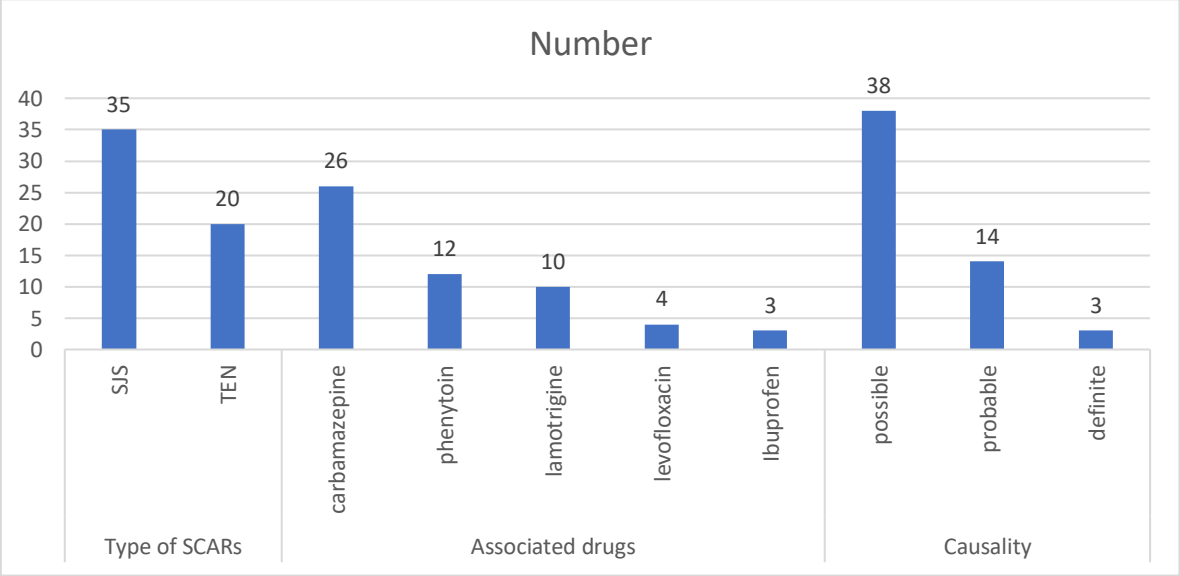
Table I shows that out of 55 patients, males were 34 and females were 21.

Table II Assessment of parameters

Parameters	Variables	Number	P value
Type of SCARs	SJS	35	0.05
	TEN	20	
Associated drugs	carbamazepine	26	0.17
	phenytoin	12	
	lamotrigine	10	
	levofloxacin	4	
	Ibuprofen	3	
Causality	possible	38	0.83
	probable	14	
	definite	3	

Table II shows that type of SCARs was SJS in 35 and TEN in 20 patients. Associated drugs were carbamazepine in 26, phenytoin in 12, lamotrigine in 10, levofloxacin in 4 and Ibuprofen in 3 cases. Causality was possible in 38, probable in 14 and definite in 3 cases. The difference was significant (P< 0.05).

Graph I Assessment of parameters



DISCUSSION

Erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) can all be caused by drug therapies; EM and SJS also have many causes not related to drug therapy.[9] These three cutaneous eruptions share many clinical features and together account for the majority of severe cutaneous reactions to drug therapies.[10,11]The present study was conducted to assess severe cutaneous adverse reactions (SCAR's) like Steven–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

We found that out of 55 patients, males were 34 and females were 21. Farhat et al[12]found that the mean age of the patients was 53.5 years. The mean surface area of denuded skin was 44% (range 30-90%). An adverse drug reaction was implicated in all patients, with mean time of TEN onset being 17 days (range 2-41 days) after initial drug exposure. The SCORTEN index was calculated in 19 patients (median SCORTEN 3, range 2-5). The SCORTEN predicted 7.3 deaths in this cohort, and 7 deaths were seen in the group of patients for whom SCORTEN was calculated. The overall mortality was 8/21 (38%). Ten

patients received corticosteroids before transfer to our centre. In the steroid-treated group 4/10 patients (40%) died, and 4/11 patients (36%) who were not treated with steroids also died. Between 1995 and 2000, patients were treated with cyclophosphamide 1.5 mg/kg/day (n=2; both died) and subsequently with ciclosporin 2.5-4 mg/kg/day (n=3; 2 deaths). From 2000, patients were treated with IVIg 0.4-1 g/kg/day (n=14; 3 deaths); the SCORTEN-predicted mortality in this group was 5 deaths. Complications included sepsis (n=18), and organisms included Enterococcus, Acinetobacter, Staphylococcus aureus and methicillin-resistant S. aureus strains). Other complications included anaemia (n=17), lymphopenia (n=11) and neutrophilia (n=9). The presence of neutropenia (n=6; 4 deaths), renal impairment (n=5; 4 deaths) and disseminated intravascular coagulation (n=4; all died) were strong risk factors for mortality. Of 12 patients with ocular involvement, 6 (50%) developed symblepharon and/or visual impairment.

We found that type of SCARs was SJS in 35 and TEN in 20 patients. Associated drugs were carbamazepine in 26, phenytoin in 12, lamotrigine in 10, levofloxacin in 4 and Ibuprofen in 3 cases. Causality was possible in 38, probable in 14 and definite in 3 cases. Chan et al[13] in their study a total of 61 suspect cases of EM, SJS, or TEN were identified. A total of 37 patients (61%) were classified as having EM, SJS, or TEN. Of these, 16 cases (43%) were attributed to drugs administered to these patients prior to hospitalization. The overall incidence of hospitalization for EM, SJS, or TEN due to all causes was 4.2 per 10(6) person-years. The incidence of TEN alone due to all causes was 0.5 per 10(6) person-years. The incidence of EM, SJS, or TEN associated with drug use were 7.0, 1.8, and 9.0 per 10(6) person-years, respectively, for persons younger than 20 years of age, 20 to 64 years of age, and 65 years of age and older. Drug therapies with reaction rates in excess of 1 per 100,000 exposed individuals include phenobarbital (20 per 100,000), nitrofurantoin (7 per 100,000), sulfamethoxazole and trimethoprim, and ampicillin (both 3 per 100,000), and amoxicillin (2 per 100,000).

Bastuji-Garin et al[14] identified seven independent risk factors for death and constituted the toxic epidermal necrolysis-specific severity-of-illness score: age above 40 y, malignancy, tachycardia above 120 per min, initial percentage of epidermal detachment above 10%, serum urea above 10 mmol per liter, serum glucose above 14 mmol per liter, and bicarbonate below 20 mmol per liter. For each toxic epidermal necrolysis-specific severity-of-illness score point the odds ratio was 3.45 (confidence interval 2.26-5.25). Probability of death was: P(death) = elogit/1 + elogit with logit = -4.448 + 1.237 (toxic epidermal necrolysis-specific severity-of-illness score). Calibration demonstrated excellent agreement between expected (19. 6%) and actual (20%) mortality; discrimination was also excellent with a receiver operating characteristic area of 82%. The Simplified Acute Physiology Score and the burn score were also associated with mortality. The discriminatory powers were poorer (receiver operating characteristic area: 72 and 75%) and calibration of the Simplified Acute Physiology Score indicated a poor agreement between expected (9.1%) and actual (26.7%) mortality.

The shortcoming of the study is small sample size.

CONCLUSION

Authors found that associated drugs were carbamazepine, phenytoin, lamotrigine, levofloxacin and Ibuprofen. To get outcome-based results, patients should be taught to refrain from re-exposure to the suspected substance or drugs.

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