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A RETROSPECTIVE STUDY ON STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS IN A TERTIARY CARE TEACHING HOSPITAL, MYSURU.

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ABSTRACT

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute life threatening adverse drug reactions (ADR's) that are commonly caused by drugs. These are potentially serious cutaneous reactions, characterized by high fever, wide-spread blistering exanthema of macules and atypical target-like lesions, accompanied by mucosal involvement. In addition to the severe skin symptoms, both diseases are accompanied by complications in numerous organs, such as liver, kidney and lungs. In this study, we aimed to identify the incidence and the causative drugs of SJS-TEN, to educate patients on nature and complications of SJS-TEN.

Objectives

Primary objectives

1. To detect the drugs implicated in SJS-TEN in our hospital and clinical outcome.

Secondary objectives

1. To create awareness among the treating physicians about the drugs implicated in life threatening reactions. Hence, to facilitate judicious use of the drugs in future.
2. To educate patients on nature and complications of SJS-TEN.

Materials and Methods: Study was carried out at Department of Skin and STD's, Mysore Medical College & Research Institute and K R Hospital, Mysore, India. A retrospective study that included 13 patients diagnosed with drug- induced SJS, SJS-TEN overlap and TEN, from August 2017 to July 2020. Data was collected from patient medical records and interview with healthcare professionals. **Result:** During the study period, 13 cases of drug induced SJS (4/13, 30.76%), TEN (8/13, 61.73%) and SJS-TEN (1/13, 0.76%) overlap reported. Total 9 males and 4 females were reported. The major group of drugs causing SJS/TEN were anticonvulsants (7/13, 53.83%), antiretroviral (2/13, 15.3%), antimicrobials (2/13, 15.3%) and non-steroidal anti-inflammatory drugs (NSAIDs) (2/13, 15.3%). 1 case of SJS-TEN overlap was reported due to aspirin. While considering individual drugs, Phenytoin (4/13, 30.76%) and Carbamazepine (3/13, 23.07%) were among the commonly reported offending drugs. **Conclusion:** In conclusion, SJS, TEN and SJS-TEN overlap are serious cutaneous adverse reaction most commonly caused by anticonvulsants, antimicrobials and NSAIDs. The risk of management is higher than other serious ADRs. Identification and withdrawal of drugs suspected to cause SJS or TEN are important.

KEYWORDS: Stevens-Johnson syndrome, toxic epidermal necrolysis, Anti-convulsants, Antimicrobials, Adverse drug reactions, Non-steroidal anti-inflammatory drugs.

INTRODUCTION

Adverse drug reactions (ADRs) hold special importance in healthcare as they account for 6% of total hospital admissions, increase in economic burden on healthcare system, withdrawal of drugs from market, and death.[1-3] Among the various ADRs, cutaneous adverse reactions like skin rashes, urticarial, itching, fixed drug eruption, angioedema, erythema multiforme, Stevens- Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) are the common ones.[4,5] Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute life- threatening adverse drug reactions (ADRs) characterized by epidermal detachment and mucositis.[6] SJS and TEN are immune-mediated reactions, due to various etiological factors like drugs, infections, malignancy and radiation therapy.[7] Drugs are most commonly implicated in 95% of cases.[7] Incidence of SJS and TEN is 0.05 to 2 persons per million populations

per year.[8,9] Incidence is higher in HIV patients than general population.[10] Clinically, SJS and TEN are characterized by polymorphic lesions like erythematous macules, papules, plaque, vesicles, and bullae predilected to distal extremities with Nikolsky's sign positive. "Target" lesion with bull's eye appearance is characteristic of SJS and TEN. Oral, genital, and conjunctival mucosa is often involved in the form of erosion or ulceration.[11] The basic difference between SJS and TEN is the percentage of body surface area (BSA) involved: <10% in SJS; >30% in TEN; 10 to 30% in SJS-TEN overlap.[7,11]

Drugs are identified as the etiologic agents of SJS, TEN and SJS-TEN overlap syndrome. Based on regisSCAR/euroSCAR registries, the high risk drugs include Allopurinol, Carbamazepine, Cotrimoxazole and other anti-infective sulphonamides, Nevirapine, Lamotrigine, Sulfasalazine, Oxicam type non-steroidal anti-inflammatory drugs (NSAID's), phenobarbital and phenytoin. Moderate risk drugs include quinolones, Macrolides, Cephalosporins and Tetracyclines. Low risk drugs, that in previous studies were not associated with a measurable risk, including beta- blockers, calcium channel blockers, Sulphanamide based thiazide diuretics, Sulphonylurea anti- diabetics, Insulin.[12,13] No confirmatory in vivo or invitro tests are available for identifying offending agents in SJS and TEN.[11]

Despite the fact that the incidence of SJS or TEN are acute life-threatening, the condition may also lead to significant financial consequences for the patients.[14] Therefore identification and withdrawal of drugs suspected to cause SJS or TEN are important.[15]

The study also helped us to know the changing pattern of most common causative agents for SJS and TEN.

MATERIALS AND METHODOLOGY

We conducted a retrospective study at Department of skin and STD's, K R hospital, Mysuru. Medical records of patients diagnosed with drug-induced SJS, TEN or SJS-TEN overlap syndrome from August 1, 2017 to July 30 2020, were recalled and included in the study. A data collection sheet was designed for the purpose of organizing collected data from patient records. Data included patient demographics, disease progression, detailed treatment regimen and suspected causative drugs as specifically mentioned in medical records by treating physicians. Incomplete patient records were excluded from the study. Incomplete patient records that excluded were due to insufficient data and improper record that is missing of suspected causative drug from the treating physicians and incomplete medical treatment records. Return informed consent form was not required because this was a retrospective observational study. No medical interventions were performed during the study. All ethical considerations were followed. No personal data were collected.

Ethical approval was obtained from the institutional ethical committee of Mysore Medical College and Research Institute, KR Hospital, Mysuru.

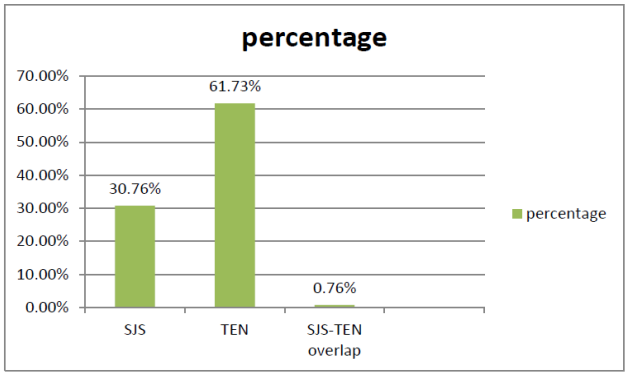
RESULTS

During the study period, 13 cases of drug induced SJS (4/13, 30.76%), TEN (8/13, 61.73%) and SJS-TEN (1/13, 0.76%) overlap reported (Graph 1). Total 9 males and 4 females were reported (Table 1). Of these 3 males and 1 female had SJS while 5 males and 3 females had TEN. Only 1 male patient of SJS-TEN overlap was reported (Table 2).

The major group of drugs causing SJS/TEN were anticonvulsants (7/13, 53.83%), antiretroviral (2/13, 15.3%), antimicrobials (2/13, 15.3%) and non-steroidal anti-inflammatory drugs (NSAIDs) (2/13, 15.3%) (Table 3). 1 case of SJS-TEN overlap was reported due to aspirin. While considering individual drugs, Phenytoin (4/13, 30.76%) and Carbamazepine (3/13, 23.07%) were among the commonly reported offending drugs. The conditions for which patients took these offending drugs were seizure, HIV, Arthralgia, Depression, cystic kidney disease, chronic diarrhoea.

Table 1: Gender Distribution of the study population.

Gender	No. of patients	Percentage
Female	4	30.76%
Male	9	69.24%
Total	13	100%



Graph 1: Condition distribution of the study population.

Table 2: Gender wise distribution of patient condition.

Condition	Male	Female
SJS	3	1
TEN	5	3
SJS-TEN overlap	1	0

Table 3: Offending drugs with respect to reactions.

Offending drugs	No. of patients with SJS	No. of patients with TEN	No. of patients with SJS-TEN	Total no. of patients (%)
Phenytoin (anticonvulsants)	1	3	0	4 (30.76%)
Carbamazepine (anticonvulsants)	1	2	0	3 (23.07%)
Efavirenz (antiretroviral)	0	2	0	2 (15.3%)
Levofloxacin (antimicrobial)	0	1	0	1 (7.69%)
Cotrimoxazole (antimicrobial)	1	0	0	1 (7.69%)
Nimesulide (NSAIDs)	1	0	0	1 (7.69%)
Aspirin (NSAIDs)	0	0	1	1 (7.69%)

DISCUSSION

In this study male preponderance (69.29% male and 30.76% female) was observed. In our study incidence rate of TEN (61.53%) is higher compared to SJS (30.76%) and SJS-TEN overlap (7.69%). Three most common groups of drugs causing eruptions were anticonvulsant drugs, antiretroviral drugs and NSAIDs. This is in agreement with the previous reports.[16,17] Phenytoin(30.76%) was the most commonly associated drug in our study as against nevirapine which have been mentioned in previous study.[18] Anticonvulsant drugs were the most common drugs causing TEN in our study they had the higher chance(62.5%) of causing severe eruption, that is TEN than antiretroviral(25%) and antimicrobials(12.5%) this is lower as compared with the previous report(81.8%).[18] Anticonvulsants(50%) was the most common group of drugs causing SJS in our study compared to antimicrobials(25%) and NSAIDs(25%). In our study SJS- TEN overlap was caused by Aspirin compared to Cotrimoxazole is the causative drug in the other study.[18]

Among NSAIDs, Nimesulide was the most common to cause the reaction in our study. But Paracetamol is described in other Indian study.[18] we did not find any Oxicam derivative as offending drug which is mentioned as most responsible among NSAIDs in American study.[19] This may be due to different genomic factors or drug utility pattern influencing both the populations.

Twenty percent cases have been excluded from the study due insufficient data or improper records. Proper record maintaining is required for such type of study involving disease of low incidence rate.

CONCLUSION

In conclusion, SJS, TEN and SJS-TEN overlap are serious cutaneous adverse reaction most commonly caused by anticonvulsants, antimicrobials and NSAIDs. The risk of management is higher than other serious ADRs. Treating physicians and pharmacists should also consider the ADRs between the medication given and the medication for other diseases that are independent from SJS, TEN and SJS-TEN overlap treatments. Furthermore, identification and withdrawal of drugs suspected to cause SJS or TEN are important.

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