

ORIGINAL RESEARCH

The clinical spectrum of cutaneous adverse drug reactions for drugs

¹Dr. Revanth BN, ²Dr. Khizerulla Sharief

¹Consultant Dermatologist, Spectrum Skin Care, Jayanagar, Bangalore, Karnataka, India

²Associate Professor, Department of Paediatrics, Akash Institute of Medical Sciences and research Centre, Bangalore, Karnataka, India

Corresponding Author

Dr. Revanth BN

Consultant Dermatologist, Spectrum Skin Care, Jayanagar, Bangalore, Karnataka, India

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Abstract

The incidence of cutaneous drug eruptions is about 2.2% and is higher among inpatients and females. Fatal reactions to drug occur even though benign reactions are common. The diagnosis of cutaneous drug reaction is based on detailed history and correlation between drug intake and the onset of rash. A stepwise approach was taken to evaluate the patients. This included an exhaustive history and clinical examination. An accurate drug history was obtained. Names of all the drugs and the duration of intake were noted. Attention was also paid to the sequence of events, to rule out other diseases mimicking drug rash. The underlying disease for which drug was taken was also noted. History of any previous drug allergies in self and family members, were also noted. The most common cutaneous adverse drug reaction seen in our patients were maculopapular rash in 23% (23/100), followed by fixed drug eruptions in 17% (17/100), urticaria in 10% (10/100), Stevens Johnson syndrome in 9% (9/100), DHS in 8% (08/100), and acneiform in 6% (06/100). A similar pattern was seen in the adult age group.

Key words: Cutaneous adverse drug reactions, fixed drug eruptions, maculopapular rash

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Introduction

Drug eruptions are in limelight today, not only because of availability of a number of drugs due to almost uninhibited, profuse proliferation of a variety of them, but also because of the great enthusiasm to use them by medical profession and people alike.

With increase in the number of drugs, adverse drug reactions have become very common in recent times. Among them the cutaneous reactions play a major role

and have attracted importance. Many epidemiological and clinical studies have thrown light on various aspects of this disorder. A large quantity of information is being added to literature regarding cutaneous drug eruptions.¹

In a large variety of ambulatory patients the Cutaneous Adverse Drug Reactions are mild and transient, and therefore go unnoticed by the patient and the treating doctor.² On the other hand cutaneous symptoms of diseases that may appear to have a temporal relationship to drug therapy are often erroneously classified as drug eruptions.³

The incidence of cutaneous drug eruptions is about 2.2% and is higher among inpatients and females. Fatal reactions to drug occur even though benign

reactions are common. The diagnosis of cutaneous drug reaction is based on detailed history and correlation between drug intake and the onset of rash.⁴ The cutaneous are visible and hence their reporting is earlier and better as compared to the drug reactions involving internal organs and other systems. Similarly the response to the treatment to the cutaneous drug reactions is also better perceived.^{5,6,7} Few prospective studies have been done in the Indian population with regards to causative drugs and the type of rash.⁸

Methodology

Patients

All patients attending the department of Dermatology, Those cases suspected of having a cutaneous adverse drug reaction were evaluated.

All the various departments of the hospital were informed about the study not only at the beginning of the study but also at regular intervals thereafter to ensure that all cutaneous adverse drug reactions were referred to our department.

Inclusion Criteria: All cases of cutaneous drug eruptions of all age groups of either sex.

Exclusion Criteria

Reactions where the drug taken are not known.

Method

A stepwise approach was taken to evaluate the patients. This included an exhaustive history and clinical examination. An accurate drug history was obtained. Names of all the drugs and the duration of intake were noted. Attention was also paid to the sequence of events, to rule out other diseases mimicking drug rash. The underlying disease for which drug was taken was also noted. History of any previous drug allergies in self and family members, were also noted.

All patients were counselled and advised HIV testing. However, the test was done only in those patients who gave consent for testing. CD4 counts were not done as

a routine. However, if a patient had a test report of CD4 counts the same was noted.

In systems review, specific attention was given to history of UTI, URTI or other intercurrent infection.

A meticulous and thorough clinical examination was done. Attention was paid to the site, nature and extent of rash, pattern of rash as to whether it was generalized, localized, flexural or sun exposed. Distribution of rash was noted. Any special or unusual finding was noted. Colour of rash and secondary changes (like necrosis or blistering) were documented. On general examination in addition to the general condition of the patient, attention was paid to the presence of features like lymphadenopathy, icterus and pyrexia. Routine investigations such as total count were done in all patients that were included. (Special investigations were done in certain individuals based on the rash category.).

Results

Table 1: Cutaneous adverse drug reactions

Rash type	Child{N=15 (%)}	Adults{N=85 (%)}	Total{N=100 (%)}
Maculopapular	03 (20)	20 (24)	23 (23)
Fixed drug eruption	02 (13)	15 (18)	17 (17)
Urticaria	02 (13)	08 (09)	10 (10)
Stevens Johnson syndrome	01 (07)	08 (09)	09 (09)
Drug hypersensitivity syndrome	01 (07)	07 (08)	08 (08)
Toxic epidermal necrolysis	02 (13)	04 (05)	06 (06)
Acne form	00 (00)	06 (07)	06 (06)
Erythema multiforme	01 (07)	03 (04)	04 (04)
Angioedema	01 (07)	02 (3.6)	03 (03)
Pruritus	00 (00)	01 (01)	01 (01)
Photosensitivity	00 (00)	02 (3.6)	02 (02)
Hyperpigmentation	01 (07)	01 (01)	02 (02)
Vasculitis	00 (00)	01 (01)	01 (01)
Exfoliative	01 (07)	01 (01)	02 (02)
Lichenoid	00 (00)	01 (01)	01 (01)
Papular	00 (00)	01 (01)	01 (01)
Eczematous	00 (00)	01 (01)	01 (01)
Hair loss	00 (00)	01 (01)	01 (01)
Psoriasis form	00 (00)	01 (01)	01 (01)
Ulcers	00 (00)	01 (01)	01 (01)
Total	15	85	100

The most common cutaneous adverse drug reaction seen in our patients were maculopapular rash in 23% (23/100), followed by fixed drug eruptions in 17% (17/100), urticaria in 10% (10/100), Stevens Johnson syndrome in 9% (9/100), DHS in 8% (08/100), and acneiform in 6% (06/100). A similar pattern was seen in the adult age group.

Among the pediatric cases, the most common drug

eruptions seen were maculopapular rash (3). There were two cases each of fixed drug eruptions and urticaria, and one cases of Stevens Johnson syndrome. Some forms of CADRs were not seen in pediatric age group like acneiform eruptions, lichenoid eruptions, photosensitive eruptions, vasculitis, eczematous eruptions, pustular eruptions, papular eruptions and hair loss.

Table 2: Comparison of common CADR with their significance values

Rash	Total number of cases	Chi-square	Significance (p-value)
Maculopapular	23	0.081	0.487
TEN	06	8.792	0.008
FDE	17	0.010	0.921
Urticaria	10	1.380	0.376
SJS	09	0.094	1.000
EMF	04	0.513	0.823
DHS	08	1.571	0.319
Others	23	3.188	0.074

Among the various CADR in adults and children the frequencies were similar in cases of maculopapular

reactions, fixed drug eruptions, and Stevens Johnson syndrome.

Table 3: CADR among males and females

Rash type	Sex		Total	Chi- square	Significance (p-value)
	Male	Female			
Fixed drug eruption	10	7	17	7.694	0.006
Maculopapular	10	13	23	0.701	0.403
Stevens Johnson syndrome	6	3	9	2.069	0.150
Urticaria	7	3	10	0.933	0.334
Acneform	4	2	6	0.767	0.381
Drug hypersensitivity syndrome	2	6	8	1.948	0.163
Toxic epidermal necrolysis	2	4	6	1.403	0.236
Angioedema	2	1	3	0.762	0.379
Photosensitivity	0	2	2	0.245	0.679
Papular	0	1	1	0.001	0.979
Erythema multiforme	1	3	4	4.448	0.025
Exfoliative	1	1	2	0.309	0.583
Pruritus	0	1	1	0.302	0.579
Hyperpigmentation	1	1	2	0.302	0.579
Lichenoid	1	0	1	0.001	0.979
Vasculitis	0	1	1	0.001	0.979
Others	2	2	4	1.042	0.232
Total	49	51	100		

Among the various rashes seen in males and females, the incidence of fixed drug eruptions was found to be significantly higher in males as compared to females. In case of erythema multiforme, however a trend towards significance was seen in females.

Discussion

Adverse drug reactions form an important and common problem in both inpatient and outpatient setting. It is important to keep oneself updated with the knowledge on latest trends in drug reaction with regards to the newer drugs, newer manifestations of older drugs, diagnosis, and management of these drug reactions.

This study was done in a tertiary care hospital with large outpatient and inpatient numbers. A total of 100, confirmed or suspected CADR in 100 patients were documented, over a period of one and half year.

The incidence of CADR in this study was found to be 2 over thousand patients. Whereas studies done by Mehta *et al.*, Mani *et al.* and Impicciatore *et al.* showed 14.6, 10 and 12 respectively per 1000 patients which is high when compared to the present study.

The incidence in the present study may be low due to the reason that there is a developing awareness among the population in this region for drug reactions. There is also decrease in taking of over the counter drugs by the patients in this region especially in the recent years which may have lead to the drop in incidence of drug reactions.⁸

Studies done by Mehta *et al.*, Mani *et al.*, Sharma *et al.* showed a ratio of 0.80:1, 0.92:1, 0.90:1 respectively implicating that there is a slight female preponderance over males. The present study showed a ratio of 0.95:1. All the studies show a slight female preponderance due to gender related differences in pharmacokinetic, immunological and hormonal factors as well as differences in the use of medications by women compared with men.^{9,10}

Conclusion

- The incidence of CADR among dermatology patients is 2 per thousand patients.
- The incidence of CADR among adults and children is 2.09 and 1.57 per thousand patients respectively.

- There is no significant difference in the sex incidence of CADR.

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