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Original Research Article

Prevalence and pattern of adverse cutaneous drug reactions presenting to a tertiary care hospital

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ABSTRACT

Background: An adverse cutaneous drug reaction (ACDR) is defined as an undesirable clinical manifestation resulting from administration of a particular drug. With an ever increasing number of drugs and varied formulations being continuously made available it is important that a close watch on the risks of adverse drug reactions is looked for, to ensure safe use of medicines in the interest of the patient. In the present study our aim is to study the prevalence & pattern of cutaneous adverse drug reactions reported to department of dermatology at MediCiti Institute of Medical Sciences, Hyderabad, India.
Methods: All suspected cutaneous adverse drug reactions reported to the department of dermatology at MediCiti Institute of Medical Sciences during the two year period from January 2013 to December 2014 were included in this study. A thorough clinical examination of all these cases & details related to the drug use and clinical manifestations of the cutaneous adverse drug reaction were documented using a structured proforma. Naranjo scale was used to assess causality in all the causes of cutaneous adverse drug reactions.
Results: The mean age of the patients was 42 years (age range: 1-64 years). Most of them were in the age group of 30-39 years. The male to female ratio was 1.78:1. The most common type of skin eruptions observed were maculopapular rash (35.55%), urticaria (26.19%) and fixed drug eruption (17.87%). The mean duration between drug intake and appearance of rash was 4 days (range: 1-120 days).
Conclusions: The pattern of ACDRs and the drugs causing them in this study were similar to that reported in other studies both in terms of disease burden and clinical pattern. Knowledge of adverse cutaneous drug reactions will help to identify common medications contributing to dermatological reactions, so as to anticipate, prevent and limit their undue consequences.

Keywords: Adverse cutaneous drug reactions, Drug rash, Drug reaction

INTRODUCTION

Cutaneous adverse drug reactions are part of skin problems reported to dermatology clinics. Systematic monitoring and surveillance of adverse drug reactions will help in ensuring safer prescription and limit the adverse effects of drugs with their undue consequences. We analysed systematically documented data on cutaneous adverse drug reactions reporting at our centre. The main aim of this study was to estimate the burden of cutaneous adverse drug reactions and to analyse the nature and causality of cutaneous adverse drug reactions in a tertiary care hospital.

The objectives of the study was to estimate the prevalence of adverse cutaneous drug reactions (ACDR) presenting to department of Dermatology at a tertiary

care hospital and to determine the pattern of ACDR and to identify the putative aetiological agents causing them.

METHODS

All patients with cutaneous adverse drug reactions presenting to the dermatology department at MediCiti Institute of Medical Sciences from January 2013 to December 2014 were included in this study. All cases of suspected drug rash presenting to the dermatology department either self-reported or referral from other departments were examined by a dermatologist. A detailed history including medication use was collected and a clinical diagnosis was made after thorough clinical examination and subjected to relevant investigations wherever required. The details of cutaneous manifestation, medication use, were recorded in the adverse drug reaction reporting form used in the National Pharmacovigilance program of India. Naranjo scale was used for assessing causality of suspected individual cutaneous adverse drug reactions. The study was approved by the Institution Ethics Committee.

RESULTS

Total number of patients reported at our centre during the period from January 2013 to December 2014 was 44,408. A total of 481 suspected cutaneous adverse drug reactions were reported during the said time period. The prevalence of cutaneous adverse drug reactions was 1.08%. The age group in this study ranged from 1year to 64 years with mean age of 42 years. The number of male patients 308 (64%) and female were 173 (36%), with a male to female ratio of 1.78:1. The mean duration between drug intake and appearance of rash was 4 days (1-120 days). The proportions of various cutaneous adverse drug reactions are shown in Table 1.

The distribution of various cutaneous drug reactions by suspected medication was provided in Table 2.

DISCUSSION

Cutaneous adverse drug reactions account for a major portion of drug reactions. Most cutaneous adverse drug reactions could impose significant physical, mental and economic burden on the patient while others may end fatally.

The prevalence of cutaneous adverse drug reactions in our study was 1.08% which is similar to that reported in literature. Studies have reported the burden of ACDRs in developed countries as 1–3% and in developing countries between 2-5%.[1] We observed a male: female ratio of 1.78:1 in the cases that reported with suspected cutaneous adverse drug reactions. Slight male preponderance in cutaneous adverse drug reactions was reported by Sharma et al.[2] A systematic review done by Patel et al concluded that association of gender is inconsistent in published literature & reported that the male preponderance to cutaneous adverse drug reactions in India could be due to the gender distribution of Indian population.[3]

The most common cutaneous adverse drug reaction observed in our study was maculopapular eruptions (34.3%). The most common drug causing maculopapular eruption was Amoxicillin, followed by Ampicillin, Cephalosporins, Phenytoin and Carbamazepine. Similar to our observation, several studies reported maculo-papular rash as the most common cutaneous adverse drug reaction.[4-6] The time of onset of maculopapular eruption after the suspected medication intake ranged from 1 day to 7 days in our study.

Table 1: Distribution of various cutaneous adverse drug reactions.

Nature of Lesion	No. of cases	Percentage
Maculopapular eruptions	171	35.55
Urticaria	126	26.19
Fixed drug eruptions (FDE)	86	17.87
Drug induced vasculitis	24	4.98
Erythema multiforme(EMF)	20	4.15
Drug Reaction with eosinophilia and systemic symptoms (DRESS)	20	4.15
Acute generalised exanthematous pustulosis (AGEP)	15	3.11
Lichenoid eruptions	10	2.07
Stevens Johnson Syndrome (SJS)	05	1.03
SJS/TEN overlap syndrome	02	0.41
Toxic epidemal necrolysis (TEN)	02	0.41
Total	481	100

The second most common cutaneous adverse drug reaction observed in our study was urticaria comprising 26.2%. Non-steroidal anti-inflammatory drugs (NSAIDs) accounted for the most cases of urticarial (40%), followed by Sulfonamides, Penicillin, Cephalosporins, Enalapril, Cetrizine and radio-contrast media. All of these medications were reported to be associated with urticaria in several previous studies.[7-10] Antihistamine like Cetrizine causing urticaria was observed in 4 cases in our study. Similar observation was reported by Calista et al.[11]

Fixed drug eruption comprised 17.9% of the total cutaneous adverse drug reactions in our study. Diclofenac contributed to the highest number of fixed drug eruptions followed by Cotrimoxazole, Ciprofloxacin, Ibuprofen, Ofloxacin, Phenytoin, Metronidazole, Carbamazepine, Levofloxacin and Sparfloxacin. These findings are in concordance with other studies.[12-14]

Table 2: Distribution of cutaneous adverse drug reactions by suspected drug.

S.no.	Type of cutaneous adverse drug reaction	Total no. of cases (N)	Name of the drug	No. of cases (n)	Percentage (%)
1	Maculo-Papular eruptions	171	Amoxicillin	68	39.77
			Ampicillin	34	19.88
			Cephalosporins	38	22.22
			Phenytoin	23	13.45
			Carbamazepine	08	4.68
2	Urticaria	126	NSAIDS	54	42.85
			Sulfonamides	22	17.46
			Penicillin	16	12.69
			Cephalosporin	14	11.11
			Enalapril	14	11.11
			Cetrizine	04	3.17
			Radio-contrast media	02	1.58
3	Fixed drug eruptions	86	Diclofenac	16	18.6
			Cotrimoxazole	14	16.27
			Ciprofloxacin	12	13.95
			Ibuprofen	10	11.62
			Ofloxacin	09	10.46
			Phenytoin	08	9.30
			Metronidazole	06	6.97
			Carbamazepine	05	5.81
			Levofloxacin	04	4.65
			Gatifloxacin	02	2.32
4	Vasculitis	24	Phenytoin	12	50.0
			Enalapril	08	33.33
			Carbamazepine	04	16.67
5	Drug reaction with eosinophilia and systemic symptoms (DRESS)	20	Cotrimoxazole	07	35.0
			Phenytoin	06	30.0
			Dapsone	04	20.0
			Carbamazepine	03	15.0
6	Acute generalized exanthematous pustulosis	15	Amoxicillin	04	26.67
			Ampicillin	04	26.67
			Cephalexin	04	26.67
			Cefpodoxime	02	13.33
			Doxycycline	01	6.67
7	Lichenoid eruptions	10	Hydroxychloroquine	07	70.0
			Diclofenac	02	20.0
			Atenolol	01	10.0
8	Erythema multiforme	20	NSAIDs	12	60.0
			Sulfonamides	06	30.0
			Phenobarbitone	02	10.0
9	Stevens Johnson syndrome (SJS) & SJS/TEN	5+2	Phenytoin	04	57.14
			Carbamazepine	03	42.85
10	Toxic epidermal necrolysis (TEN)	2	carbamazepine	01	50.0
			Phenytoin	01	50.0

A study done by Nandha et al in north India observed predominantly maculopapular rash followed by fixed drug eruption & urticaria, whereas in our study we noted maculopapular rash dominance followed by urticaria & fixed drug eruption.[15]

Drug induced vasculitis comprised 4.98% of the total cutaneous adverse drug reactions. The most common offending agent associated with drug induced vasculitis was Phenytoin, followed by Enalapril and Carbamazepine.

Drug Reaction with eosinophilia and systemic symptoms (DRESS) comprised 4.15% of the cutaneous adverse drug reactions. The most common drugs suspected was Cotrimoxazole followed by Phenytoin, Dapsone and Carbamazepine. DRESS has been shown to be associated with the use of antiepileptics and sulphur compounds. Similar observations made by Akpinar et al.[14]

Acute Generalized exanthematous pustulosis comprised 3.11% of the total cutaneous adverse drug reactions. Amoxicillin was associated with the most number of cases followed by Ampicillin, Cephalexin, Cepodoxime and Doxycycline. These observations are similar to those observed by Sidoroff et al.[16]

Erythema multiforme comprised 4.15% of the adverse cutaneous drug reactions. Drugs noticed are NSAIDs, sulphonamides and phenobarbitone. Our observations are in concordance with previous studies in India which have reported an incidence of Erythema multiforme ranging from 0.4% to 3.57%.[17,18]

Lichenoid eruptions comprised 2.07% of the cutaneous adverse drug reactions. Hydroxychloroquine was associated with the majority cases, followed by Diclofenac and Atenolol.

Stevens Johnson syndrome (SJS) comprised a small fraction (1.03%) of reported cutaneous adverse drug reactions. About 57% of SJS was associated with the use of Phenytoin and 43% with the use of Carbamazepine. Toxic epidermal necrolyis (TEN) comprised 0.4% of the total cutaneous adverse drug reactions. There were only 2 cases of TEN, one each associated with the use of Phenytoin and Carbamazepine. SJS/TEN overlap syndrome was seen in 2 patients only. These findings are in concordance with reports implicating antiepileptics, similar to review done by Patel et al.[19]

The patients who had adverse drug reaction like toxic epidermal necrolysis, Stevens Johnson syndrome, SJS/TEN overlap syndrome, DRESS syndrome & acute generalised exanthematous pustulosis were treated as in-patients. One patient with TEN survived and the other died. The Scorten in the patient who survived was 3, whereas the Scorten was 4 in the patient who died.

All the cutaneous adverse drug reactions noted in our study had a score ranging from 1-4 using the Naranjo algorithm for causality assessment.[20] Thus, suggesting that the cutaneous adverse drug reactions noted in our study were probable in terms of causality.

CONCLUSION

The pattern of cutaneous adverse drug reactions observed in this study are similar to that reported in various studies in India. Further, the medications predominantly antibiotics & anticonvulsants that were found to be possibly associated with the cutaneous adverse drug reactions in our study have been reported in literature to be similarly associated with cutaneous drug reactions both in India and abroad.

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