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STUDY OF ADVERSE CUTANEOUS DRUG REACTION IN DERMATOLOGY DEPARTMENT AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: An adverse cutaneous drug reaction (ACDR) contributes approximately 3% of all disabling injuries during hospitalisation, increases morbidity and complications of drug therapy. The pattern of cutaneous reactions and the drugs causing various reactions are changing continuously over the period of time due to introduction of newer drugs and changing trends in the use of drugs. There is scarcity of such data in India which includes aspects like demographic details, type of cutaneous adverse drug reactions, pharmacological agents responsible for it, causality and severity assessment of reactions etc. **Methods:** 150 patients were enrolled from dermatology department at tertiary care teaching hospital over period of 6 months. Confirmed cutaneous adverse drug reaction details were recorded. Causality grading was done by using Naranjo's Algorithm Scale and severity grading was done by using The Modified Hartwig And Siegel Scale. The variety of skin manifestations and agents causing cutaneous drug reactions were also noted. **Results:** Study population affected (%) by Cutaneous Adverse Drug Reactions in this study was maximum with maculopapular rash (30.04%) and least with Steven Johnson syndrome (0.02%). Drug classes responsible were antimicrobial agents(50.02%), NSAIDs(29.12%), steroids(9.54%),anti-epileptic agents(3.01 %), anti-retroviral agents(2.23%), acid suppressors(ranitidine, omeprazole)(1.69%), haematinics(0.08%) and others(4.31%). The causality assessment by Naranjo's Algorithm Scale shown in present study was probable category (60.14%), possible (36.98%), doubtful (2.87%) and definite (0.01%). Study population showed moderate severe level 3(48.43%) followed by mild level 1 (34.63%), mild level 2(16.91%), moderate level 4 (0.02%) and severe level 5 (0.01%). **Conclusions:** In our study we found maximum maculopapular rash in study population and agents found culprit for highest contribution were antimicrobial agents showing concern of rational use of antimicrobials. Causality grading showed probable category maximum and severity grading showed moderate severe level 3 like many other similar studies. This result of the present study helps to health care professionals in policy making regarding rational use of drugs, rational prescription and adverse drug monitoring on regular basis.

KEYWORDS: Adverse cutaneous drug reaction (ACDR), Causality, Severity.

INTRODUCTION

Cutaneous reactions are the most common manifestations of ADRs.[1] An adverse cutaneous drug reaction(ACDR) caused by a drug is any undesirable change in the structure or function of the skin, its appendages or mucous membranes, and it encompass all adverse events related to drug eruption, regardless of the aetiology.[2] Cutaneous adverse drug reactions (ADR) can be caused by a wide variety of agents. They are responsible for approximately 3% of all disabling injuries during hospitalisation and complications of drug therapy are the most common type of adverse event in hospitalised patients. There is a wide spectrum of cutaneous ADR ranging from a transient maculopapular rash to fatal toxic epidermal necrolysis (TEN). They affect the patient in the form of prolonging or requiring hospitalization, systemic complications, mortality, and economic burden.[3,4] Atopy, genetic variations in drug metabolism, HLA variation, comorbidities, underlying disease, active viral infection, immune status of the patient, and concomitant intake of other drugs can alter the rate, presentation, course, and the outcome of cutaneous drug reactions. Many of the commonly used drugs have reaction rates above one percent.[1] The common group of drugs responsible for adverse cutaneous reaction are antimicrobials, anticonvulsants, NSAIDs, antimalarials, beta blockers and others. Knowledge of drugs that can cause cutaneous ADR can help physicians in choosing safer drugs and therefore can be helpful to society at-large. However there is a lack of comprehensive data regarding it. The inadequacy of data could be attributed to reason such as diagnostic

dilemmas and lack of awareness to report. The prevalence, patterns of ACDR and their causative drugs vary greatly among the different populations previously studied in Europe, Israel, and Asia.[5,6,7,8,9,10,11,12] The epidemiological data based on intensive monitoring studies and analysis are limited for the cutaneous adverse drug reactions in India. Most of earlier Indian studies focused only on types and causative drugs of cutaneous drug reactions.[13] The aim of this study is also to analyse severity and causality of drug induced cutaneous reactions in Indian population. Only about 50% of drug reactions can be detected in the premarketing trials.[2] The Pharmacovigilance Programme of India was launched in 2010, and it operates through spontaneous reporting system to monitor ADRs. There are several advantages of this system in terms of being less cumbersome; generation of early safety signals about newer drugs, and identification of serious as well as rare ADRs.[14] So the present study is planned to generate more data by spontaneous reporting system and to analyse severity and causality of cutaneous ADRs.

MATERIALS AND METHODS

Study Design

It was a cross-sectional, observational, and non-interventional study.

Ethical Approval

The study protocol, permission letter from dermatology department, participant information sheet and informed consent form (in English and vernacular languages) were submitted and approved by the scientific review committee and human research and ethics committee of the Institution. IEC approval no. Permission/NCHS/505/2018 Dated 21/02/18.

Study Subjects and procedure

150 subjects (patients) were enrolled from dermatology department at tertiary care teaching hospital over period of 6 months after getting approval from ethics committee. Patients were selected after getting confirmation of cutaneous adverse drug reactions from clinician of dermatology department. Participant Information sheet was given to all the patients, written consent was taken and they enrolled for the study based on following criteria.

Inclusion criteria

1) Patients of either sex or age group attending skin OPD and wards.
2) Patients willing to give consent for the study.

Exclusion criteria

Patient not willing to participate.

Recognized and confirmed (by Skin & V.D. professional) cutaneous drug reaction details were filled in the Suspected Adverse Drug Reaction Reporting Form. Causality grading was done by using Naranjo's Algorithm Scale[15] and severity grading was done by using The Modified Hartwig And Siegel Scale.[16] The variety of skin manifestations and agents causing cutaneous drug reactions were also noted.

Statistical Analysis

Data were analysed using descriptive statistics and Microsoft excel.

RESULTS

Table 1: General characteristics of the patients.

Out of 150 patients, 78 male, 70 female and 2 paediatric patients confirmed with cutaneous drug reactions. There was not much difference found between male and female.

Study Population	Total(150)	Average Age in years
Male	78	45
Female	70	37
Paediatric	2	2

Table 2: Study Population affected (%) by Cutaneous Adverse Drug Reactions.

Study population affected (%) by Cutaneous Adverse Drug Reactions in this study was maximum with maculopapular rash(30.04%) followed by urticaria(21.79%), pruritus(15.32%), atopic dermatitis(8.76%), erythema multiforme(7.10%), fixed Drug eruption(7.01%), acneiform eruptions(3.70%), hyperpigmentation(3.56%), phototoxicity(2.70%) and steven johnson syndrome(0.02%).

Cutaneous Adverse Drug Reactions	Study Population affected (%)
Maculopapular rash	30.04
Urticaria	21.79
Pruritus	15.32
Atopic dermatitis	8.76
Erythema Multiforme	7.10
Fixed Drug Eruption	7.01
Acneiform Eruptions	3.70
Hyperpigmentation	3.56
Phototoxicity	2.70
Steven Johnson Syndrome	0.02

Table 3: Drug classes causing Cutaneous Adverse Drug Reactions.

Drug classes causing Cutaneous Adverse Drug Reactions were antimicrobial agents(50.02%), NSAIDs(29.12%), steroids(9.54%), anti-epileptic agents(3.01%), anti-retroviral agents(2.23%), acid suppressors(ranitidine, omeprazole)(1.69%), haematinics(0.08%) and others(4.31%).

Cutaneous Adverse Drug Reactions	Study Population affected (%)
Antimicrobial Agents	50.02
NSAIDs	29.12
Steroids	9.54
Anti-epileptic agents	3.01
Anti-retroviral agents	2.23
Acid suppressors(Ranitidine, omeprazole)	1.69
Haematinics	0.08
Others	4.31

Table 4: Causality grading by Naranjo's Algorithm Scale.

The causality assessment by Naranjo's Algorithm Scale shown in present study was probable category (60.14%), possible (36.98%), doubtful (2.87%) and definite(0.01%).

Causality Grading	Cutaneous Adverse Drug Reactions(%)
Definite	0.01
Probable	60.14
Possible	36.98
Doubtful	2.87

Table 5: Severity Assessment By The Modified Hartwig And Siegel Scale.

Study population showed moderate severe level 3(48.43%) followed by mild level 1 (34.63%), mild level 2(16.91%), moderate level 4 (0.02%) and severe level 5 (0.01%).

Severity Grading		Cutaneous Adverse Drug Reactions(%)
Mild	Level 1	34.63
	Level 2	16.91
Moderate	Level 3	48.43
	Level 4	0.02
Severe	Level 5	0.01
	Level 6	0
	Level 7	0

DISCUSSION

The introduction of many new drugs are successful and associated with potential benefits to patients but serious side-effect profile of the same is cumbersome for patients, healthcare professionals and the industry. Fitzgerald stated it truly, 'the safety of drugs is of paramount importance to patients and healthcare professionals'.[17] Adverse cutaneous drug reactions (ACDR) are the commonly reported type of ADR.[18] The pattern of cutaneous reactions and the drugs causing various reactions are changing continuously over the period of time due to introduction of newer drugs and changing trends in the use of drugs.[19] There is scarcity of such data in India which includes aspects like demographic details, type of cutaneous adverse drug reactions, pharmacological agents responsible for it, causality and severity assessment of reactions etc.

In our study, out of 150 patients, 78 male, 70 female and 2 paediatric patients confirmed with cutaneous drug reactions. There was no significant difference between males and females observed with CADRs which is in same line with the several studies previously conducted.[3,5,8,9,20,21] Both the genders were almost equally affected in one prospective study conducted previously.[22] High prevalence of ADRs has been found in elderly than nonelderly age groups in various systematic reviews.[23,24,25] Some study indicates that age groups do not modify the incidence of cutaneous reactions.[4] In our study majority of the study population were middle aged.

Study population affected (%) by Cutaneous Adverse Drug Reactions in this study was maximum with maculopapular rash(30.04%) followed by urticaria(21.79%), pruritus(15.32%), atopic dermatitis(8.76%), erythema multiforme(7.10%), fixed Drug eruption(7.01%), acneiform eruptions(3.70%), hyperpigmentation(3.56%), phototoxicity(2.70%) and Steven Johnson syndrome(0.02%). The study conducted previously showed the most commonly observed CADRs were maculopapular rash, urticaria, and FDEs in study population[4] which is the common observation found in indian population.

The major suspect groups were antimicrobials (45.46%), NSAIDs (20.87%), antiepileptics (14.57%) and corticosteroids (3.87%) in the previous study.[4] Drug classes causing Cutaneous Adverse Drug Reactions in our study were antimicrobial agents(50.02%), NSAIDs(29.12%), steroids(9.54%), anti-epileptic agents(3.01%), anti-retroviral agents(2.23%), acid suppressors(ranitidine, omeprazole) (1.69%), haematinics(0.08%) and others(4.31%). Most common drug group which caused cutaneous drug reactions was antimicrobials in 41.5% cases, followed by NSAIDs in 26.8% cases in previous study.[22] which is in the same line with our study. Other studies showed anti-microbial and antiepileptic drugs as commonly suspected groups.[3,19,26] In the present study, antiepileptic were at forth position.

The causality assessment by Naranjo's Algorithm Scale shown in present study was maximum fell in probable category (60.14%) followed by possible (36.98%), doubtful (2.87%) and only 0.01% were definite which showed similarity with previous study.[22] Majority of the studies cant established definite type of causal relationship of drug and adverse reaction as it needs careful history taking, examination, filling of ADR forms, follow up and re challenge status.

On evaluation of the severity of ADRs by Hartwig et al., scale it was evident that most of the ACDR reported in the study were of moderate severity in many studies including us.[27] In our study maximum study population showed moderate severe level 3(48.43%) followed by mild level 1 (34.63%), mild level 2(16.91%), moderate level 4 (0.02%) and severe level 5 (0.01%). We didn't record severity level 6 and level 7 cutaneous adverse drug reactions. The reason behind it is design of study as in long prospective study it is possible to record more and more severe forms of ADR s with prolong hospitalization, morbidity, mortality etc. Our study is a cross sectional study so there are less chances to record severity of level 6 and level 7.

Limitation

We have taken data from dermatology department only as per our study planning. So many cutaneous drug reactions from other departments were missed.

CONCLUSION

In our study we found maximum maculopapular rash in study population. The agents found culprit for highest contribution were antimicrobial agents showing concern of rational use of antimicrobials. Causality grading showed probable category maximum and severity grading showed moderate severe level 3 like many other similar studies. This result of the present study helps to health care professionals in policy making regarding rational use of drugs, rational prescription and adverse drug monitoring on regular basis.

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