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Original Research Article

A study on cutaneous adverse drug reactions in a tertiary care center in Rajnandgaon, Chattisgarh

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ABSTRACT

Background: Cutaneous reactions are one of the most common types of adverse drug reactions which may vary from mildly discomforting to those that are life-threatening.
Methods: This prospective, observational study was done in the department of dermatology. Patients with suspected drug rash, of either sex or all age groups were included in the study.
Results: A total of 114 patients were enrolled in the study. The most common presenting symptoms of cutaneous adverse drug reactions (CADRs) were itching, burning sensation and pigmentation with 61.31%, 13.87% and 10.22% respectively. A total of 21 different CADRs were observed. The common causative agents were of anti-microbial, nervous system and musculoskeletal class in both outdoor and indoor patients with 51 (37.22%), 21 (15.32%) and 25 (18.24%) respectively.
Conclusions: The most common CADR observed in the study was antimicrobials and NSAIDs were the most common causative drugs.

Keywords: Causative drugs, Cutaneous adverse drug reactions, Maculopapular rash, Antimicrobials

INTRODUCTION

Drug reactions are unwanted reactions that occur following the administration of drugs and are not characteristic of the desired pharmacodynamics effects of the drug.[1] Cutaneous reactions are one of the most common types of adverse drug reactions (ADRs).[2] Cutaneous ADRs (CADRs) may vary from mildly discomforting to those that are life-threatening.[3] They affect the patient in the form of prolonging or requiring hospitalization, systemic complications, mortality, and economic burden.[4,5] The disability such as blindness as a consequence of severe CADR could affect employment and quality of life.[6] Most of the reactions often are underreported, and many questions regarding the pathogenesis are yet to be addressed. Despite attempts at monitoring by the government and by the pharmaceutical industry, it is very difficult to obtain proper and detailed information about the incidence of drug reactions.

Cutaneous ADRs (CADRs) are common, comprising 10-30% of all reported ADRs and its incidence in hospitalized patients is estimated to be 2-3%.[2,7] They vary from localized and transient erythema to severe forms. The commonly reported CADRs are maculopapular rash, fixed drug eruptions (FDEs), and urticaria.[5] The wide range of pharmacology group of drugs can cause CADRs and its patterns could change due to different prescribing patterns, use of newer drugs, self-medications, and referral bias.[8,9] Serious CADRs endangering patient's life

are Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematouspustulosis (AGEP).[10] SJS has mortality rate <5%, whereas the rate for TEN approaches 20-30%.

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.[11] However, it is less reliable to estimate incidence and other clinical characteristics due to under-reporting. Prospective intensive monitoring can overcome these drawbacks and is also an important tool to identify the pattern and causative drugs of CADRs.

The common offending drugs are antimicrobials, non-steroidal anti-inflammatory drugs (NSAIDs), anti-epileptic drugs, and anti-gout agents. The morphology of drug-induced lesion gives us a clue for early identification of serious drug reaction, and hence, it is mandatory for a dermatologist or treating physician to pick up these early signs and prompt withdrawal of drug if possible. The purpose of the study was to identify the pattern of drug-induced cutaneous adverse reactions in patients and establish the causal link between the drug and reaction.

METHODS

This prospective, observational study was conducted at Department of Dermatology, Government Medical College, Rajnandgaon (C.G.), India. Patients with CADR for the study selected from outdoor (Department of Dermatology) and indoor (Department of Medicine, Surgery and Pediatrics). Most common pattern of reaction and offending drug(s) were identified.

Inclusion criteria

All subjects showing any signs and symptoms of drug reaction where taken for the study.

Exclusion criteria

Subjects on any long term illness or on long term medications were excluded.

Patients were clinically evaluated and recruited for the study if they fulfilled the inclusion and exclusion criteria and gave willing consent for participation. The study was commenced after acquiring clearance from the institutional ethics committee and conducted from January 2017 to December 2018 (2 years) at the patients not giving consent for the study, patients who developed drug reactions following intake of homeopathic, Ayurveda, and indigenous medicines were excluded from the study.

Confidentiality of the information obtained was assured throughout the study. Information of all the patients including relevant history, clinical examination details, and drug therapy were noted in the pretested proforma. List of drugs taken before the appearance of reaction, whether monotherapy or polytherapy, presenting complaints, period, duration of symptoms, severity, the reason for drug intake, history, and drug-involved were recorded. The WHO causality definitions were used to assess the suspected offending drug. It classifies ADRs into "certain," "probable," "possible," "unlikely," "unclassified," or "unclassifiable.

Data collection

A proforma was used to collect data of demography, diagnosis, investigations, adverse reactions, their clinical morphology, causative drugs with dosage, route, frequency, and duration of administration, lag period to develop reaction (period between administration of drugs and appearance of lesions), its treatment and cost, outcome, severity and concomitant medications. Data was recorded in MS Excel and checked for its completeness and correctness then it was analysed by using statistical methods.

RESULTS

Out of total 137 study subjects, 54.74% were males and 45.26% were females [Table 1].

Table 1: Incidence of cutaneous adverse drug reaction.

Gender	No.	%
Male	75	54.74
Female	62	45.26
Total	137	100

Table 2: Age distribution of the study subjects.

Age group (in years)	No.	%
<21	39	28.47
21-40	57	41.61
41-60	23	16.79
>60	18	13.14
Total	137	100.00

Table 3: Presenting symptoms of cutaneous adverse drug reactions.

Symptom	No.	%
Itching	84	61.31
Burning	19	13.87
Pigmentation	14	10.22
Erythema	13	9.49
Pain	11	8.03
Soreness	6	4.38

*Multiple responses.

Majority of the subjects were in the age group of 21-40 years followed by <21 years [Table 2].

The most common presenting symptoms of CADRs were itching, burning sensation and pigmentation with 61.31%, 13.87% and 10.22% respectively [Table 3].

A total of 21 different CADRs were observed. The most commonly observed CADRs were maculopapular rash 41 (29.93), urticarial 32 (23.36), and FDEs 20 (14.60) in both outdoor and indoor patients [Table 4].

Table 4: Frequency distribution of observed cutaneous adverse drug reactions.

Type of CADR	No.	%
Maculopapular rash	41	29.93
Urticaria	32	23.36
FDEs	20	14.60
EM	6	4.38
Urticaria with angioedema	7	5.11
Pruritus	6	4.38
Bullous FDEs	6	4.38
Stevens-Johnson syndrome	5	3.65
Angioedema	4	2.92
Acneiform eruption	4	2.92
Oral ulcer	3	2.19
Exfoliative dermatitis; bullous reactions; photosensitivity reaction	2	1.46
Palmoplantar exfoliation; local erythema; anaphylactic reaction; Cushing's syndrome; dapsone syndrome; DRESS; hyperpigmentation; lichenoid reaction	1	0.73

Table 5: Causative drugs of cutaneous adverse drug reactions.

Suspected drugs	No.	%
Anti-microbial for systemic use (fluoroquinolones, penicillin, cephalopsporins, sulfa)	51	37.22
Musculoskeletal system (NSAIDs)	25	18.24
Nervous system drugs (analgesics, antiepileptic drugs)	21	15.32
Antiparasitic products (nitroimidazole, antimalarial)	15	10.94
Alimentary tract and metabolism	19	13.86
Other drugs	11	8.02
Unknown	16	11.67

*****Multiple responses.

The common causative agents were of anti-microbial, nervous system and musculoskeletal class in both outdoor and indoor patients with 51 (37.22%), 21 (15.32%) and 25 (18.24%) respectively [Table 5].

DISCUSSION

In our study, 54.74% were male and 45.26% of females which is in accordance with the study done by Agrawal et al and Sharma et al.[12,13] Most of the patients in our study were in the age group of 21-40 years comprising 41.61% of the study population which was in accordance with a study done by Jha et al.[14] In the present study, patients <21 years of age contributed 28.47% and only 13.14% of patients were >60 years which correlates well with the study done by Jhaj et al.[15]

In our study, the most common presenting symptoms of CADRs were itching, burning sensation and pigmentation which was in accordance with the study done by Thakkar et al.[16]

In our study, 41 patients were of maculopapular rash (29.93%) followed by 32 patients of urticarial rash (23.36%) which was comparable to the study by Raksha et al.[17] This is in accordance with the study by Pudukadan et al who reported 31.1% of patients with FDE followed by maculopapular rash in 12.2%.[4] Anjaneyan et al in their study found 23% of cases due to FDE which was almost double to our study.[18] Radhika et al reported most common reaction as FDE in 36.67% of patients.[19]

In a study done by Thakkar et al, single drug was culprit in 110 cases. Anti-infective and musculoskeletal drugs were observed as a single causative agent in 27 (24.54%) and 20 (15.45%) cases, respectively, among which fluoroquinolones and diclofenac were most common.[16]

In our study, 37.22% of the total reactions were due to antimicrobials followed by 18.24% due to NSAIDs which was in accordance with the study by Patel et al.[5] In a study by Sharma et al the most common classes of drugs implicated were antimicrobials in 40% of patients followed by NSAIDS in 35.3%.[13] According to Nandha

et al antimicrobials were implicated as the major causative factor for CADR followed by NSAIDS.[20] Jhaj et al reported antimicrobials to be most frequently associated with cutaneous adverse events. Thus according to the various studies, the results inferred that a variety of drugs caused CADR.[15] Due to growing infections, the use of antibiotics has increased, leading to adverse reactions in almost all the studies quoted above. All drugs are capable of producing any type of reaction in susceptible individuals, but some drugs are more likely to induce certain reaction patterns, and this can also give a clue regarding the likely causative drug and prompt withdrawal. Beta-lactams and diclofenac were the most commonly implicated drugs causing urticaria, followed by fluoroquinolones and ibuprofen.

CONCLUSION

There is no gold standard investigation available for diagnosing CADR, but taking a proper history such as duration of drug intake, reaction time, response of drug eruption to withdrawal of the suspected drug and any past history of similar reactions can help in diagnosing CADRs. The risk of using drug should be carefully monitored. Awareness must be brought among people so that, the mortality and morbidity related to drug use is reduced. Patients should be educated to avoid self-medication of drugs to prevent dangerous or serious situation. ADR should be reported to the manufacturer and the regulator agency, especially if the skin eruption is rare, serious or unexpected. Prescribing a drug to a previously sensibiliser patient or prescribing a related medication with cross-reactivity are the most common medicolegal pitfalls, therefore should never be over-looked.

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