



Original Research Article

A prospective study of incidence and assessment of Adverse Cutaneous Drug Reactions as a part of Pharmacovigilance from a rural northern Indian medical school

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How to cite this article: Jai Krishna, G. Chitti Babu, Shewtank Goel, Abhishek Singh, Aakansha Gupta, Sanjeet Panesar, Avinash Surana, Deepak Pathania, Lalit Kumar Singh. A prospective study of incidence and assessment of Adverse Cutaneous Drug Reactions as a part of Pharmacovigilance from a rural northern Indian medical school. IAIM, 2015; 2(6): 108-115.

Available online at www.iaimjournal.com

Received on: 02-06-2015

Accepted on: 06-06-2015

Abstract

Background: The wide and indiscriminate use of drugs has increased the incidence and the modes of presentation of cutaneous drug reaction. Understanding the nature of ACDRs may help narrow down the search for the offending agent.



Aim- The study aimed to evaluate incidence, assessment of causality, severity and preventability of Adverse Cutaneous Drug Reactions as a part of Pharmacovigilance from a rural northern Indian medical school.

Material and methods: The current survey was executed by the department of Pharmacology in collaboration with Department of Dermatology, MSDS Medical College, Fatehgarh among 7692 patients attending Dermatology OPD during March-December 2014. CDSCO ADR Reporting Form, WHO causality assessment scale, Hartwig and Siegel's Assessment scale and Modified Schomock and Thronton's preventability assessment scale were used as study tools. All the doctors, residents, interns and students were encouraged to notify any suspected ACDRs. Patients were screened and recruited if they presented with visible skin lesions suspected to be drug related. As per Modified Schumock and Thornton Scale, 43.5% of ACDRs were 'Definitely preventable' followed by 'Probably preventable' (30.4%) and 'Not preventable' (26.1%).

Results: 23 patients (0.3%) were detected to have one or other type of ACDRs. Fixed drug eruption was most common form (34.8%) of ACDRs followed by Acneform eruption and Urticaria in 21.7% and 13% respectively among study subjects. The most common drugs responsible for ACDRs were prednisolone, betamethasone and isoniazid for Fixed drug eruption, while metronidazole, cotrimoxazole and paracetamol for acneform eruption. Antimicrobials, other steroids and NSAIDs were responsible for other spectrum of ACDRs. On assessment of Causality of ACDRs, it was noted that more than half (52.2%) of them fall under probable category. Severity assessment of ACDRs revealed that majority (65.3%) of them was moderate in nature.

Conclusion: Awareness on part of the physician can help in timely detection of cutaneous reactions, thereby restricting damage from them. Pharmacovigilance activity is significantly effective in increasing the reporting of ADRs. Study with long-term follow-up and monitoring of the patients with bigger sample size is warranted.

Key words

Adverse cutaneous drug reaction, Causality of Adverse Drug Reactions, Severity of ADR, Preventability of ADR, Pharmacovigilance.

Introduction

Drug eruptions are among the most common cutaneous disorders encountered by the dermatologist [1]. There is a wide spectrum of Adverse Cutaneous Drug Reactions (ACDRs) varying from transient maculopapular rash to fatal toxic epidermal necrolysis and acneform eruption. An ACDRs caused by a drug is any undesirable change in the structure or function of the skin, its appendages or mucous membranes and it encompasses all adverse events related to drug eruption, regardless of the etiology. Pharmacovigilance is "The Pharmacological science relating to the

detection, assessment, understanding and prevention of adverse effects, particularly long term and short term side effects of medicines [2]."

Development of medicine is never static and new drugs continue to be developed, there is potential for the occurrence of an increasing number of cutaneous drug reactions. True incidence of drug eruptions is difficult to determine, as mild and transitory reactions are often goes unrecorded. On the other hand, skin changes due to other etiology are sometimes incorrectly attributed to drugs. There are chances of adverse unexpected outcomes to

newly introduced drugs, causing inconvenience to both patients and physicians.

The wide and indiscriminate use of drugs has increased the incidence and the modes of presentation of cutaneous drug reaction [3]. Understanding the nature of ACDRs may help narrow down the search for the offending agent. There is paucity of data and literature regarding out-patient department on this particular aspect. The inadequacy of data is due to lack of awareness to report Adverse Drug Reaction (ADR). Therefore this study was conducted to evaluate incidence, assessment of causality, severity and preventability of Adverse Cutaneous Drug Reactions as a part of Pharmacovigilance from a rural northern Indian medical school.

Materials and methods

The current survey was planned and executed by the department of Pharmacology in collaboration with Department of Dermatology, MSDS Medical College, Fatehgarh among patients attending Dermatology OPD.

Study area: Out Patient Department of Dermatology, MSDS Medical College, Fatehgarh

Study population: Patients attending Dermatology OPD

Study design: Prospective study

Study period: March-December 2014

Sample size: 7692

Exclusion criteria

Subjects who complained of only symptoms without visible skin lesions, those who could not recall the name of the suspect medicines consumed, and those whose lesions turned out to be disease related on closer examination. A few subjects who reported to have taken indigenous (ayurvedic and homeopathic) medicines were also excluded.

Study tools

- **CDSCO ADR Reporting Form [4]:** 'CDSCO ADR Reporting Form' captured details like drug history and information like onset and nature of reaction, associated drugs and past history of similar or other allergic reactions. Incidence rate was calculated and the ACDRs were classified on the basis of age, sex and most common drug causing them.
- **WHO causality assessment scale [5]:** Causality assessment was done by WHO causality assessment scale, classifying ADR in to certain, probable, possible, unlikely, unclassified and unassessible. ACDRs reported under certain, probable and possible were included in study.
- **Hartwig and Siegel's Assessment scale [6]:** Severity assessment was done by modified Hartwig and Siegel's scale, which classifies severity of ADR as mild, moderate or severe based on factors like necessity of change in treatment, increased duration of hospital stay and disability produced by ADR.
- **Modified Schomock and Thronton's preventability assessment scale [7]:** Assessment of preventability was done by modified Schomock and Thronton scale. According to this scale detected ACDRs were categorised in to definitely preventable, probably preventable and not preventable.

Study strategy

All the doctors, residents, interns and students were encouraged to notify any suspected ACDRs by closely observing patients attending Dermatology out Patient Department by either telephonic direct reporting to the Dept. of Pharmacology. Patients were screened and recruited if they presented with visible skin lesions suspected to be drug related and provided written informed consent for inclusion.

Reporting was to be done during the study period on daily basis strictly according to 'CDSCO ADR Reporting Form' only. All the persons involved in this study were briefed about the variables of CDSCO ADR Reporting Form prior to commencement of the study. For quality assurance, findings were cross-checked by senior faculty member of the Dermatology department at the same time. Dept. of Pharmacology and Dept. of Dermatology were actively involved and shared their observations and reports on daily basis. Permission of Institutional ethics committee (IEC) was sought before the commencement of the study. Informed consent was obtained from the study participants.

All the proformas were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data in Microsoft Excel, analysis was done using Statistical Package for Social Sciences (SPSS), version 21 (IBM, Chicago, USA). The results were expressed using appropriate statistical variables.

Results

Out of 7692 patients attending the dermatology OPD during the study period 23 patients (0.3%) were detected to have one or other type of Adverse Cutaneous Drug Reactions. The most common age group affected was 20 -35 years with preponderance in male gender.

Fixed drug eruption was most common form (34.8%) of ACDRs followed by Acneform eruption and Urticaria in 21.7% and 13% respectively among study subjects. The most common drugs responsible for ACDRs were prednisolone, betamethasone and isoniazid for Fixed drug eruption, while metronidazole, cotrimoxazole and paracetamol for acneform eruption. Antimicrobials, other steroids and

NSAIDs were responsible for other spectrum of ACDRs. (Table - 1)

On assessment of Causality of Adverse Cutaneous Drug Reactions, it was noted that more than half (52.2%) of them fall under probable category. Certain ACDRs were 30.4%. (Table - 2)

Severity assessment of Adverse Cutaneous Drug Reactions revealed that majority (65.3%) of them was moderate in nature. (Table - 3)

As per Modified Schumock and Thornton Scale, 43.5% of Adverse Cutaneous Drug Reactions were 'Definitely preventable' followed by 'Probably preventable' (30.4%) and 'Not preventable' (26.1%). (Figure - 1)

Discussion

The current study was planned with an approach to reveal pattern of ACDRs with simultaneous vision of establishing impact of Pharmacovigilance activity in our tertiary care centre. The incidence of ACDRs reported was 0.3%. This is lower than the figures reported in earlier Indian studies, such as those by Chatterjee, et al. (26 per 1000) and Ghosh, et al. (285 per 1000) [8, 9].

A probable reason for lower incidence rate could be better drug prescribing method or still lack of awareness regarding ADR reporting. Another probable explanation for this low incidence rate could be, the study was conducted in a tertiary center, so minor rashes may not have come to the dermatology OPD or patients could have been treated by physicians in other disciplines. Furthermore, certain excluded patients from the final evaluation in spite of having recognizable features of CADR, largely because they failed to state the names of the offending drugs or took indigenous medicines with non-declared or non-identifiable active ingredients. Another



significant factor for lower incidence rate was no patient of ACDRs caused by antiretroviral drugs because the department that provides antiretroviral therapy managed skin reactions on their own without referral to the dermatology department.

Another study from south India [10] revealed that most common age group was 20-39 years followed by 40-59 years with higher incidence in female (M:F = 0.87:1), similarly in our study most common age group was 20-35 years but with male preponderance, However another study from Chandigarh have reported the high male female ratio [11].

Regarding clinical spectrum of ACDRs, Fixed drug eruption was most common form (34.8%) of ACDRs followed by Acneform eruption and Urticaria in 21.7% and 13% respectively. Others have noted maculopapular rash and FDE as the most common ACDRs [8, 9]. Antimalarials and fluoroquinolones were the most common drugs responsible for FDE, which has already been reported [12]. A review from Pakistan had documented sulfonamides and tetracycline as the most common causative agent [13].

It was observed in the current study that steroids and anti-tubercular drugs were responsible for acneform eruption. Causative agents for SJ syndrome in this study were antipsychotics. The result of this study is in agreement with previous study by Noel MV and Nayak S [1, 14]. Other causative agents for ACDRs revealed by this study were antimicrobials, steroids and NSAIDs, which is in concordance to results of other studies [15, 16].

Causality assessment revealed 30.4% were certain, 52.2% were probable and 17.4% were possible which was comparable to Chatterjee, et al. [8]. Hartwig severity assessment showed 4.3% of total reported ACDRs were severe.

Importantly, in this study preventability assessment was done by modified Schomock and Thronton scale which was lacking in other studies done on ACDRs.

Assessment of Adverse Cutaneous Drug Reactions as a part of Pharmacovigilance was taken up in a rural northern Indian medical college is strength of this study. A constant check on quality reporting is another favorable aspect of this survey. On the other hand, this study centre caters primarily to a lower socioeconomic stratum therefore exposure to most newer drugs was limited in our study population. This is one most evident limitation of current survey.

Conclusion

Fixed drug eruption and acneform eruption were the most frequently observed ACDRs. Most common drugs responsible were corticosteroids, isoniazid, rifampicin, metronidazole, fluoroquinolone and antimalarial drugs. Awareness on part of the physician can help in timely detection of cutaneous reactions, thereby restricting damage from them. Pharmacovigilance activity is significantly effective in increasing the reporting of ADRs. Study with long-term follow-up and monitoring of the patients with bigger sample size is warranted.

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Source of support: Nil

Conflict of interest: None declared.

Table - 1: Profile of Adverse Cutaneous Drug Reactions detected among study subjects.

Type of Adverse Cutaneous Drug Reactions*	Number of patients	Drugs Responsible
Fixed drug eruption	8	Prednisolone, Betamethasone, Chlorpromazine, Clobetasol, Isoniazid, tinidazole
Acneform eruption	5	Cotrimoxazole, Diclofenac, Metronidazole, Mefenemic acid, Paracetamol, Quinine, Levofloxacin
Urticaria	3	Aceclofenac, Cephalosporin, Paracetamol, Propofol, Multivitamin, ramipril
SJ syndrome	2	Ciprofloxacin, Septran, Ofloxacin, Allopurinol
Bullous eruption	2	Carbamazepine, Furosemide, Ibuprofen, Diclofenac
Maculopapular rash	2	Ofloxacin, Isoniazid, Levofloxacin
Eczematous drug eruption	1	Indomethacin, Sparfloxacin, Betamethasone
Hypertrichosis	1	Betamethasone
Swelling of lips	2	Ceftriaxone, Carbamazepine
Acne rosacea	1	Clobetasol
Vesicular eruption	1	Azithromycin, Levofloxacin
Hypo-pigmentation	2	Betamethasone, Chlorpromazine
Pellagrous dermatitis	1	Isoniazid
*More than one type of Adverse Cutaneous Drug Reactions were noted		

Table - 2: Assessment of Causality of ACDRs detected using 'WHO causality assessment scale' among study subjects.

Assessment	Category	No. of ADRs	Percentage
Causality	Certain	7	30.4%
	Probable	12	52.2%
	Possible	4	17.4%

Table - 3: Assessment of Severity of ACDRs detected using 'Hartwig and Siegel's Assessment scale' among study subjects.

Assessment	Category	No. of ADRs	Percentage
Severity	Mild	7	30.4%
	Moderate	15	65.3%
	Severe	1	4.3%

Fig. 1- Pie diagram showing Preventability of ACDRs by Modified Schumock and Thornton Scale (n=23)

