International Journal of Basic & Clinical Pharmacology
Gupta D et al. Int J Basic Clin Pharmacol. 2021 Jun;10(6):664-667
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20212075

Original Research Article

A study and evaluation of cutaneous adverse drug reaction in the patients attending dermatology department of tertiary care teaching hospital in Eastern Uttar Pradesh

Dharmender Gupta, Bikash Gairola*, Bijay Kumar, Masuram Bharath, Mohd Shadab Ansari

Department of Pharmacology, Varun Arjun Medical College, Shahjahanpur, Uttar Pradesh, India

Received: 02 April 2021
Revised: 30 April 2021
Accepted: 01 May 2021

***Correspondence:**
Dr. Bikash Gairola,
Email: drbikashgairola@gmail.com

ABSTRACT

Background: Cutaneous adverse drug reactions (CADRs) are most frequently reported type of ADRs and can be caused by variety of drugs. The clinical patterns of adverse cutaneous drug reactions and the drug responsible for them is changing every year due to the emergence of newer molecules and changing trends in the use of drugs.
Methods: This was a prospective, cross-sectional and observational study done for a period of 6 months to evaluate the clinical pattern of CADRs and their causative drugs in the tertiary health care.
Results: Over all 55 patients were detected with cutaneous adverse drug reaction. The majority of CADRs were in the age group of 18-35 years (63.46%). Fixed drug eruptions (FDE) being the most common adverse cutaneous drug reaction (34.68%) followed by maculopapular rash (23%), NSAIDs being the most common, followed by antimicrobial agents.
Conclusions: Knowledge of these drug eruptions, the causative drugs are essential for the clinicians and implementing the ADRs reporting and monitoring system, one can promote drug safety and better patients care, among health care professionals.

Keywords: Cutaneous adverse drug reaction, NSAIDs, VAMCRH, FDE

INTRODUCTION

As defined by WHO, ADR is a response to a drug that is noxious and unintended and occurs at doses, used in man for prophylaxis, diagnosis or therapy of a disease or for modification of physiological functions.[1] ADRs are claimed to be the fourth leading cause of death highest than pulmonary disease, AIDS, accidents and automobiles death. The growing number of newly approved drugs coupled with the complex treatment modalities have contributed to an increased risk of ADRs. Pharmacovigilance is usable in educating doctors about ADRs and in the authorized regulation of drug use. Its main motive is to reduce the risk of drug related loss to the patients. Cutaneous ADRs being most common in present time, are thought to occur up to 3% of medical in patients.[2] CADRs are a frequent and challenging clinical issue in our daily practice in dermatology, involving complex and incompletely understood pathophysiology and manifest under different clinical patterns varying from mild to severe life-threatening CADRs.[3] CADRs can mimic skin diseases like lichen planus, psoriasis, lupus erythematosus

or phemphigus vulgaris, which usually are not drug induced. The time course of the different CADRs is also very variable occurring within minutes, hours, days, weeks or even months after drug administration and lasting about a few hours to weeks, months or years. Moreover, virtually any drug can induce CADRs, of several clinical patterns and there is no universal test to confirm drug hypersensitivity.

METHODS

This study was done by department of pharmacology in collaboration with department of dermatology in the patients attending the VAMC and RH, dermatology OPD, covering the population in Eastern UP, India from November 2020 to March 2021 (6 months). This was a prospective, cross-sectional and observational study was approved by the ethics committee of the institute. Demographic data such as patients, age, gender, occupation were recorded along with the diagnosis. The diagnosis of CADRs was based on examination done by consultant dermatologist. The patient who consumed medicine other than allopathic medications (like ayurvedic/homeopathic) and who are not able to recall the name of suspected medicine consumed (improper drug history) were excluded from the study. Detailed history of the patients including present illness and past or concurrent systemic illness were also taken.

The criteria for the diagnosis of ACDRs were as follows.[4] The time interval between the introduction of the drug and the onset of a reaction should be within a specific time maculopapular rash <7 days, urticaria 7-21 days, Steven Johnson syndrome/toxic epidermal necrosis (SJS/TEN) and erythema multiforme 1-3 weeks, drug hypersensitivity syndrome 2-6 weeks, photodermatitis up to 1 year, exfoliative dermatitis 1-6 weeks, FDE 30 min-16 hours; improvement is the condition of the patient after de-challenge/withdrawal of the suspected drug; drug rechallenges producing similar reaction again.

To establish the etiological agents for ACDRs, attention was paid to the drug history, temporal correlation with the drug, duration of the rash, pattern of lesion, improvement of lesion on withdrawal of drug and recurrence of lesion on re-challenge if possible. Re-challenge was not undertaken in any of our cases because of the possible associated risks. If more than one drug was thought to be responsible, the most likely offending agent was noted and the impression was confirmed by subsidence of the reaction with time or on withdrawing the drug. Finally, data was recorded in CDSCO form and was compiled and analysed.[5] According to the WHO causality definition ADRs were categorized as certain, probable, possible and unlikely.

Statistical methods

As the sample size was too small therefore result was concluded on microsoft excel and was expressed as percentage values.

RESULTS

In our study 52 patients were included after applying inclusion and exclusion criteria. The mean age of the patients developing CADRs was 39.36±16.77 (range 2-70 years). A majority of patients were in the age group of 21-40 years. Males accounted for 44.23% (23) of CADRs and females accounted for 55.76% (29). The male and female ratio was 0.79:1. Age and gender wise distribution of patients reporting with CADRs is summarized in Table 1. FDE being the commonest CADR accounting for 34.68% (18) followed by maculopapular rash 23.0% (12), SJS/TEN 11.56% (6), acneform eruption 11.5% (6), urticaria 8.38% (4), erythema multiforme 7% (4) and less common pattern are hyperpigmentation (3.88%). The most common drugs responsible for CADR in prospective study were metronidazole, paracetamol and levofloxacin for FDE, while diclofenac and levofloxacin for maculopapular rash. Antimicrobial 32.69% (24) other NSAID 50% (20) and steroid were responsible for other various CADRs (Table 2). According to WHO causality assessment 13 were certain (25.23%), 30 were probable (57.69%) and 10 were possible (9%) in nature. On severity assessment by modified Hartwig and Siegel`s scale, out 52 CADRs 8 (16.08%) were mild 42(80%) were moderate and 2 (3.84%) were severe.

Table 1: Age and sex wise distribution of patients who developed CADRs in prospective study.

Age group (in years)	Male	Female	Total	Percentage (%)
1-17	05	06	11	21.15
18-35	15	18	33	63.46
36-53	03	05	08	15.38
54-71	00	00	00	00
Total	23	29	52	100

Table 2: Drug responsible for CADRs in prospective study (n=52).

Type of reactions	Number of patients	Percentage of patients (%)	Drug`s (group) responsible
Fixed drug eruption	18	34.68	Antimicrobial (10)
			NSAIDs (8)

Continued.

Type of reactions	Number of patients	Percentage of patients (%)	Drug`s (group) responsible
Maculopapular rash	12	23.0	NSAIDs (6) Antimicrobials (4) Antiepileptic (2)
Acne-form eruption	06	11.50	Steroid (4) Antimicrobial (2)
SJS/TEN syndrome	06	11.56	NSAIDs (4) Antimicrobial (2)
Erythema multiforme	4	7.0	Antimicrobial (2) NSAIDs (2)
Urticaria	4	8.38	NSAIDs (2) Antibiotic (1) Anaesthetics (1)
Hyperpigmentation	2	3.88	Antileprotics (1) NSAIDs (1)

Table 3: Drug responsible for CADRs.

Drugs	Number of patients	Percentage (%)
Antimicrobial	17	32.69
NSAIDs	26	50
Antiepileptic	4	7.69
Steroids	3	5.76
Others	2	3.84

DISCUSSION

In our study CADRs with higher incidence in adult age group between 21-40 years (63.46%) CADRs and in previous studies higher CADRs reported of 21- 35 years.[6,7] There were 29 (55.76%) females and 23 (44.23%) males in our studies. Female cases were already reported in many studies.[8-10] In our study conducted for duration of 12 months, CADRs were most commonly observed with NSAIDs (50%) in our study. NSAIDs were the main age group of drugs (42.6%) to cause various types of drug induced reaction in previous study, supporting our study.[6] In our study sulphonamide, fluroquinolones and penicillin were the main antibiotic to cause CADRs. Similar to this previous study reported that sulphonamides, penicillins and quinolones were found to be the major cause of CADRs.[6] In our study SJS (3 cases) and FDE (2 cases) with cotrimoxazole and EM (2 cases) with sulphadiazine. Three (3) patients on ofloxacin developed maculopapular reaction in our study. 2 patients on furazolidone produce FDE in our study which may be due to structural similarity to sulphonamides. Sulphonamide have been noticed to develop EM, exofoliative dermatitis and SJS supporting our study.[11-14] Among fluroquinolones ciprofloxacin produced SJS (2 cases) and ofloxacin EM (1 case) and ofloxacin maculopapular reaction (3 cases) in our study. Doxycycline produce hyperpigmentation. Photosensitivity, hypersensitivity reactions, erythema multiforme, FDE and several skin reactions have been reported with fluoro-quinolones by several authors.[15-17] Mostly CADRs were found in newer drug like cephalosporines and fluroquinolones when compared to the reports of previous studies with older antibiotics.[7]

In other studies, incidence of CADRs with NSAIDs were 21%, 35%, 30% and 38% respectively.[7,8,11] The most common reaction were purpose, macula papular eruption and FDE and common drug were ibuprofen and acetaminophen.[7,11,18,19] In our study incidence of CADRs with NSAIDs were (n=32.69) which occurred with nimesulide (3 cases) and diclofenac sodium (2 cases). Drug involved in CADRs were antiepileptics and the incidence was n=7.69 in our study. In other studies, the incidence was reported as 23.8% and 25% respectively which was higher than our study.[7,8] We observed maculopapular rash (1 case) with phenytoin sodium in our study. Similarly, several studies had shown that SJS, FDE and DHS (drug hypersensitivity syndrome) were the main CADRs seen with phenytoin sodium.[7,17,20] We got ADRs only with phenytoin sodium, whereas other studies reported ADRs with phenytoin as well as with carbamazepine.[7,14,17] In our study according to Naranjo`s causality scale, 3 ADRs (n=5.76) were definite, 38 ADRs (n=73.07) were probable and 11 ADRs (n=21.15) were possible. The study of Guwahati by Lihite et al showed higher cases of probable ADRs similar to our study.

Limitations

As this study sample size was very small in size due to limited OPD in coronal pandemic therefore these resets cannot be applied on general population for which bigger

sample size and probably multicentre study should be done.

CONCLUSION

It was concluded from our study that dermatological ADR was a common occurrence and awareness for them is essential for diagnosis and prevention. The dermatological ADRs varied in their appearance, duration, causality, severity and preventability. NSAIDs and antimicrobial agents were the most common implicated drug class. NSAIDs group diclofenac, aceclofenac and nimesulide were most commonly responsible drug for produce CADRs. Antimicrobial group such as fluroquinolones and ciprofloxacin were the most common drugs for produce CADRs. Depending upon nature of ADRs, actions against suspected drug along with symptomatic treatment were given whenever found significant. Most of ADRs gets unreported due to lack of interest in ADRs monitoring and reporting at hospital settings. By present piece of work, pharmacist contributed patient's safety and rational use of drug by assessing, reporting and treating ADRs. Causality assessment also resulted in high score of probable categories. The healthcare system should promote the spontaneous reporting of dermatological adverse drug reaction to pharmacovigilance centres for ensuring drug safety. ADRs study will provide useful information of adverse cutaneous drug reaction to the existing information of CADRs.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Edwards RI, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. Lancet. 2000;356(9237):1255-9.
2. Raksha MP, Marfatia YS. Clinical study of cutaneous drug eruptions in 200 patients. Indian J Dermatol Vereal Leprol. 2008;74(1):80.
3. Roujeau JC, Stern RS. Severe adverse cutaneous reaction to drugs N Engl J Med. 1994;331(19):1272-85.
4. Noel MV, Sushma M, Guido S. Cutaneous adverse drug reaction in hospitalized patients in tertiary care centre. Indian J Pharmacol. 2004;36(5):292-5.
5. Central Drugs Standard Control Organisation. Fact sheet: Adverse drug reaction reporting form. Available at: https://cdsco.gov.in›Pdf-documents›ADRRF_2. Accessed on 19 March 2021.
6. Smidt NA, McQueen EG. Adverse reactions to drugs: a comprehensive hospital in-patient survey. NZ Med J. 1972;76(487):397-401.
7. InamdarAC, Palit A. Serious cutaneous adverse drug reactions: pathomechanisms and their implications to treatment. Indian J Dermatol Venereol Leprol. 2003;69(3):205-8 .
8. Swarte RD. Drug allergy-problems and strategies. J Allergy Clin Immunol. 1984;74:209-24.
9. Naldi L, Conforti A, Venegoni M, Trancon MG, Caputi A, Ghiotto E, et al. Cutaneous reactions to drugs: an analysis of spontaneous reports in four Italian regions. Br J Clin Pharmacol, 1999;48(6)839-46.
10. Abebe W. Herbal medication: potential for adverse interactions with analgesic drugs. J Clin Pharmacy Ther. 2002;27:391-401.
11. Stephens MDB. The diagnosis of adverse medical events associated with drug treatment. Adverse Drug React Acute Poisoning Rev. 1987;6(1):1-35.
12. Lanctot KL, Naranjo CA. Computer-assisted evaluation of adverse events using a Bayesian approach. J Clin Pharmacol. 1994;34(2):142-7.
13. CA Naranjo, U Busto. et.al A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45.
14. Sharma VK, Sethuraman G, Kumar B. Cutaneous adverse drug reactions: clinical pattern and causative agents-a 6 year series from Chandigarh, India-brief report. J Post Grad Med. 2001;47(2):95-9.
15. Sushma M, Noel MV, Ritika MC, James J, Guidos. Cutaneous adverse drug reactions: a 9-year study from a South Indian hospital. Pharmaco Epidemiol Drug Safety. 2005;14(8):567-70.
16. Tran C, Knowless SR, Liu BA, Shear NH. Gender differences in adverse drug reactions. J clin Pharmacol. 1998;38(11):1003-9.
17. Modi A, Desai M, Shah S, Shah B. Analysis of cutaneous adverse drug reactions reported at the regional adr monitoring center. Indian J Dermatol. 2019;64(3):250.
18. Kelkar PS, Li JT. Cephalosporin allergy-review. N Eng J Med. 2001;345(11):804-9.
19. Ding WY, Lee CK. Cutaneous adverse drug reactions seen in a tertiary hospital in Johor, Malaysia. Int J Dermatol. 2010;49(7):834-41.
20. Gimnig JE, MacArthur JR, M'bang'ombe M, Kramer MH, Chizani N, Stern RS, et al. Severe cutaneous reactions to sulfadoxine-pyrimethamine and trimethoprim-sulfamethoxazole in Blantyre district, Malawi. Am J Trop Med Hyg. 2006;74(5):738-43.

Cite this article as: Gupta D, Gairola B, Kumar B, Bharath M, Ansari MS. A study and evaluation of cutaneous adverse drug reaction in the patients attending dermatology department of tertiary care teaching hospital in Eastern Uttar Pradesh. Int J Basic Clin Pharmacol 2021;10:664-7.