Original article

Prevalence and types of cutaneous drug reactions in two institutes

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Abstract

Introduction: Adverse drug reaction is one of the growing concerns of today's health practice. The purpose of the study was to find out the prevalence and types of cutaneous drug reactions at Tribhuvan University Teaching Hospital (TUTH) and DI Skin Hospital and Research Centre.

Methods: It was a prospective, cross sectional study conducted at Department of Dermatology of TUTH and DI Skin Hospital and Research Centre from 14th April 2010 to 14th October 2010. All the suspected cases of cutaneous drug reaction above 14 years were included. Naranjo Algorithm was used to establish the causality and Modified Hartwig and Siegel Scale was used to access the severity of the cutaneous drug reaction. Clear purpose of the study was described and a patient consent form was produced before them while collecting the data and ethically approved from Institutional Review Board, Institute of Medicine.

Results: Prevalence of cutaneous drug reaction was found to be 0.258%. The male: female ratio was 2.1:1. The highest percentage of CDR was seen in 15-34 years age group. Antibiotics were the group of drug involved in most CDR followed by anticonvulsant. Phenytoin, ibuprofen+paracetamol combination and betamethasone were mostly associated with CDR. 51.61% of the cases were of moderate III rd level which was followed by moderate IV (b) level. 51.62% were assessed to be probable and 48.38% were possible. Out of 13 admitted cases, 6 cases were admitted for 7-9 days. Maculopapular rash was the most common clinical presentation observed followed by Steven's Johnson Syndrome.

Conclusion: The study estimated the average rate of cutaneous drug reaction in two major hospitals of Nepal. It also determined the most common type of manifestation of the cutaneous drug reaction.

Key words: Cutaneous drug reaction, DI Skin Hospital, prevalence, Tribhuvan University Teaching Hospital.

Introduction

The wonders of pharmacology are numerous. However, medications are a double-edged sword. All drugs have adverse effects and carry the potential of causing injury, even if used properly.

Adverse drug reaction (ADR) is defined by WHO as 'any noxious, unintended and undesired effect of a drug which occurs at doses used in humans for prophylaxis, diagnosis or therapy'.[1]

Skin is the outer protective layer of the body. An intact skin is essential for the life and well being of human beings. The adverse drug reaction manifested in the skin is known as the Cutaneous Drug Reactions (CDR). The skin and the mucosa are the commonest sites for initial presentation of many adverse drug reactions. Adverse Drug Reactions is a

disease due to treatment. Prompt recognition of severe reactions, right drug withdrawal, and appropriate therapeutic interventions can minimize toxicity.

Adverse drug reaction has been reported to occur in 10%-20% of hospitalized patients with cutaneous eruptions occurring in 2%-3% of the cases.[2]

In addition to their human costs, ADRs are expensive to the health-care system. Two studies conducted independently arrived at estimates of about $2000 per event. Preventable events were even more costly, approximately $4500 per event.[3]

Method

This was a prospective, cross sectional study conducted in Dermatology Department of Tribhuvan University Teaching Hospital and DI Skin Hospital and Research Centre over the period of six months (from 14th April 2010 to 14th October 2010). It included all the patients above 14 years of age with the suspected cases of cutaneous drug reactions in Dermatology Department of TUTH and DI Skin Hospital and Research Center.

An ADR reporting form designed using the reference of ADR reporting form of Department of Drug Administration, TUTH and KIST Medical College was used to collect the information. Naranjo Algorithm[4] was used to establish the causality while Modified Hartwig and Siegel scale[5] was used to categorize the cutaneous drug reactions into different levels of severity. The data were collected with the help of patients and their relatives in the hospital ward. The study used interview and observation methods for data collection. The interview was conducted with the admitted and out patient (OPD patients) on the basis of the ADR reporting form while observation of treatment was done using cardex and record files. All the patients were followed up till in wards and outcome was documented.

The clear purpose of the study was described before interviewing the patients. Social and cultural values were respected and information was collected under condition of assumed anonymity and confidentiality. Besides, a patient consent form was produced while collecting the data and ethical approval was taken from Institutional Review Board, Institute of Medicine.

To each patient, fulfilling the criteria for selection of the study was given a case number. Similarly, name, age, gender, address, to the patients, and date of attending the Dermatology Department were recorded. After collecting the data, the variables were classified and tabulated. Similarly, data analysis and interpretation were done.

Result

Out of 11,984 cases observed in the Dermatology Department of TUTH and DI Skin Hospital and Research Center during the data collection period, 31 cases were cutaneous drug reaction cases. Hence, the prevalence was 0.258 %

Out of 11,984 cases meeting the criteria, 9984 cases were observed in Dermatology Department of TUTH and 2000 cases were observed in DI Skin Hospital and Research Center. Out of 31 CDR cases, 24 CDR cases were from Dermatology Department of TUTH of which, 13 cases (41.93%) were admitted and 11 cases were OPD patients. 7 cases were obtained from DI Skin Hospital and Research Center. There were no admitted cases at DI Skin Hospital and Research Center during the study period.

68% (21 cases) of the cutaneous drug reaction were observed in male while only 32% (10 cases) of cutaneous drug reaction were observed in female in this study. The male to female ratio was found to be 2.1:1.

Fig. 1: Overall cases by gender

38.70% (12 cases) were observed in patients of age group (15-24) years and was the most common age group having the cutaneous drug reaction.

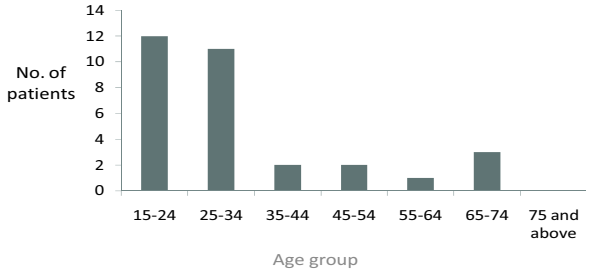

Fig. 2: Age distribution of the cutaneous drug reactions

Only one case (3.22%) was found to be severe. Most of the cases (16 cases) were found to be of moderate III level which is 51.61% followed by moderate IV (b) level (14 cases) which is 45.61% as per modified Hartwig and Siegel scale.

Fig. 3: Severity assessment of the cutaneous drug reactions

Phenytoin, paracetamol + ibuprofen, and betamethasone were found to be the drug most frequently associated with cutaneous drug reactions in the study. Betamethasone, clobetasone, fluconazole and terbinafine were used topically while other drugs were used systemically.

Table 1: Individual drug involved in the cutaneous drug reactions

	Individual drugs	Number of cases	Percentage
1.	Phenytoin	3	9.67
2.	Ibuprofen + paracetamol	3	9.67
3.	Betamethasone	3	9.67
4.	Ciprofloxacin	2	6.45
5.	Dapsone	2	6.45
6.	Amoxycillin	2	6.45
7.	Clobetosone	2	6.45
8.	Fluconazole	2	6.45
9.	Carbamazepine	2	6.45
10.	Allopurinol	1	3.22
11.	Ofloxacin	1	3.22
12.	Terbinafine	1	3.22
13.	Lamotrigine	1	3.22
14.	Ceftrioxone	1	3.22
15.	Tinidazole	1	3.22
16.	Lithium + sodium valporate	1	3.22
17.	Anti TB regimen	1	3.22
18.	Ayruvedic	1	3.22
19.	Unidentified	1	3.22
	Total	31	100.00

Maculopapular rash was the most common clinical presentation observed in 11 cases (35.58%) during the study period.

Table 2: Clinical presentation of cutaneous drug reactions

Clinical presentation	Number of cases	Percentage
1. Erythema multiforme (maculopapular rashes)	11	35.58
2. Stevens Johnson's syndrome	8	25.80
3. Erythema + atrophy	4	12.90
4. Urticaria	3	9.60
5. Fixed drug eruption	1	3.22
6. Angioedema	1	3.22
7. Exfoliative dermatitis	1	3.22
8. Dapsone hypersensitivity	1	3.22
Total	1	100.00

There were altogether 13 admitted cases. Out of them, most of the cases (46.15%) were admitted for 7-9 days.

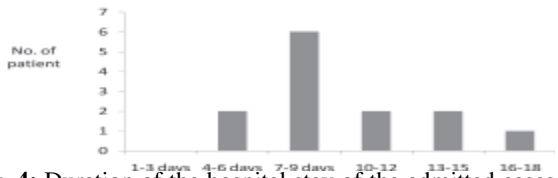

Fig. 4: Duration of the hospital stay of the admitted cases due to the cutaneous drug reaction

Antibiotics (32.23%) were the most common group of drug involved in the cutaneous drug reaction followed by anticonvulsant drugs (19.35%) and corticosteroid (16.12%).

Table 3: Group of drug involved in the cutaneous drug reactions

Group of drug	Number of cases	Percentage
1. Antibiotic	10	32.23
2. Anticonvulsant	6	19.35
3. Corticosteroid	5	16.12
4. NSAIDS	3	9.6
5. Antifungal	3	9.6
6. Antipsychotic	1	3.2
7. anti rheumatoid	1	3.2
8. Ayurvedic	1	3.2
9. Unidentified	1	3.2
Total	31	100.00

16 cases (51.61%) were assessed to be probable and 15 cases (48.38%) were assessed possible according to the Naranjo algorithm.

Discussion

In the study, number of cases of male cutaneous drug reaction was found more than female cutaneous drug reaction. The female: male ratio was found to be 1: 2.1. This result is different from other studies. One of the studies had female: male of 1.8: 1.[6] However, a study from the western Nepal showed that the ratio was 1: 1.2.[7] There are periods in females when there is alteration of pharmacokinetics of drugs: menarche, pregnancy, lactation and menopause. This might be the reason why women may be at higher risk than men for experiencing drug reactions.[8]

The study showed the highest reports of cutaneous drug reactions to be in the age group 15-34 years. In a study in a South Indian hospital, the majority of patients experiencing cutaneous ADRs were in the age group 21–40 years.[9] Another study in a tertiary care center in South India identified the age group 20–39 years as being more predisposed to cutaneous ADRs. [10]The results of these studies are more or less in agreement with our study.

In this study, antibiotics were implicated for majority of the cutaneous drug reactions (32.20%) and antiepileptics were implicated for the second major cause of cutaneous drug reactions (19.35%). In the study by Pudukadan et al., the main drug group implemented for cutaneous drug reactions was also antibiotics.[10] This was also seen in the study by Fiszensin-Albala et al. [11] However, a study by Noel et al. [12] implicated antiepileptics as the major cause of cutaneous ADRs followed by antibiotics. Another study by Ramesh et al.[13] reported cardiovascular drugs to be the most commonly implicated drugs (18.3%). However, this study included all types of ADRs and not just the cutaneous drug reactions. Understanding the major class of drugs leading to ADRs will be a potent tool in prevention and early diagnosis of ADRs. It also helps the clinician to counsel the vulnerable patients regarding the possibility of ADRs.

Maculopapular rash (35.58%) was the most common type of cutaneous ADRs encountered in this study followed by Stevens Johnsons Syndrome (25.80%). This result is in conformity with the studies by Sushma et al.[9] and Puavilai et. al.[6] In the study by Fiszensin-Albala and colleagues, however, exanthematous was the principal cutaneous reaction.[11] In an Italian study the most frequent serious reaction was angioedema. [14]

The majority (51.61%) of the cutaneous ADRs in this study were found to have a probable association with the suspected drug/s as per the Naranjo algorithm. In a retrospective study by Sushma et al., 95% of the diagnosed cutaneous ADRs had certain or probable causal association with the drugs implicated.[9] Establishing the causality helps the clinician to conclude that a particular drug has caused an ADR. Based on this the treating clinician can stop, withhold, reduce the dose or change the suspected drug causing the adverse drug reactions.In this study, majority (51.61%) of the reported cutaneous drug reactions were classified as moderate (level 3) as per the modified Hartwig and Siegel scale. In a study in Iran to assess the factors associated with preventability, predictability, and severity of ADRs, 86.3% of the reported ADRs were also classified as moderate.[15] Establishing the severity is very much essential in pharmacovigilance studies as the management pattern of the ADRs including the hospitalization is mainly based on the severity of an ADR. Moreover, severe ADRs require special attention by the clinician and may require an emergency intervention.

Out of the thirteen admitted cases, majority (46.15%) of the cases were admitted for 7-9 days. In a study conducted by P. Mishra et al. the majority (36.84%) of patients required an average of 6 to 10 days of the treatment for the reported cutaneous ADRs.[16] Again, since no similar study could be found, this result also could not be compared.

Conclusion

Cutaneous drug reaction is one of the major health problems. The study estimated the average rate of cutaneous drug reaction in two major hospitals of Kathmandu, Nepal. With the increasing number of people using the drug therapy, more people are likely to suffer from adverse drug reactions. However, only little work has been in this field in our country.

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