ISSN 0378-6323
E-ISSN 0973-3930

Indian Journal of Dermatology, Venereology & Leprology

Vol 74 | Issue 1 | Jan-Feb 2008

The Indian Journal of Dermatology, Venereology and Leprology (IJDVL) is a bimonthly publication of the Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) and is published for IADVL by Medknow Publications.

The Journal is **indexed/listed** with Science Citation Index Expanded, PUBMED, EMBASE, Bioline International, CAB Abstracts, Global Health, DOAJ, Health and Wellness Research Center, SCOPUS, Health Reference Center Academic, InfoTrac One File, Expanded Academic ASAP, NIWI, INIST, Uncover, JADE (Journal Article Database), IndMed, Indian Science Abstract's and PubList.

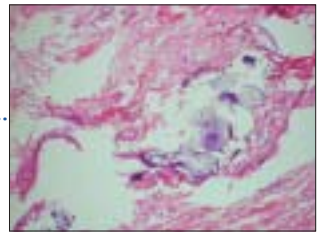
EDITORIAL OFFICE
Dr. Uday Khopkar
Editor, IJDVL, Department of Dermatology, 117, 1st Floor, Old OPD Building, K.E.M. Hospital, Parel, Mumbai - 400012, India.
E-mail: editor@ijdvl.com

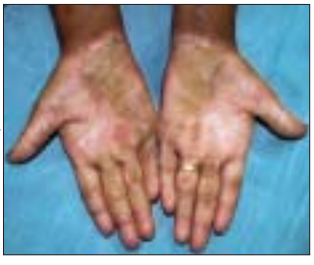
Published for IADVL by
MEDKNOW PUBLICATIONS
A-109, Kanara Business Centre, Off Link Road, Ghatkopar (E), Mumbai - 400075, India.
Tel: 91-22-6649 1818 / 1816
Website: www.medknow.com

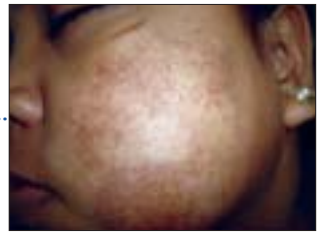
www.ijdvl.com
www.journalonweb.com/ijdvl
www.bioline.org.br/dv

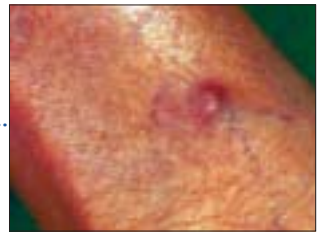
Indian Journal of
Dermatology, Venereology & Leprology
Journal indexed with SCI-E, PubMed, and EMBASE
Vol 74 | Issue 1 | Jan-Feb 2008

CONTENTS

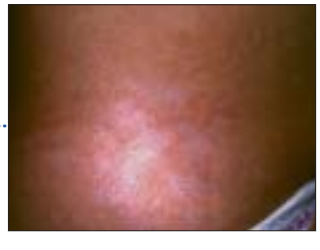


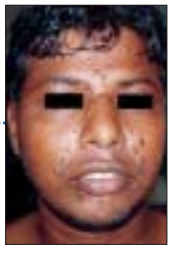


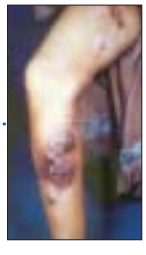


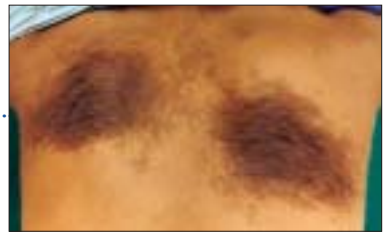


LETTERS TO THE EDITOR



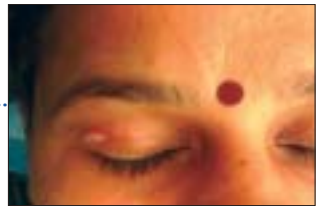




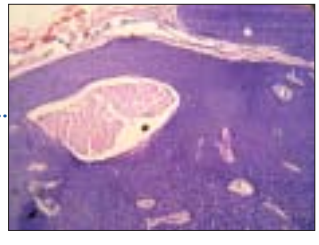


FOCUS

E-IJDVL



QUIZ



Clinical study of cutaneous drug eruptions in 200 patients

M. Patel Raksha, Y. S. Marfatia
Department of Skin and V. D, Medical College, Vadodara, India

Address for correspondence: Dr. M. Patel Raksha, R-3, Doctor's Quarters, Jail Road, Vadodara - 390 001, India.
E-mail: rakshamp@yahoo.co.in

ABSTRACT

Two hundred patients (112 males and 88 females) with cutaneous drug eruption were studied. The aim was to recognize the offending drug, to evaluate mortality and morbidity, educate the patient and avoid self-administration and readministration of drugs. Fixed drug eruption was the commonest reaction, seen in 61 patients; other reactions being urticaria and angioedema, morbilliform rash in 37, pruritus in 25, Stevens Johnson Syndrome (SJS) in 6, purpura in 6, exfoliative dermatitis in 5, photosensitivity in 5, toxic epidermal necrolysis in 2, acneiform eruption in 3, erythema multiforme in 2. Maximum patients belonged to the age group 41-50, followed by 21-30 and 31-40 years. The youngest was 1 year old and the oldest was 80 years old. Period of development of lesion after intake of drug varied from 1 day to 45 days. Cotrimoxazole was the commonest drug, in 26 cases; followed by Ibuprofen in 20 cases.

Key Words: Adverse drug reaction, Cutaneous drug eruption

INTRODUCTION

Cutaneous drug eruptions have become very common in recent times. The incidence of cutaneous drug eruptions is about 2.2% and is higher amongst inpatients and females.[1] Fatal reactions to drugs occur even though benign reactions are more common. The incidence increases in proportion to the number of drugs prescribed.

The best history comes not from asking 'What do you take?' but from asking 'What do you take for fever, cold, sinuses or headache?'

Cutaneous drug eruptions are the most common adverse reactions attributed to drugs. Any skin disorder can be imitated, induced or aggravated by drugs. The present study was carried out to know the age, sex incidence and clinical pattern of drug reactions, to recognize the offending drug (self-medication or prescribed), to evaluate mortality and morbidity associated with drugs, to educate the patients, to avoid self-administration of drugs and readministration of offending drugs. The diagnosis of cutaneous drug eruptions is based on detailed history and correlation between drug intake and the onset of rash. The history-taking for drug intake is an art, which includes direct, indirect, suggestive, evocative and repetitive questioning. It takes time, but answers are golden in case of cutaneous drug reactions and drug-induced dermatitis.

METHODS

A prospective study comprising of 200 cases of drug reaction was carried out from July 1997 to June 2006. The diagnosis was based on detailed history and clinical examination.

Patients with cutaneous drug reactions attending Skin-V.D. Department, SSG Hospital, Vadodara, were studied. Precise history of drug ingestion, including allopathic, homeopathic, herbal remedies, and self-medication was taken. Careful history of symptoms, other existing skin and systemic diseases, atopy, and past history, family history of drug reaction or any other illness were taken. Thorough clinical examination was carried out. Skin, hair, nail and mucosa (eye, oral and genital) were examined.

The diagnosis of cutaneous drug reaction was based on

How to cite this article: Patel Raksha M, Marfatia Y S. Clinical study of cutaneous drug eruption in 200 patients. Indian J Dermatol Venereol Leprol 2008;74:80.
Received: March, 2007. **Accepted:** July, 2007. **Source of Support:** Nil. **Conflict of interest:** None declared.

history of drug ingestion, clinical findings and exclusion of other similar disorders. Diagnosis was confirmed by observing disappearance of signs and symptoms after discontinuation of drugs. Re-challenge was done as and when possible in less severe types of reactions.

Complete blood count, routine and microscopic examination of urine and stool were carried out in all patients. Specific or relevant investigations such as liver function test (LFT), renal function test (RFT), VDRL and ELISA for HIV were carried out in selected patients.

RESULTS

Two hundred patients (112 males and 88 females) were studied. Maximum patients belonged to the age group of 41-50 years, followed by 21-30 and 31-40 years [Table 1]. The youngest patient was 1 year old and the oldest was of 80 years old. Period of development of lesions after intake of drug varied from 1 day to 45 days.

Table 1: Age and sex distribution of drug eruption in the present study

Age group (In years)	Male	Female	Total	Percentage (%)
0-10	12	04	16	08
11-20	10	12	22	11
21-30	20	22	42	21
31-40	26	14	40	20
41-50	22	22	44	22
51-60	08	08	16	08
61-70	06	05	11	5.5
71-80	08	01	09	4.5
Total	112	88	200	100

Cotrimoxazole was the most implicated drug, in 26 cases; followed by Ibuprofen in 20 cases. The commonest pattern of cutaneous drug reaction observed was FDE (Fixed Drug Eruption) (30.5%), followed by urticaria in 18.5%, morbilliform rash in 18% and pruritus in 12.5% [Table 2].

FDE [Table 3] occurred most commonly due to cotrimoxazole (29.5%), followed by NSAIDs (nonsteroidal anti-inflammatory drugs) in 22.8%, urticaria in 18.5%, morbilliform rash in 18% [Table 4] and pruritus in 12.5%. NSAIDs were also the main culprit in causing urticaria, angioedema [Table 5] and morbilliform rash.

Twenty-five cases presented with pruritus, out of which two were because of antituberculous therapy [isoniazid (INH), rifampicin, pyrazinamide, ethambutol] and three were due to cotrimoxazole. Others were due to drugs like ampicillin, ibuprofen, APC (aspirin, paracetamol and codeine), hydroxyzine hydrochloride, vitamin A and chloroquine.

There were seven cases of SJS, out of which three (42.8%) were due to ibuprofen. Two cases of SJS were severe, but they

Table 2: Clinical pattern of drug eruption in the present study

Clinical Pattern	Present study (n = 200)		Malhotra *et al.*[2] (n = 54)%	Jhal *et al.*[3] (n = 379)%
	No.	%		
FDE	61	30.5	–	–
Urticaria	37	18.5	9.26	21.5
Morbilliform rash	36	18	29.63	50
Pruritus	25	12.5	–	–
SJ Syndrome	06	03	22.22	13.9
TEN	02	01	–	4.9
Erythema multiforme	02	01	–	–
Purpura	06	03	–	–
Exfoliative dermatitis	05	2.5	–	–
Photosensitivity	05	2.5	–	–
Acneiform eruption	03	1.5	–	–
Oral ulcer	03	1.5	–	–
DDS syndrome	01	0.5	–	–
Bullous drug reaction	01	0.5	–	–
Hemorrhagic cystitis	03	1.5	–	–
Angular cheilitis	01	0.5	–	–
Eczematous reaction	01	0.5	–	–
Erythema nodosum	01	0.5	–	–
PR like DE	01	0.5	–	–

FDE - Fixed Drug Eruption, SJ Syndrome - Stevens Johnson Syndrome, TEN - Toxic Epidermal Necrolysis, DDS Syndrome - Sulfone Syndrome, PR - Pityriasis Rosea, DE - Drug Eruption

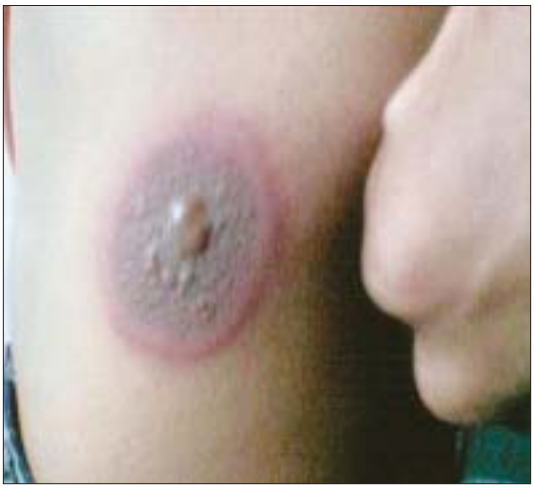


Figure 1: Fixed drug eruption due to cotrimoxazole

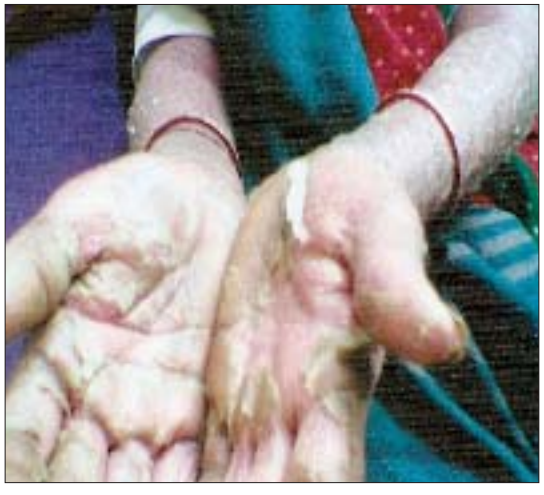


Figure 2: Exfoliative dermatitis due to NSAIDs

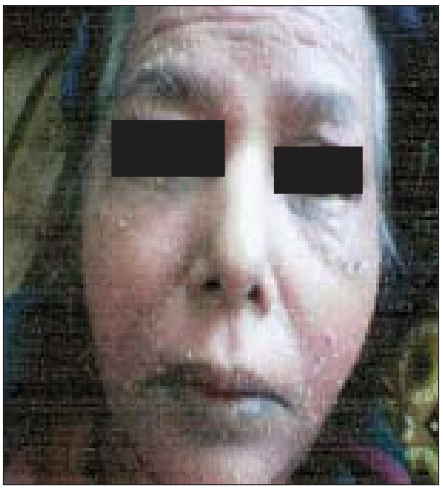


Figure 3: Exfoliative dermatitis due to NSAIDs

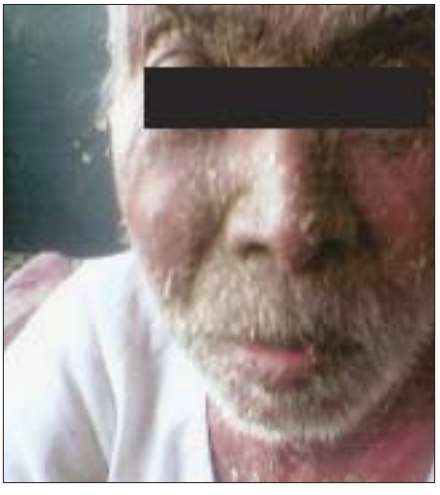


Figure 4: Sulfone syndrome

were managed successfully with intensive care. In addition to this, there were two cases of TEN (Toxic epidermal necrolysis), out of which one case due to rifampicin was severe but responded well to treatment and one case of TEN because of unknown drug proved fatal.

Photosensitivity was seen in four cases, mainly due to ciprofloxacin and sparfloxacin. Five cases of exfoliative dermatitis (2.5%) occurring due to carbamazepine (two), ibuprofen and NSAIDs and dapsone were seen. There were four cases of purpura, the culprit drugs being aspirin, chloroquine, griseofulvin and an unknown drug. One case of angular cheilitis presented due to isotretinoin.

Other than cutaneous drug reactions, we had three cases of hemorrhagic cystitis and one case of aplastic anemia due to cyclophosphamide.

Re-challenge was done in 40 cases of mild cutaneous drug reaction, out of which positive results were found in 29 cases.

Patients were given a list of common drugs causing particular types of reactions and advised to avoid these drugs, chemically related drugs and OTC (over-the-counter) products.

They were instructed that even ayurvedic and other alternative medicines can cause adverse drug reactions. Even their family members were advised to avoid particular groups of drugs.

DISCUSSION

The most common drugs causing reactions were NSAIDs,

in 42 cases (21%); followed by sulpha in 28 cases (14%) in our study. Pudukadan *et al.* reported cotrimoxazole (22.25%), followed by dapsone (17.7%), as the commonest culprit.[2]

The commonest pattern was FDE (30.5%), followed by urticaria (18.5%) and morbilliform rash (18%). Similar to this, Pudukadan D *et al,* reported the commonest pattern to be FDE (31.1%), followed by maculopapular rash (12.2%).[2] Malhotra *et al,* reported morbilliform rash in 29.63%, SJS/TEN in 22.22% and urticaria in 9.26% cases as common patterns of reaction.[3] Jhaj *et al.* reported 50% cases of morbilliform rash, 21% cases of urticaria, 13.9% cases of SJS and 4.9% cases of TEN.[4]

Most of the patients had taken medicine for pain, fever and infection. Cotrimoxazole was the commonest cause of FDE in our study, similar to that found in the study by Singh *et al.*[5] NSAIDs and cotrimoxazole were also found to be the common cause of cutaneous drug reaction in the study by Shrivastav *et al.*[6]

Additives and preservatives are common causes of urticaria. The exact percentage of reactions to additives is not known but is considered to be important in fewer than 10% of

Table 3: Drugs causing fixed drug eruptions

Offending drug	No. of patients (%) present study	Singh *et al.*[4]
Antimicrobials		
Cotrimoxazole	18 (29.5%)	08 (50%)
Sulfadiazine	02 (3.2%)	–
Amoxicillin	02 (3.2%)	–
Doxycycline	01 (1.6%)	02 (12.50%)
Rifampicin	–	01 (6.25%)
Griseofulvin	01 (1.6%)	01 (6.5%)
Antipyretic, analgesic, anti-inflammatory		
Ibuprofen	05 (8.1%)	–
Oxyphenbutazone	–	04 (25%)
Diclofenac sodium	03 (4.9%)	–
Other NSAIDs	06 (9.8%)	–
Paracetamol	02 (3.2%)	–
Analgin®	02 (3.25)	–
Tramadol	01 (1.6%)	–
Antiepileptics		
Carbamezepine	02 (3.2%)	–
Phenytoin sodium	01 (1.6%)	–
Unknown	14 (22%)	–
OTC	01 (1.6%)	–
Total	61 (100%)	16 (100%)

Analgin® is a pyrazolone derivative made available by IDPL with the same generic name in the market

Table 4: Morbilliform rash

Offending drugs	No. of patients (%)
Antimicrobials	
Cotrimoxazole and sulfadiazine	02 (5.5)
Ciprofloxacin	03 (8.3)
Norfloxacin	01 (2.7)
Sparfloxacin	03 (8.3)
Ofloxacin	01 (2.7)
Amoxycillin	02 (5.5)
Metronidazole	01 (2.7)
Albendazole	01 (2.7)
NSAIDS	
Ibuprofen	03 (8.3)
Diclofenac	01 (2.7)
Valdicoxib	01 (2.7)
Other NSAIDS	01 (2.7)
Folic acid (yellow)	01 (2.7)
Vit.B complex (yellow)	03 (8.3)
Magnesium trisillicate (yellow)	01 (2.7)
Antiepileptics	
Carbamazepine	02 (5.5)
Phenytoin/Phenobarbitone	01 (2.7)
Others	
Oral corticosteroid	01 (2.7)
Chloroquine	01 (2.7)
Nevirapine	01 (2.7)
Hazmola*	01 (2.7)
Unknown	01 (2.7)
Total	37 (100)

*Ayurvedic medicine with multiple ingredients

Table 5: Urticaria and angioedema

Offending drugs	No. of patients (%) present study
Antipyretic, Antinflammatory	
Ibuprofen	05
Aspirin	01
Diclofenac	03
Paracetamol	03
Valdicoxib	01
Unknown NSAIDS	07
Antimicrobials	
Cotrimoxazole	01
Tetracycline	01
Cephalexin	02
Ciprofloxacin	01
Dapsone	01
Others	
Loperamide	01
Omeprazole	01
Vitamin AD (red color)	02
Bisacodyl (yellow color)	01
Total	35 (100%)

patients with chronic urticaria. Most frequently implicated food additives are tartrazine, other azo-dyes including amaranth and sunset yellow.[7]

One case of sulfone syndrome (DDS Syndrome - exfoliative dermatitis, fever, generalized lymphadenopathy and raised LFT) [Figure 4] was observed in our study, while dapsone (sulfone) syndrome was observed in 10 (1.6%) out of 604 patients over a period of 4 years in the study by Prasad PV.[8]

Quinolones were a common cause of morbilliform rash and photosensitivity in our study, which might be because of increased use of quinolones.

Ibuprofen was the commonest cause of erythema multiforme (EM) and (Stevens Johnson's syndrome) SJS in our study, whereas one case of SJS was reported due to paracetamol. Halevi *et al,* reported TEN due to acetaminophen,[9] while carbamazepine was the commonest cause of TEN and SJS in the study by Devik *et al.*[10]

The incidence of acneiform eruptions induced by INH was 0.53% in the study by Sharma PP,[11] while we had two cases of acneiform eruptions due to INH.

One case of pruritus was probably induced by (1%) hydroxyzine hydrochloride.

Every drug must be regarded as potentially hazardous. For each patient, the risk must be weighed against the expected therapeutic benefit.

REFERENCES

1. Sehgal S, Balachandran C, Shenoi SD. Clinical study of cutaneous drug reaction in 80 patients. Indian J Dermatol Venereol Leprol 2003;69:6-7.
2. Pudukadan D, Thappa DM. Adverse cutaneous drug reactions: Clinical pattern and causative agents in a tertiary care centre in South India. Indian J Dermatol Venereol Leprol 2004;70:20-4.
3. Malhotra S, Chopra SC, Dogra A, Gupta C. Cutaneous adverse drug reactions- one year pharmacovigilance study in a tertiary care hospital. Indian J Pharmacol 2004;36:S41-2.
4. Jhaj R, Uppal R, Malhotra S, Bhargava VK. Cutaneous adverse reactions in in-patients in a tertiary care hospital. Indian J Dermatol Venereol Leprol 1999;65:14-7.
5. Singh KK, Shrinivas CR, Krupashankar DS, Naik RPC. Study of thirty three cases of fixed drug eruption, Indian J Dermatol Venereol Leprol 1990;56:123-4.
6. Shrivastava D, Kumar A, Singh SK. Adverse drug reaction monitoring in patients attending skin O.P.D at a teaching hospital. Indian J Pharmacol 2004;36:S42.
7. Pollock I, Young E, Stoneham M, Slater N, Wilkinson JD, Warner JO. Survey of colorings and preservatives in drugs. BMJ 1989;299:649-51.
8. Prasad PV. A study of Dapsone syndrome at a rural teaching hospital in south India. Indian J Dermatol Venereol Leprol 2001;67:69-71.
9. Halevi A, Ben-Amitai D, Garty BZ. Toxic epidermal necrolysis associated with acetaminophen ingestion. Ann Pharmacother 2000;34:32-4.
10. Devi K, George Sandhya, Criton S, Suja V. Carbamazepine-The commonest cause of toxic epidermal necrolysis and Steven Johnson syndrome: A study of 7 years. Indian J Dermatol Venereol Leprol 2005;71:325-8.
11. Sharma RP, Kothari AK, Sharma NK. Acneform eruptions and Antitubercular drugs. Indian J Dermatol Venereol Leprol 1995;61:26-7.