ORIGINAL ARTICLE

Prevalence of Cutaneous Drug Eruption in Hospitalized Patients: A Report from Sina Hospital of Tabriz

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Abstract

Background: Cutaneous drug reaction seems to be relatively common The aim of the study was to recognize offending drugs, evaluate patients' characteristics and educate the patients to avoid self-administration and re-administration of drugs.

Methods: We retrospectively and prospectively analyzed data from Sina hospital in Tabriz (2000-2005) to determine the number of hospitalizations and visits with primary diagnoses of skin conditions that are often attributed to drugs. A physical examination was done by a dermatologist who completed a standardized questionnaire. Requested information included patient characteristics (associated disorders, severity scores), drug intake and characteristics of the skin reaction (type, course).Using statistical methods for surveys, we determined the demographic characteristics of patients with these diagnoses.

Results: Three hundred patients (148 males and 152 females) with cutaneous drug eruption were studied. The most common eruptions were erythroderma (41.3%) and maculopapular rash (26%) and the most common offending drugs were carbamazepine (28%), carbamazepine-valproate (20%) and Co-Ttrimoxazole-carbamazepine-diclofenac sodium combination (26.7%). The highest number of the patients belonged to the age group of 30-39 years (15%). The interval between developing lesions and intake of the offending drug varied from 1 day to 45 days. Drug reactions showed that 20-30% of the ADRs from anticonvulsants, 15-25% of the ADRS from sulfonamides, 10% of the ADRs from antibiotics, and 7% of the ADRs from non-steroidal anti-inflammatory and anti-hypertensive drugs were dermatological.

Conclusion: The pattern of ADRs and the drugs causing them is remarkably different in our population. Knowledge of these drug eruptions, the causative drugs and the prognostic indicators is essential for clinicians. It is recommended to advise patients to carry a card or some other form of an emergency identification in their wallets that lists drug allergies and/or intolerances, especially if they have had a severe reaction. *(Iran J Dermatol 2009;12: 16-19)*

Keywords: adverse drug reaction, cutaneous drug eruption, hospitalization

Introduction

An adverse cutaneous reaction caused by a drug is any undesirable change in the structure or function of the skin, its appendages or mucous membranes and encompasses all adverse events related to drug eruption, regardless of the etiology. Drug reactions can be classified into immunologic and non-immunologic etiologies.[1-3]

Adverse cutaneous reactions to drugs are common, affecting 2 to 3 percent of hospitalized patients.[4] It is estimated that 1 in 1000 hospitalized patients has a serious cutaneous drug reaction.[5] In one study, the rate of cutaneous drug eruptions was reported to be about 2.2% and was higher amongst inpatients and females.[6] Incidence increases in proportion to the number of drugs prescribed and polypharmacy.

The present study was carried out to determine age, sex, incidence and clinical pattern of drug reactions, to recognize offending drugs (self-medication or prescribed), to evaluate mortality and morbidity associated with drugs, and to educate the patients to avoid self-administration of drugs and re-administration of offending drugs.

Carbamazepine and phenytoin were the most common offenders in previous studies. The common offending drug groups were antimicrobials (34.10%), anticonvulsants (32.88%), and anti-inflammatory drugs (21.51%). Other less frequent ones were antipsychotics, antidepressants, antihypertensives, oral contraceptives, antidiabetics, insulin, vaccines, radio contrasts, pancreatic enzyme supplements, homeopathic and ayurvedic preparations.[7] Stern *et al*. and Sullivan *et al*. also noted exanthematous eruptions to be the most common type of drug eruptions.[8,9] In a study by Thappa et al.[10-11] the most common eruptions were fixed drug eruption (31.1%) and maculopapular rash (12.2%).

Patients and Methods

Our survey was cross-sectional and we analyzed data from Sina hospital in Tabriz (2000-2005) to determine the number of hospitalizations and visits with primary diagnoses of skin conditions often attributed to drugs. A physical examination was done by a dermatologist who completed a standardized questionnaire. Requested information included patient characteristics (associated disorders, severity scores), drug intake and characteristics of the skin reaction (type, course). Hematological and biochemical investigations (serum electrolytes, blood sugar, liver and renal function tests) were done in all cases. The VDRL test and HIV-Ab (ELISA) test were performed where the underlying risk factors were present. Other similar disorders were excluded. Diagnosis was confirmed by the disappearance of signs and symptoms after discontinuation of drugs. Re-challenge was done when possible in less severe types of reactions,with permission of the patient after giving written consent from. Using statistical methods for surveys, we determined the demographic characteristics of the patients with these diagnoses.

Result

Three hundred patients (148 males and 152 females) were studied. The highest number of the patients belonged to the age group of 30-39 years (78 cases, 26%) (Table 1). The interval between developing lesions and intake of the offending drug varied from 1 day to 45 days. The most common causes were carbamazepine (28%), carbamazepine-valproate (20%) and Co-trimoxazole- carbamazepine-diclofenac sodium combination (26.67%).

There were one hundred and twenty four cases of erythroderma, seventy eight cases of maculopapular rash. Twenty one cases of SJS were seen due to anticonvulsants, antibiotics and NSAIDs. In addition, there were twenty five cases of TEN (Toxic Epidermal Necrolysis), out of whom eleven cases who had administered sulfasalazine and hydroxyzine hydrochloride had vasculitis.

Re-challenge was done in 150 cases with mild cutaneous drug reactions and positive results were seen in 80 (56.2%) of them.

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

In 80 out of the 300 patients, the suspected drug was withdrawn and the skin lesions subsided in 26.6% of them. Re-challenge (with carbamazepine, methotrexate, diclofenac sodium and Co-trimoxazole in 1 case each) was done only in four cases with doubtful or negative dechallenge results and the results were positive in all of them.

Various types of drug eruptions are shown in Table 2. This drug combination was due to multiple drug intake in patients because of several underlying medical conditions.

Complications were seen in 46 of the 300 patients (15.3%) with these drug eruptions, mostly in SJS and TEN, and included septicemia, urinary tract infections, ocular involvement, oral candidiasis, and renal infection.

Table1: *Age and sex distribution of drug eruptions*

Age group (yr.)	Male	Female	Total	Percentage (%)
0-9	17	13	30	10
10-19	15	15	30	10
20-29	20	23	43	14.3
30-39	33	45	78	26
40-49	21	23	44	14.7
50-59	14	12	26	8.7
60-69	9	10	19	6.3
70-79	18	12	30	10
Total	148	152	300	100

Table2: *Clinical patterns of drug eruption*

Eruption pattern	Drugs	Number of patients (n)	Percent (%)
Erythroderma	Anticonvulsants-Antipyretic, Herbal drugs, Valproate-Carbamazepine, Phenytoin-Ibuprofen, Methoxsalen-ferrous sulfate, Dimenhydrinate-Metoclopramide, Ampicillin-Indomethacin-Allopurinol, Amitriptyline, Clonidine, Phenytoin-Haloperidol-Cephalexin, Co-Trimoxazole-Carbamazepine-Diclofenac	124	41.3
Maculapapular	Co-Trimoxazole, Penicillin, Methyldopa, Amoxicillin-Co-Trimoxazole, Anticonvulsant-Azithromycin, Cephalexin-Co-Trimoxazole, Ceftizoxime-Gentamicin, Penicillin-Enalapril-Warfarin, Ampicillin-Enalapril-Triamterene H, Carbamazepine -Metoclopramide-Phenytoin	78	26
Erythemo Multiforme	Carbamazepine	31	10.3
Toxic Epidermal Necrosis (TEN)	Antibiotics	25	8.4
Steven Johnson syndrome (SJS)	Phenytoin, Valproate-Ampicillin, Theophylline-Triamterene H-Dilitiazim	21	7
Vasculitis	Sulfasalazine-Hydroxyzine	11	3.6
Vesiculobullous	Anti-Ashmatic Spray	5	1.7
Exfoliative dermatitis	Ceftizoxime-Propranolol-Ibuprofen	5	1.7

Discussion

The majority of patients in this study belonged to the 30-39 age group, as also observed by Sharma et al.[12] Solensky et al observed that adults aged 20-49 were at greatest risk of antibiotics-related drug eruptions, probably due to increased exposure to antibiotics.[13] However, Leape et al and Hafner et al studies noted that the elderly are more commonly affected.[14,15] Adverse reactions to drugs increase with age.[16] This may be due to the increased use of medications by the elderly and an increased potential for drug-drug interactions. The difference in various studies may be related to the regional variation in the health care seeking behavior of the population.[17]

Every drug must be regarded as potentially hazardous. For each patient, the risk must be weighed against the expected therapeutic benefit. After a cutaneous drug eruption has been diagnosed and treated, clear information must be provided to the patient regarding his/her drug rash.

Adverse drug reactions are influenced by several factors such as prolonged hospital stay, the classes of drugs used and polypharmacy.[18] This might be extrapolated to other age groups as well.

Adverse cutaneous drug reactions vary in their patterns of morphology and distribution. In previous studies, the most common morphologic patterns have been reported to be exanthematous, urticaria and/or angioedema, fixed drug eruption and erythema multiform.[8] Sullivan *et al* and Kauppinen *et al* have noted exanthematous eruption to be most common type of drug eruptions.[9,10] This variation could be due to different patterns of drug usage and different ethnic group characteristics.

The most common causes were carbamazepine (28%), carbamazepine-valproate (20%) and Co-trimoxazole- carbamazepine-diclofenac sodium combination (26.67%) in our assay. Pudukadan et al. reported Co-trimoxazole (22.25%), followed by dapsone (17.7%), as the commonest culprits.[11]

In our study, the most common patterns were erythroderma (41.3%) and maculopapular rash (26%). Malhotra et al reported morbilliform rashes in 29.63%, SJS/TEN in 22.22% and urticaria in 9.26% of the cases as common patterns of reaction.[19] Jhaj et al reported that 50% of the cases had a morbilliform rash, 21% of the cases had urticaria, 13.9% of the cases had SJS and 4.9% of the cases had TEN.[20]

Most of the patients had taken medicine for pain, fever and infection. Carbamazepine-valproate was the commonest cause of erythroderma in our study, similar to the findings of a study by Singh et al. [21] Carbamazepine, NSAIDs and Co-trimoxazole were also found to be the common causes of cutaneous drug reactions in a study by Shrivastav et al.[22]

In our study, carbamazepine and phenytoin were the commonest causes of erythema multiform (EM) and Stevens Johnson's syndrome (SJS), respectively. However, one case of SJS was reported due to acetaminophen. Halevi et al. reported TEN due to acetaminophen,[24] while carbamazepine was the commonest cause of TEN and SJS in a study by Devik et al.[25]

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 the patients with chronic urticaria. Most frequently implicated food

additives are tartrazine, other azo-dyes including amaranth and sunset yellow.[23]

It is recommended to advise patients to carry a card or some other form of an emergency identification in their wallets that lists drug allergies and/or intolerances, especially if they have had a severe reaction. The names of the medication, potentially cross-reacting drugs that can be safely taken, are an important part of the evaluation. The predisposition to some drug-induced eruptions may be genetic and family counseling is part of the care plan. This can be important especially in SJS, TEN, and drug hypersensitivity syndromes. Finally, cutaneous drug reactions should be reported to the manufacturer and the regulator agencies, especially if the skin eruption is rare, serious or unexpected.

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