ORIGINAL CONTRIBUTIONS

CUTANEOUS ADVERSE REACTIONS IN IN-PATIENTS IN A TERTIARY CARE HOSPITAL

R Jhaj, R Uppal, S Malhotra, V K Bhargava

Cutaneous reactions were monitored by spontaneous adverse reaction monitoring system among inpatients in Nehru Hospital, over a period of 3 1/2 years. A total of 379 adverse drug reactions were reported during this period, of which 144 (40%) were cutaneous reactions. Maculopapular rashes (50% of cutaneous reactions), and urticaria (21.5%) were the most common eruption. Stevens -Johnson syndrome (13.9%) and toxic epidermal necrolysis (TEN 4.9%) were the serious cutaneous reactions. There were 4 fatal cutaneous reactions (all due to TEN). Antimicrobials (caused 56.9% reactions), radiocontrast dyes (14.6% reactions) and antiepileptics (15.3% reactions) were the most prominent drugs responsible for these eruptions.

Key words : Skin rashes, Cutaneous reactions, Adverse drug reactions

Introduction

Cutaneous reactions are among the most frequently reported adverse drug reactions, occurring in 2-3% of hospitalised patients.[1,2] The reported percentage of potentially serious cutaneous reactions varies greatly, but probably about 1 in 1000 hospitalised patients has a serious cutaneous drug reaction.[3] Such reactions may result in substantial morbidity or even death, unless promptly recognised and treated. It is for this reason that an awareness of possible adverse cutaneous effects of drugs is important, as well as a knowledge of drugs most frequently associated with these reactions.

In this study, we present the data on cutaneous adverse reactions in hospitalised patients, reported over a period of 3 1/2 years.

From the Department of Pharmacology, PGIMER, Chandigarh-160 012.

Address correspondence to :
Dr. V.K Bhargava

Materials and Methods

Data on adverse drug reactions (ADRs) including cutaneous reactions was collected from 1-4-1994 to 31-12-1997 by the system of spontaneous monitoring of adverse drug reactions.[4] Patients admitted in the wards of Nehru Hospital, which is a 1174 bed hospital attached to Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, were covered. Letters/ notices were circulated to all clinical departments, asking for reports of any ADRs encountered. ADRs were reported to the department of Pharmacology on ADR forms, available in the hospital wards. On receiving such reports, team members from Pharmacology went to the wards to follow up the patients. All reactions were reviewed by a dermatologist and classified into different morphological patterns using ADR terms developed by the USA Food and Drug Administration (COSTART). [5] Patients with generalised pruritus with hepatic and/or renal failure or lymphoma were excluded. Also patients with alopecia due to anticancer drugs were excluded from this study.

In patients receiving more than 1 drug, the possible cause of the cutaneous reaction was based on the algorithm devised by Kramer.[6,7] Broadly, the relative reaction rates for cutaneous reactions due to different drugs, the specific morphologic pattern, timing of the reaction and rechallenge were the chief elements used in implicating a drug. Rechallenge was not given to any patient.

Results

Out of 379 adverse drug reactions reported during the period of study, there were 144 (40% of all adverse reactions) cutaneous reactions.

Morphological types of cutaneous reactions :

Maculopapular rashes were the most common reactions, reported in 72 (50% of all cutaneous reactions) patients (Table 1). Urticaria was reported in 31 (21.5%) patients . Twenty patients (13.9%) developed Stevens - Johnson syndrome (SJS) , while in 7 toxic epidermal necrolysis (TEN) was reported, 4 out of 7 cases of TEN were fatal.

Other reactions included pruritus without a rash, contact dermatitis, purpura, erythema multiforme, fixed drug eruption and acneiform eruptions.

Drugs implicated in cutaneous reactions

Antimicrobials were most frequently associated with cutaneous adverse events, being responsible for 82 (56.94%) reactions (Table II) . b- lactum (38 reactions), ciprofloxacin (15) and antituberculosis therapy (ATT,10) were prominent among the antimicrobials causing cutaneous reactions. Radio contrast dyes urograffin 76% and conray 420 (21 reactions), carbamazepine and phenytoin (a total of 22 reactions), were other drugs implicated in adverse cutaneous reactions.

There were 4 deaths due to cutaneous side effects - all due to TEN. Children aged 12 years or below made up 16.0% of the cases while 7.6% of the skin reactions were reported in the elderly i.e. 60 years or more. Thirty patients (20.8%) were on more than 1 drug. Only 3 patients reported skin rashes due to topical administration (all 3 contact dermatitis).

Discussion

Despite its limitations eg. Under - reporting, biased reporting and failure to provide incidence rates, spontaneous adverse reaction monitoring system is the only drug surveillance system which can monitor safety of all drugs throughout their life as therapeutic agents.[8]

In the present study, the most frequent cutaneous reactions reported were maculopapular rashes and urticaria. These morphological patterns are the predominantly reported drug-induced eruptions, including those reported in several case series and intensive surveillance studies .[1,2,9-11] Stevens-Johnson syndrome (SJS) was reported in a larger number of patients (13.9%) compared to earlier studies. In the series reported by Kauppinen and Stuble,[9] SJS was reported in 8 out of 446 reactions, while Kuokkanen,[10] in a series of 464 cases, reported SJS in 4%.

Among the drugs which were responsible for the cutaneous reactions, antimicrobials, particularly of the b-lactum group, were the chief culprits, as reported in earlier studies too. [1,2,9-11] Most of these earlier reports include sulphonamides along with penicillin as the predominant antimicrobials. Antimicrobials were also the inducing agents in 5 out of 7 cases of a serious cutaneous reaction i.e toxic epidermal necrolysis (TEN). All 4 fatal cases of TEN were receiving an antimicrobial (sulphamethoxazole - trimethoprim, tetracycline, ciprofloxacin or amoxicillin). Ciprofloxacin, carbamazepine alone and carbamazepine with phenytoin were the inducing agents in the 3 non -fatal cases of TEN. Previous studies too have identified anti-microbials and anticonvulsants as major inducing agents of TEN. [3,12,13]