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ORIGINAL ARTICLE

A cross-sectional study of cutaneous drug reactions in a private dental college and government medical college in eastern India

C Chattopadhyay, N Chakrabarti[1]

Department of Pharmacology, KPC Medical College and Hospital, [1]General Medicine, NRS Medical College and Hospital, Kolkata, India

Abstract

Background: Cutaneous drug reactions are a common impediment in therapy, the incidence ranging from 2% to 8%. This cross-sectional study was designed to compare different trends of cutaneous drug reaction in two different socio-economic groups of patients in the same region.

Aims: The aim was to evaluate common drugs implicated in causing reactions, describe the adverse cutaneous drug reactions, study the characteristics of patients presenting with the reactions. Study Design: This is an observational study of cross-sectional type.

Materials and Methods: The study was carried out in the department of Oral and Maxillofacial surgery in a Private dental College and department of General Medicine in a Medical College only on outdoor basis for 3 years. Out of 2000 patients observed in each college for their necessary treatment 75 patients in the dental College and 200 patients in the Medical College were reported to have various types of cutaneous drug reactions. Diagnosis was based on detailed history including temporal correlation between drug intake and onset of rash and thorough clinical examination Apart from history of drug intake, information regarding associated other allergy, comorbidity and severity (whether hospitalization was required or not) was recorded. Rechallenge with the drug was not possible due to ethical problem.

Results: Out of 2000 patients observed in each college 75 patients in dental College and 200 patients in Medical College were documented to have different kinds of cutaneous drug reactions. A total of 30 were male and 45 female in dental college whereas 90 male and 110 female patients were enrolled in Medical College. The age group of the patients in both the colleges ranged from 18 to 75 years. Common culprits observed in this study were antibiotics and NSAIDs. They had contributed 53% and 40% of the total skin reactions respectively in dental college and 47.5% and 45% in Medical College. We encountered 6 patients of systemic lupus erythematosus (SLE), 20 patients with allergic rhinitis and 12 patients with bronchial asthma in the whole proceedings. The duration of drug intake varied from 15 minutes to 2 weeks. The most common reaction noted was maculopapular rash 37 (50.5%), urticaria 15 (20%), fixed drug eruption (FDR) 15 (20%), angioedema 6 (8%) in dental College whereas a little different trend was observed in the medical college. Hospitalization was required in two cases of Steven--Johnson syndrome caused by NSAIDS in the dental College whereas 11 patients were hospitalized for the same indication in the medical College. Except for maculopapular rash, all other skin reactions were observed more frequently with NSAIDS in dental College whereas Steven--Johnson syndrome is predominantly observed in Medical College with anticonvulsants. In all the cases causative drugs were withdrawn. A total 40% of the patients required only antihistaminic, 35% required antihistaminic and topical corticosteroid and rest required a combination of antihistaminic, oral and topical corticosteroids.

Conclusion: Commonest drugs causing drug reactions are antibiotics mainly beta lactams and quinolones. Severe reactions were seen in our series with anticonvulsants and NSAIDS. Association with other diseases could not be inferred due to this modest patient pool.

Address for correspondence:
Dr. Chandan Chattopadhyay,
358, NSC Bose road, Kolkata-700 047, India.
E-mail: rivuc2006@gmail.com

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Introduction

Cutaneous drug reactions are among the most frequent side effects of drugs. Few of them can be life threatening but most are benign. In everyday dental practice one has to prescribe antibiotics, analgesics, antifungals and antivirals mostly via oral route whereas in medical college wider ranges of drugs are prescribed. The percentage of reactions in commonly used drugs is not above1%-2%.[1,2] Prompt recognition of reactions, appropriate management and withdrawal of the causing agent can minimize the drug reaction and prevent death due to severe drug reactions.

We had set forward to study, compare and find an association between different types of cutaneous drug reactions in two different socio-economic groups of patients in the same region.

Objectives

The objectives of this study were as follows: to evaluate common drugs responsible for causing reactions, describe the adverse cutaneous drug reactions, to study the characteristics of patients presenting with the reactions.

Materials and Methods

This hospital-based study was carried out in outdoor departments of Oral and Maxillofacial Surgery and Pharmacology in a Dental teaching institute and Department of General Medicine in a Govt. Medical College for a span of 3 years. This was an observational study of cross-sectional type. All patients suspected of having drug reactions seen in dental and medicine outpatient departments during the period of three years were evaluated by us. In every case a detailed history was elicited and a thorough clinical examination was carried out as suggested by Sacerdots *et al*.[3] To establish the etiologic agent for a certain type of reaction, attention was given to drug and addiction history, duration of the rash, temporal correlation with the drug, average incubation period, morphology of the eruption, status of lesions on withdrawal of drug, associated mucosal or systemic involvement and recurrence of lesions on accidental rechallenge. Comorbidity and severity of drug reaction (whether hospitalization was required or not) was recorded and history of drug intake-associated other allergies was noted. Reactions where the drugs taken were not known were excluded. Hematological and biochemical investigations (serum electrolytes, blood sugar, liver and renal function tests) were done in all cases. The VDRL test and HIV (ELISA) test were performed where the underlying risk factors were present.

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 rash on withdrawing the drug. The rashes were attributed to a drug following the guidelines of Boston collaborative drug reaction surveillance program.[4]

Results

We had observed 2000 patients (both male and female) age groups ranging from 18 years to 75 years in each college within a span of 3 years. (patient below age of 18 reported to the department of Pediatrics and those above 75 years have deranged immune function ,hence excluded from the study). A total of 75 patients were enrolled in dental outdoor department with drug reactions in the span of 3 years [Table 1]. Thirty were male and 45 were female [Figure 1]. Common culprits observed in this study were antibiotics and NSAIDS [Table 1]. They had contributed 53% and 40% of the total skin reactions respectively. Antifungals (3%) and antivirals (4%) had also contributed a small number of affected. We encountered 2 patients of SLE, 2 patients with allergic rhinitis and 3 patients with bronchial asthma in the whole proceedings in dental college. The duration of drug intake varied from 15 minutes to 2 weeks. Commonest reaction noticed was maculopapular rash 37 (50.5%). Urticaria 15 (20%), fixed drug eruption (FDR) 15 (20%), angioedema 6 (8%) were the other lesions encountered in this study. Hospitalization was required in two cases who had suffered from Steven--Johnson syndrome due to NSAIDS. Except for maculopapular rash, all other skin reactions were observed more frequently with NSAIDS. 40% of the patients required only antihistaminic, 35% required antihistaminic and topical corticosteroid and rest required a combination

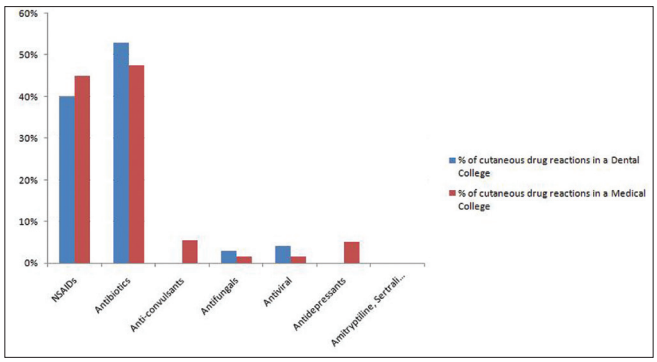

Figure 1: Comparative assessment of percentage of different drugs responsible for cutaneous drug reactions in two colleges

Table 1: Relationship between the drugs and clinical spectrum of adverse cutaneous reactions

Causing drugs	Maculopapular rash	Urticaria	Fixed drug reactions	Angioedema	Steven Johnson Syndrome	Total
Beta lactams	15	05				20
Quinolones	06	01		02		09
Metronidazole	04	01				05
Erythromycin	02					02
Doxycycline			04			04
Non steroidal anti-inflammatory drugs	05	08	11	04	02	30
Antifungals	02					02
Antivirals	03					03
Total	37	15	15	06	02	75

FDR = Fixed drug reactions; SJS = Steven johnson syndrome

Table 2: Relationship between the drugs and clinical spectrum of adverse cutaneous reaction in a Medical College

Causing drugs	Maculopapular rash	Urticaria	FDR	Angio-edema	Photo-allergy	Steven--Johnson syndrome	Total
Beta-lactams	25	6	-	4	-	-	45
Fluroquinolones	20	5	-	-	-	-	25
Metronidazole/tinidazole	10	-	5	-		-	15
Erythromycin/azithromycin	-	-	-	-		-	-
Doxycycline	5				5		10
Non steroidal anti-inflammatory drugs	40	16	10	23		1	90
Antifungals	3						3
Antiviral	2						2
Anti-depressants (For Chronic pain)	10						10
Anticonvulsants (Phenytoin, carbamazepine,)	-	-	-	-	-	10	10
Antimalarial	-	-	-	-	-	-	-
Total	115	27	15	27	05	11	200

NSAIDs = Non steroidal anti-inflammatory drugs, FDR = Fixed drug reaction

Table 3: Percentage of different drugs responsible for different drug reactions in two colleges

Drugs	% of cutaneous drug reactions in a dental college	% of cutaneous drug reactions in a medical college
Non steroidal anti-inflammatory drugs	40	45
Antibiotics	53	47.5
Anticonvulsants	0	5.5
Antifungals	3	1.5
Antiviral	4	1.5
Antitubercular	-	-
Antimalarial	-	-
Antidepressants Amitryptiline, sertraline	-	5%

of antihistaminic , topical and systemic corticosteroids. Of 2000 patients observed in the span of 3 years in Medical College, 200 patients were enrolled with cutaneous drug reaction [Table 2]. The most common morphological types of ACDRs was maculopapular rash (57.5%) [Table 3]. Stevens--Johnson syndrome was the most serious acute cutaneous drug reactions (ACDRs). Antimicrobials (47.5%), nonsteroidal anti-inflammatory drugs (NSAIDs) (45%), antidepressants (5%), and antiepileptic drugs (5%) were the most prominent group of drug responsible for cutaneous Drug reactions. [Figures 2 and 3, Table 4] We encountered 4 patients of SLE, 18 patients with allergic rhinitis, and 9 patients with bronchial asthma in the whole proceedings in the medical college

Discussion

Cutaneous reactions[5] arise as a result of immunologic or nonimmunologic mechanisms. Immunologic reactions designated as drug allergy require activation of host immunological pathways. Nonimmunologic mechanisms may be due to side effects, overdosage, exacerbation of preexisting conditions, etc. Specifying pathogenic

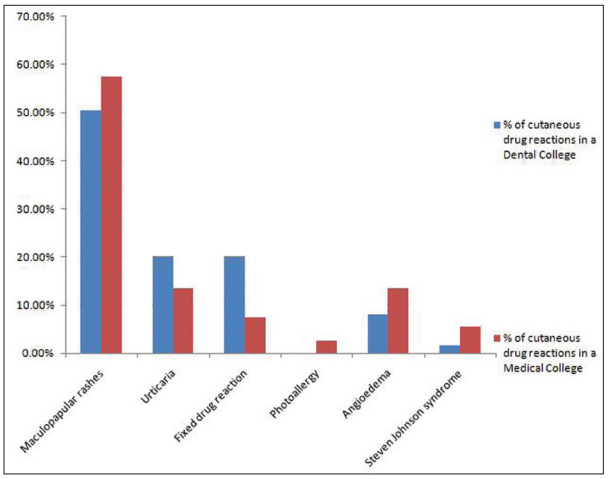

Figure 2: Comparative assessment of percentage of different drugs responsible for cutaneous drug reactions in two colleges

Table 4: Percentage of different cutaneous drug reactions in two colleges

Types of cutaneous drug reaction	% of cutaneous drug reactions in a dental college	% of cutaneous drug reactions in a medical college
Maculopapular rashes	50.5%	57.5%
Urticaria	20%	13.5%
Fixed drug reaction	20%	7.5%
Photoallergy	-	2.5%
Angioedema	8%	13.5%
Steven--Johnson syndrome	1.5%	5.5%

mechanisms are extremely difficult because skin responds through limited number of reaction patterns to a variety of stimuli. Thus our endeavor was to study these reaction patterns and implicate causative drugs without going into pathogenic mechanisms.

Most of the patients in Medical College were in the age group of 30-60 years. Female patients had predominance over male patients [Figure 1, Table 5]. In this study, most cases had reaction time between 15 minutes to 14 days. The most common morphological types of reaction was maculopapular rash (57.5%) [Stevens--Johnson syndrome was the most serious reaction for which hospitalization was required. Antimicrobials (47.5%), nonsteroidal anti-inflammatory drugs (NSAIDs) (45%), antidepressants (5%), and antiepileptic drugs (5.5%) were the most prominent group of drugs responsible for cutaneous reactions. Among antiepileptics, phenytoin was implicated in 5 (2.5%) and carbamazepine in 5 (2.5%) cases [Table 3].

Pudukadan,[6] Chatterjee *et al*,[7] and Sharma[1] reported antimicrobials as a major group producing cutaneous drug reactions followed by antiepileptics and NSAIDs. This indicates regional differences in drug reactions with a study in Gujrat.[8] The maximum number of cases in the Gujrat-based study, i.e., 15 (21.4%) were due to cotrimoxazole. In our institutions cotrimoxazole was not prescribed. Among NSAIDs, the maximum number cases were due to diclofenac followed by ibuprofen. Among antiepileptics, phenytoin was implicated in 5 (2.5%) and carbamazepine in 5 (2.5%) cases. Out of 75 patients in the dental college, all (100%) were cured either due to withdrawal of offending drug or due to appropriate drug therapy to the patients. In the medical college six patients developed chronic urticaria (3%) in spite of getting all forms of therapy. Rest of the patients were (194) completely cured after withdrawal of offending drug and after getting medications. A causal relationship between the drug and the reaction was assessed by using WHO-UMC classification for causality assessment depending upon the lag period between the start of the drug and appearance of the reaction (reaction time), and the available data about the drug.

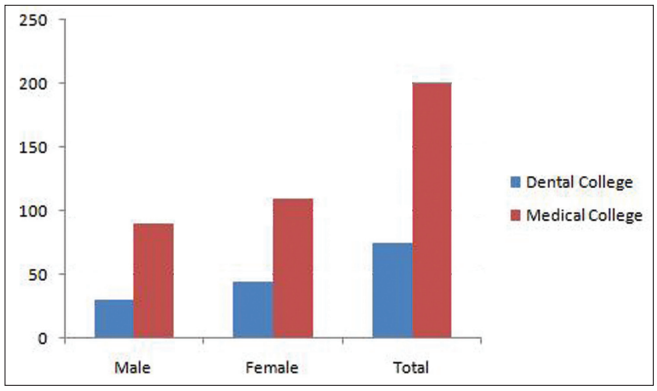

Figure 3: Demographic (sex) distribution in dental and medical colleges

Table 5: Sex distribution of patients in dental and medical colleges

	Male	Female	Total
Dental college	30	45	75
Medical college	90	110	200

In our series we observed a female preponderance in a patient profile with maximum number of cases being in the third and fourth decade in dental College.[1] Maculopapular rashes were also the commonest lesions seen.[1] This is a well-established fact observed in all studies conducted in these lines followed by Fixed Drug reactions, urticaria, angioedema, and Steven--Johnson Syndrome. Drugs used in everyday dental practice included B lactams, Quinolones, Metronidazole/Tinidazole, analgesics, and less commonly antifungal, antiviral. Thus the patterns of drugs involved in causing reactions were slightly different from established series. Preponderance of sulfonamides among antibiotics was not observed in our study due to its dwindling use in a sphere. Similarly antimalarials and antitubercular drugs which prominently figure in notable studies are absent here. Quinolones and Beta lactams are taking pride of place in our

list of culprits. Severe reactions with mucosal involvement name SJS/TEN occur much lesser in this dental series. Since most of the patients attending Govt Medical College belong to relatively poor socio-economic status, the pattern of drug usage amongst them is mostly restricted to drugs that are supplied free of cost from the hospital. This was an important limitation of this study as the suspected drug information generated from this study may not be truly reflective of the pattern in other health care centers catering to patients of higher socio-economic status. To eliminate that, we have observed patients with drug reactions in a Private dental College and surprisingly observed similar nature of drug reactions in the same region though socioeconomic status of the patients changed considerably.

The observations made in our study emphasize the need for a strict and efficient pharmacovigilance system which could curtail the incidence of cutaneous drug reactions in clinical practice.

With the emergence of newer molecules and changing trend in use of drugs it is possible that cutaneous adverse drug reaction patterns and causative drugs will undergo constant change.

Conclusion

Commonest drugs causing drug reactions are antibiotics mainly Beta lactams and Quinolones.[1] Maculopapular rashes were the commonest presentation. Severe reactions were seen in our series with NSAIDS and anticonvulsants. Association with other diseases could not be inferred with this modest patient pool. It may be concluded that the clinical patterns and the drugs causing ADR are remarkably similar to those observed in other countries except for minor variations. Drugs used for treatment of tropical diseases like malaria, diarrhoea and tuberculosis contributed less than 10% of all adverse drug reactions. It is obvious that the cutaneous ADR patterns and the drugs causing various reactions are changing every year which may be due to the emergence of newer molecules and changing trends in the use of drugs.

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