Original Article

Pattern of Adverse Cutaneous Drug Reactions (ACDR) to Systemic Drugs

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Abstract

Adverse cutaneous drug reaction (ACDR) is a common issue in dermatology practice and it is crucial for every medical practitioner to remain updated of its pattern. It was a hospital based crosssectional observational study, conducted over 130 patients with adverse cutaneous drug reactionin the outpatient department of dermatology of Bangabandhu Sheikh Mujib Medical University (BSMMU). Majority of reaction was developed within one week of taking drug. Fixed drug eruption (FDE) was present in 18.5% cases followed by maculo-papular, Stevenson-Johnson-Syndrome-Toxic epidermal necrolysis (SJS-TEN), urticaria, urticaria + angioedema, lichenoid drug reaction, erythema multiforme, acneiform eruption, exfoliative dermatitis, pityriasiform, hyperpigmentation, acute generalized exanthematous pustulosis, drug induced hypersensitive syndrome, vasculitis, purpura, photosentivity, psoriasiform and other non-specific reactions. Anti convulsants (26.9%), NSAIDs (20.0%) and anti amtimicrobials (17.7%) are the most common drug group causing adverse cutaneous reaction. Many of the ACDR caused by anticonvulsants, NSAID and antimicrobials are even life threatening.

Key words: *ACDR, drug reaction.*

INTRODUCTION

Adverse drug reaction is defined as "Any response to a drug which is noxious and unintended which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function".[1] In every day practice physicians face different unwanted response of medicines they prescribed for patients in hospitals. Globally ADR is the cause of hospital admission in roughly 5.8%.[2] Skin is one of the most important sites to be affected with adverse drug reaction.[3]

The frequency, type and extent of drug reaction are variable from drug to drug.[4] In past studies it was reported that 7–11.2% of ADRs result in hospitalization.[5-7] Every year so many new drugs are included in the prescribing list and the prescription pattern are changing as well as physicians are facing newer adverse events on their patients. So it is important to update the current trend of drug reaction.

The incidence of ACDR varies from 3.31-16% in hospital admitted patients.[8-9] but such data of out-patients are scarce. Cutaneous adverse drug reactions (CADR) are the commonest ADR (30.45%) and responsible for about 2% of hospital admissions.[10-11] The current study was carried out to see the pattern of cutaneous drug reactions in BSMMU hospital.

MATERIALS AND METHODS

In the current hospital-based cross-sectional observational study 130 patients with adverse cutaneous drug reaction were studied who were recruited from the outpatient department of dermatology of Bangabandhu Sheikh Mujib Medical University (BSMMU). Cases with history of taking vaccine, any unknown drug, homeopathy, herbal, Ayurveda and reaction due to over dose were excluded and only those giving informed written consent with history of taking prescribed drugs were enrolled. Each patient was examined by one or all authors. Detailed history (age, sex, primary disease or condition for which the suspected drug was taken, suspected drug, time taken to develop reaction after drug taken, dose of drug, duration of drug taken, use of herbal or homeopathy or home remedy, previous drug reaction, re-exposure to a drug and exacerbation of eruption, changes after drug stop or decreasing the dose, other systemic disease, family history of drug reaction and contact with any chemical or physical agents) was taken and physical examination was done. Venous blood was

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taken for hematological (complete blood count) and biochemical tests (Urine for routine analysis, serum creatinine, SGPT, blood sugar and serum electrolyte). The type, extent (total surface area, mucosal or internal organ involvement) of adverse cutaneous drug reaction was diagnosed by the expert team mostly according to morphology of the lesion and skin biopsy (if needed).Where more than one drug was suspected the mostly suspected drug was noted and was confirmed according to reduction of reaction after withdrawal.

RESULTS

Among patients with drug reaction 11.5% were under age 20 years, 23.9% from the age group 21-40 years, 27.7 % from 41-60 years group and 34.6% above the age 60 years. Mean age was 45.2±1.3 with a range from 2 to 74 years (table I).

Table I: Age distribution of the patients (n=130).

Age	Frequency (%)
<20 years	18(11.5)
21-40	31(23.9)
41-60	36(27.7)
>60	45(34.6)
Total	130(100.0)

Mean (range): 45.2±1.3 (2-74)Adverse cutaneous drug reaction was seen in 42.3% male and 57.7% female patients; male female ratio was 1:1.4. In 28.5% cases drug reaction was developed within one day of drug consumption, 59.2% developed between one day to one week and 12.3% developed after one week (Table II).

Table II: Onset of reaction following drug intake (n=130).

Onset (Day)	Male (%)	Female (%)	Total (%)
1	17(13.1)	20(15.4)	37(28.5)
2-7	31(23.8)	46(35.4)	77(59.2)
>7	7(5.4)	9(6.9)	16(12.3)
Total	55(42.3)	75(57.7)	130(100)

Fixed drug eruption (FDE) was present in 18.5% cases, other offending types of reactions were, maculo-papular (9.2%), SJS-TEN (6.9%), urticaria (8.5%), urticaria + angioedema (4.6%), lichenoid drug reaction (5.4%), erythema multiforme (7.7%), acneiform eruption (6.9%), exfoliative dermatitis (5.4%), pityriasiform (4.6%), hyper-pigmentation (1.5%), acute generalized exanthematous pustulosis (2.3%), drug induced hypersensitive syndrome (4.6%), vasculitis (1.5%), purpura (2.3%), photosentivity (2.3%), psoriasiform (1.5%) and other non-specific reactions (6.2%) (Table III).

Table III: Type of drug reaction (n=130).

Type of drug reaction	Frequency (%)
FDE	24 (18.5)
Maculo-papular	12(9.2)
SJS-TEN	9(6.9)
Urticaria	11(8.5)
Urticaria + angioedema	6(4.6)
Lichenoid	7(5.4)
Erythema multiforme	10(7.7)
Exfoliative dermatitis	7(5.4)
Hyperpigmentation	2(1.5)
Pityriasiform	6(4.6)
Acute generalized exanthematous pustulosis	3(2.3)
Acneiform eruption	9(6.9)
Drug induced hypersensitive syndrome(4+2)	6(4.6)
Vasculitis	2(1.5)
Purpura	3(2.3)
Photosentivity	3(2.3)
Psoriasiform	2(1.5)
Non specific	8(6.2)

Anti-convulsant (26.9%), NSAIDs (20.0%) and antimicrobials (17.7%) are the most common drug group causing adverse cutaneous reaction. Other offending drugs include allopurinol (6.2%), sulfasalazin (2.4%), dapsone (0.8%), antihypertensive (3.9%), systemic corticosteroid (6.9%), anticancer drugs (6.2%) and others (9.2%).

Table IV: Drugs causing adverse cutaneous reaction (n=130).

Name of drug		Frequency (%)
Anti-convulsants (Carbamezepine, Phenytoin, Phenobarbital)	FDE 3 (2.3) Maculo-papular 5(3.8) SJS-TEN 5 (3.8) Hypersensitive syndrome 4(3.1) Exfoliative dermatitis 3 (2.3) Pityriasiform 6 (4.6) Urticaria 2 (1.5), Urticaria+angioedema 2 (1.5) Vasculitis 2(1.5) Erythema Multiforme 3(2.3)	35(26.9)
Paracetamol and NSAIDs (naproxen, ibuprofen, tramadol, indomethacin, ketoprofen, diclofenac)	FDE 8 (6.2) Maculo-papular 2(1.5) Exfoliative dermatitis 2(1.5) EM 3(2.3) Acute generalized exanthematous pustulosis 2(1.5) Lichenoid 3(2.3) Urticaria+angioedema 2(1.5) SJS-TEN 2(1.5) Psoriasiform 2(1.5)	26(20.0)
Anti-microbial agents (Ciprofloxacin, Amoxicillin, Cotrimoxazol, tetracycline, Doxicycline, Metronidazole and Anti-TB drugs)	FDE 5(3.9) Maculo-papular 3(2.3) Photosentivity 2 (1.5) SJS-TEN 2(1.5) Urticaria 1(0.8) hypersensitive syndrome 2(1.5) Erythema multiforme 2(1.5) Acute generalized exanthematous pustulosis 1 (0.8) Nonspecific 2(1.5) Purpura 1(0.8) Hyperpigmentation 2 (1.5)	23(17.7)
Allopurinol	FDE 3(2.3) Urticaria 2(1.5) Maculo-papular 2(1.5) Nonspecific 1(0.8)	8(6.2)
Sulfasalazin	Erythema multeforme 2(1.5) Exfoliative dermatitis 1(0.8)	3(2.4)
Dapson	Exfoliative dermatitis 1(0.8)	1(0.8)
Antihypertensive	Lichenoid 2(1.5) Photosensitivity 1(0.8) FDE 2(1.5)	5(3.9)
Systemic corticosteroid (Prednisolone, Deflazacort and Injection Triamcinolone) anti-cancer drugs Others	Acneiform eruption 9(6.9) Purpura 2(1.5) Urticaria 5(3.8) Non-specific 1(0.8) Urticaria 1(0.8) FDE 3(2.3) Lichenoid 2(1.5) Urticaria+angioedema 2(1.5) Non-specific 4(3.1)	9(6.9) 8(6.2) 12(9.2)

FDE: Fixed drug eruption, NSAIDs: Nonsteroidal anti-inflammatory drugs, SJS-TEN: Stevens-Johnson syndrome-Toxic epidermalnecrolysis.

DISCUSSION

Among patients presented with adverse cutaneous drug reaction (ACDR) mean age was 45.2 ±1.3 years; majority was of age above 60 years. Youngest patient was 2 years age and oldest one was 74. This is in accordance with previous studies.[12-13] People of advanced age need to take more daily medications and incidence adverse drug reactions are more among them.[14] Some studies found lower age groups as common sufferer.[15] Male female ratio was 1:1.4 as no sex difference of drug reaction was found in previous studies.[12-13] Though some studies found female as predominant sufferer of ACDR.[16-17]

Most of the ACDRsappeared between one to seven days. In a series by Jonardan and Shailendra, average time of development of reaction was four days.[18] Most common type of drug reaction was fixed drug eruption (FDE) mostly caused by NSAID (table III and IV) which is in accordance with previous study.[19] In some previous studiesmaculopapular rash was found as the commonest type (67.7%).[12,20-21]

In a previous study by Jonardan and Shailendra, urticarial drug reaction was found in a higher rate whereas in the current study urticaria found in 8.5% and urticaria + angioedema in 4.6%.[18] In an Iranian study acute urticaria was the most common clinical presentation (59.2%)[22].In another study urticaria and FDE was the commonest pattern.[23] In the current study SJS-TEN was found in 6.9% cases which is closer to the previous studies.[12, 24-25] Acneiform eruption was found in both male and female patients and all were with history of use systemic corticosteroid (6.9%). Mahatme and Narasimharao found acneiform reaction in 10% cases in both male and female caused by oral contraceptives, isoniazide and prednisolone.[26] Lichenoid drug reaction was found in 5.4% developed with antihypertensive and NSAIDs, previously Mahatme and Narasimharao; and Mahapatra and Keshri, found lichenoid reaction in 3-4% cases due to NSAID and hydroxichloroquin.[26-27] Erythema multiforme was found in 7.7% whereas in previous studies EM found in 0.4% to 4.15%.[18,27-28] Anticonvulsant (26.9%) is the commonest group of drug followed by NSAIDs(20.0%) and anti-microbials (AMA) (17.7%). Anticonvulsants (Carbamezepine, Phenytoin, Phenobarbital) was frequent culprit drug for ACDR in earlier studies[18-26].In a study by Chaterjee et al common agents were antimicrobials (34.10%), anticonvulsants (32.88%), anti-inflammatory drugs (21.51%).[23] Antimicrobials was the leading cause of ACDR in study by Mahatme and Narasimharaofound[26].Aamong the patients taken anticonvulsants (Carbamezepine, Phenytoin, Phenobarbital) more faced more severe reactions like SJS-TEN, hypersensitive syndrome and exfoliative dermatitis.Three patients developed acute generalized exanthematous pustulosis (AGEP) due to NSAID (naproxen and diclofenac) and antibiotic (amoxicillin + clavulanic acid). In the study by Mahatme and Narasimhara2% had AGEP due to amoxicillin + clavulanic acid.[25] Exfoliative dermatitis was developed in seven (5.4%) patients due to carbamezepine(3), diclofenac (1), tramadol (1), sulfasalazine (1) and dapson (1). In a study by Talib et al, 8.2% developed exfoliative dermatitis.[12]

CONCLUSIONS

Commonly used drugs are associated with different adverse cutaneous drug reactions. Among them some are life threatening and disabling. It is important to be remain updated about potential adverse effects.

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