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Original Article

Evaluation of demographic and clinical features of the patients admitted with drug reactions

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Abstract

Background Prevalence of cutaneous adverse drug reactions varies depending on genetic background, geographical location, demographic features of the patients and prescribed drugs. This study is conducted to evaluate demographic and clinical features of the patients admitted with drug reactions in dermatologic ward of Afzalipour hospital in Kerman.

Methods This is a retrospective study on two-hundred and forty patients who were admitted with drug reactions in dermatology ward of Afzalipour hospital in Kerman, from 2010 to 2018. Demographic features of the patients and types of the prescribed drugs and drug reactions were recorded. Descriptive data were demonstrated by frequency and mean ±Standard deviation. Correlation between clinical patterns of cutaneous adverse drug reactions with demographic features of the patients were assessed by Fisher's exact test.

Results Most of the patients were in the fourth decade of their lives (24.2%) and female to male ratio was 1.7 to 1.The most common drug reactions were maculopapular eruptions (52.8%), Stevens-Johnson syndrome /toxic epidermal necrolysis (18.7%) and fixed drug eruption (13.6%).The most culprit drugs were antibiotics (76.6%) and antiepileptic classes (14.4%).There was no correlation between age (P. value=0.432) or sex (P. value=0.65) of the patients with types of drug reactions.

Conclusion In the present study, most of the patients were female and in the fourth decade of their lives. Maculopapular eruptions were the most frequent clinical pattern of cutaneous adverse drug reactions. Antibiotics (ceftriaxone) and anticonvulsants (carbamazepine, phenobarbital) were the most frequent culprit drugs for cutaneous adverse reactions.

Key words
Cutaneous; Drug reaction; Maculopapular eruptions.

Introduction

Cutaneous adverse drug reactions (CADRs) are the most common type of drug reactions (30% of total drug reactions) that include unwanted changes in function and structure of skin and mucosa. Incidence of CADRs varies depend on genetic background, age and sex of the patients, concurrent diseases, immune status, duration of treatment, route of administration as well as numbers and type of prescribed drugs.[1-6] Prevalence of CADRs in the developing countries are higher (approximately 2-5%) compared to the developed countries (1-3%).[1] It has been estimated that approximately 5% and 2% of dermatologic administrations and consultations is related to CARDs, respectively.[7,8] Furthermore, mortality rate due

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to the systemic or cutaneous adverse reactions is approximately 0.1-0.3% of the cases. Mechanism of drug reactions is categorized to immunologic and non-immunologic types. Most of the drug reactions are related to immunologic mechanisms (90-94%).[5-10] Severity of CADRs varies from mild and self-limited such as exantematous drug reaction, also known as maculopapular eruption (MPE), to severe and life-threatening reactions. Severe cutaneous adverse reactions (SCARs) include toxic epidermal necrolysis (TEN), generalized bullous fixed drug eruption (FDE), drug reaction with eosinophilia and systemic syndrome (DRESS) and acute generalized exantematous pustulosis (AGEP).[1,9] In this study, we decided to evaluate demographic features and clinical patterns of the patients admitted with drug reactions in dermatologic ward of Afzalipour hospital in Kerman.

Material and methods

This is a retrospective study on the patients admitted with drug reactions in dermatology ward of Afzalipour hospital in Kerman, from 2010 to 2018.This proposal was approved with ethical code of IR.KMU.AH.REC.1397.167 in ethics committee of Kerman University of medical sciences. Demographic features of the patients (age and sex) and types of prescribed drugs and drug reactions were recorded. Data were analyzed by SPSS 16 (software IBM, Armonk, NY, USA). Descriptive data were demonstrated by frequency and mean ± standard deviation.Correlation between clinical patterns of CADRs with age and sex was assessed by Fisher's exact test.

Results

Two hundred and fourteen patients with drug reactions were admitted from 2010 to 2018 in dermatology ward of Afzalipour hospital, Kerman. Mean age of the patients was 30.6±1.2 years (range 1 month-89 years). Most of the patients were female (63.6%) and in the fourth decade (24.3%) **(Table 1)**. The most common drug reactions were MPE (52.8%), Stevens-Johnson syndrome (SJS)-TEN (18.7%) and FDE (13.6%) **(Table2)**. The most common offending drugs were antibiotics (76.6%) and antiepileptic drugs (14.4%). The most common culprit drugs from antibiotic class were ceftriaxone (24.3%), vancomycin (13.1%) and cefazolin (11.7%).The most common offending drugs from antiepileptic class were carbamazepine (5,1%), phenobarbital (5.1%) and phenytoin (4.2%) **(Table3)**. There was no significant correlation between age (P. value=0.432) or sex (P. value=0.65) of the patients with types of drug reactions.

Table 1 Demographic features of the patients with cutaneous drug adverse reaction.

Variables	*Frequency (number)*	*Percentage*
Sex		
Female	136	63.6
Male	78	36.4
Age (years)		
0-10	9	4.2
10-20	23	10.7
20-30	49	22.9
30-40	52	24.3
40-50	41	19.2
50-60	19	8.9
More than 60	21	9.8

Table 2 Frequency of cutaneous adverse drug reactions.

Variables	*Frequency (number)*	*Percentage*
Maculopapular eruption	113	52.8
SJS/TEN	40	18.7
FDE	29	13.6
Urticaria-angioedema	11	5.1
AGEP	9	4.2
DRESS	8	3.7
Erythema multiform	4	1.9

Abbreviations: STS-TEN, Stevens-Johnson syndrome/toxic epidermal necrolysis; AGEP, acute generalized exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms.

Table 3 Frequency of culprit drug classes based on type of drug reaction

Variables	*Anti-biotics*	*Anticonvu-lsants*	*NSAIDS*
Maculopapular eruption	90	16	7
SJS-TEN	33	4	3
FDE	24	3	2
Urticaria-angioedema	6	3	2
AGEP	5	2	2
DRESS	3	2	3
Erythema multiform	3	1	0
Total	164	31	19

Abbreviations: STS-TEN, Stevens-Johnson syndrome/toxic epidermal necrolysis; FDE, fixed drug eruption; AGEP, acute generalized exanthematous pustulosis; DRESS, drug reaction with eosinophilia and systemic symptoms.

Discussion

This study evaluated demographic features and clinical patterns of drug reactions in patients admitted in Afzalipour hospital, Kerman. Most of the patients were female that was consistent with most of the studies.[1,4,10-14] More prevalence of drug reactions in female gender can be explained by disparity in pharmacokinetics and metabolism of drugs due to hormonal effects as well as difference in body mass index between two genders.[9]

Previous studies have demonstrated that elderly patients are more susceptible to adverse drug reactions. This can be due to increased number of taking drugs that predispose them to drug interactions.[9] Furthermore, changes in drug metabolism relative to increased age and underlying diseases such as renal and liver failure can be responsible for more adverse drug reactions in these patients.[15] In the present study, most of our patients were in the fourth decade that was compatible with most of the other studies in Iran and India. Difference in patterns of prescribed drugs and more self-administration by younger patients in our community can explain the cause of more CADRs in this age group in the current study.[1,4,9,11-15]

The most common drug reactions in the present study were MPE (52.8%) and SJS -TEN (18.7%) and FDE (13.6%). In most of the studies, MPE were the most common CADRs. In one study by Talib in Malaysia, the most common CADRs were MPE (22.4%), SJS-TEN (14.2%), and FDE (8.9%) that was nearly compatible to our study.[16]

In another study by Dhanani in India, the most common drug reaction was MPE (38%), followed by urticaria (19%), FDE (12%) and SJS-TEN spectrum (12%). The second most common drug reaction in Dhnani study was urticaria whereas in our study urticaria was the fourth common drug reaction (5.1%). Dhnani study was done on outpatients, but our study was done on inpatients, thus can explain more prevalence of urticaria and less prevalence of SJS-TEN in Dhnanistudy.[1] In another study by Pinto Gouveia in Portugal, the most common drug reactions were DRESS (28%), MPE (21.2%) and SJS-TEN (9.1%). Difference in genetic background of the patients between two studies can be attributed to high prevalence of DRESS in Pinto Gouveia study in comparison to the current study (3.7%).[10]

In the previous studies, the most common culprit drugs for CADRs were antibiotics, anti-convulsantsand non-steroidal anti-inflammatory drugs (NSAIDS).[13,17] In the present study, NSAIDS, antibiotics and anticonvulsants were the most commoncauses of CADRs. Likewise, Ehsani *et al*. in Iran, reported that antibiotics (42.2%), anticonvulsants (36.4%) and NSAIDS (12.4%) were the most common culprit drugs. In Ehsani study, the most common drugs that caused CADRs were anticonvulsants and antibiotics classes [carbamazepine (17.4%) and penicillin (16.5%), respectively]. In the present study, ceftriaxone (24.3%) as well as

carbamazepine and phenobarbital (5.1%, each) were the most common culprit drugs from antibiotics and anticonvulsants classes, respectively.[13]

In the present study, severe cutaneous adverse reactions (SCARs) consisted 40.2% of total CADRs that was nearly similar to the study by Pinto Gouveia *et al*. (49.2%).[10] In another study by Talib, SCARs constituted less percentage of the CARDs (24.5%) compared to the current study. Talib study was conducted on outpatients, but present study was done on inpatients, thereby this can explain lower number of SCARs in the latter study. Mokhtari *et al*. reported SCARs constituted 50.4% of the cases and the most common cause of SCARs were anticonvulsants. In the present study, the most common cause of SCARs were antibiotics.[16]

Conclusion

In the present study, most of the patients admitted with CADRs were female and in the fourth decade of age. MPE, SJS-TEN and FDE were the most clinical patterns of CADRS. Antibiotics and anticonvulsants were the most frequent culprit class of drugs. Furthermore, there was no significant correlation between clinical patterns of CARDs with demographical features of the patients.

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