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THE SPECTRUM OF CUTANEOUS ADVERSE DRUG REACTIONS AND IMPLICATED DRUGS: A CLINICAL STUDY

***Ayman Al Qa'qaa' MD, Rahmeh Fayez MD, Bashar Jarrar MD, Ahmad Alkhaz'ali MD and Hossam Al Salim MD**

Dermatology Section / Dept. of Medicine King Hussein Medical Center Royal Medical Services – Jordan.

***Corresponding Author: Dr. Ayman Al Qa'qaa'**

Dermatology Section / Dept. of Medicine King Hussein Medical Center Royal Medical Services – Jordan.

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ABSTRACT

Background: Skin reactions to drugs are commonly encountered in daily practice at dermatology clinics and emergency rooms and can be caused by any class of medications. These reactions in most of the cases are unpredictable and cannot be avoided. They present with diverse morphological patterns of variable severity, ranging from mild transient rashes to severe longer lasting reactions and even with systemic involvement and eventually death as an outcome. **Objective**: To assess the clinical presentation and morphology of skin reactions attributed to drugs and the causative agents among outpatients attending dermatology clinics at the Royal Medical Services of Jordan Armed Forces. **Materials and Methods**: This is a retrospective study. The case files of 720 patients who attended the out-patient dermatology clinics and were diagnosed of having cutaneous adverse drug related reactions between January 2015 and January 2017 were revised. Each patient's recorded data as gender, age, morphology of cutaneous reaction, history of previous allergies or reactions and the offending drug(s) were analyzed. **Results**: A total of 720 case files have been revised (378 males Vs 342 females). Males were slightly more affected (ratio 1.0 to 0.9). The commonest age group affected was between 41-50 years (33%). Fixed drug eruption was the commonest presentation (37%). Antibiotics were the commonest drugs to cause skin reactions in 283 patients (39.3%). Co-trimoxazole was the offending drug in 157 patients (21.8%). **Conclusion**: Cutaneous adverse drug reactions are common and widely encountered in daily practice. Patients and treating physicians should be aware of the possible skin reactions that might be induced by drugs.

KEYWORDS: drugs, cutaneous adverse drug reactions.

INTRODUCTION

Skin reactions to drugs are commonly encountered in daily practice at dermatology clinics and emergency rooms and can be caused by any class of medications. These reactions in most of the cases are unpredictable and cannot be avoided. They present with diverse morphological patterns of variable severity, ranging from mild transient rashes to severe longer lasting reactions and even with systemic involvement and eventually death as an outcome.[1,2] They are responsible for 5 to 9% of all hospital admissions.[3,4]

To identify the causative agent for suspected drug induced skin reaction is of a significant challenge in a lot of cases especially in patients with chronic diseases taking multiple medications at the same time. Factors that may help identifying an accused drug may include the time between starting the medication and onset of reaction, improvement of the condition with the discontinuation of the suspected medication, history of similar or different skin reaction(s) with the same medication, recurrence of the rash with the re-introduction of the accused medication and that the reaction is being known to be induced by that particular medication.[5,6] Taking history from the patient is of great value in identifying the causative drug and helps in planning a treatment strategy and predicting the outcome and prognosis.

Antibiotics in general, particularly aminopenicillines and nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly incriminated to induce skin reactions. New eruptions are consistently emerging with the introduction and use of newly developed medications especially chemotherapeutic agents and biologics.[7]

MATERIAL AND METHODS

This is a retrospective study, carried out in dermatology clinics at four military hospitals in Jordan operated by the Royal Medical Services of Jordan Armed Forces (RMSJAF). King Hussein Medical Center which is the main and the largest military hospital in Jordan, located in the capital Amman. The 2nd hospital is in the eastern part of Jordan, in Zarka. The 3rd hospital is in Irbid which is the largest northern city and the 4th hospital is in the southern city, Al-Karak. The case files of 720 patients

who attended these dermatology clinics and were diagnosed of having cutaneous adverse drug related reactions between January 2015 and January 2017 were revised. Each patient's recorded data as gender, age, morphology of cutaneous reaction, history of previous allergies or reactions and the offending drug(s) were analyzed. An approval from the ethical committee of the RMS-JAF was obtained to conduct this study.

RESULTS

A total of 720 case files have been revised. The analysis showed that men were slightly more affected than females (378 males Vs 342 females) with a ratio of (1.0: 0.9). But no difference in the pattern of skin affection was noted between the two genders.

The age of affected patients ranged from 14 – 69 years, with the maximum affection in the age group of 41-50 years (33%) followed by the age group 51-60 (28%) and 24% for the age group 31-40 years. Table (1) shows age and sex distribution of the study group.

Table 1. Age and Sex Distribution of the Study Group

Age group (years)	Male (%)	Female (%)	Total (%)
10 - 20	15 (3.9)	7 (2.0)	22 (3.0)
21 - 30	27 (7.2)	23 (6.7)	51 (7.0)
31 – 40	89 (23.5)	85 (24.9)	173 (24)
41 - 50	123 (32.5)	115 (33.6)	237 (33)
51 - 60	103 (27.4)	99 (29)	201 (28)
61 - 70	21 (5.5)	13 (3.8)	36 (5.0)
Total	378 (100)	342 (100)	720 (100)

The commonest cutaneous drug reaction was fixed drug eruption (37%), followed by exanthematous eruptions (23%) and urticarial reactions (19%). The results are illustrated in table 2.

Table 2. Clinical presentation of skin reactions in our Study Patients

Pattern of Reaction	No. of patients	(%)
Fixed drug eruption	267	37
Exanthematous eruptions	165	23
Urticarial reactions	137	19
Erythema multiforme	50	7
Erythroderma	16	2.2
Acute Generalized Exanthematous Pustulosis	7	0.97
Steven-Johnsons syndrome	6	0.83
Toxic epidermal necrolysis	2	0.28
Various other reactions	70	9.72

Antibiotics were the commonest drugs to cause skin reactions in 279 patients (38.7%) and co-trimoxazole was the incriminated antimicrobial in 157 patients (21.8%), followed by aminopenicillins in 91 patients (12.6%) and ciprofloxacin in 27 patients (3.7%).

Non-steroidal anti-inflammatory drugs (NSAIDs) caused 30.4% (219 patients) of the reactions. Ibuprofen was accused in 103 patients (14.3%) followed by diclofenac sodium in 93 patients (12.9%). Antiepileptics came in the third place causing 13.6% of the reactions (98 patients) and allopurinol 3.3% (24 patients). In 81 patients (11.25%) the offending drug was unknown. Table 3 shows the class of medications and incriminated drugs to cause skin reactions.

Table 3. Common drugs to cause skin reactions in our study

Group (%)	Drugs (%)	No. of patients (%)
Antimicrobials 279 (38.7%)	Co-trimoxazole	157 (21.8)
	Aminopenicillins	91 (12.6)
	Ciprofloxacin	27 (3.7)
	Others	4 (0.6)
NSAIDs 219 (30.4 %)	Ibuprofen	103 (14.3)
	Diclofenac sodium	93 (12.9%)
	Naproxen	21 (2.9%)
	Meloxicam	2 (0.3%)
Antiepileptics 98 (13.6%)	Carbamazepine	69 (9.6%)
	Phenytoin	23 (3.2%)

	Lamotrigine	6	(0.8%)
Xanthine oxidase inhibitors	Allopurinol	24	(3.3%)
Antispasmodics	Hyoscine butylbromide	12	(1.7%)
Chemotherapeutics	Tarceva	4	(0.6%)
Homoeopathic medicine		3	(0.4%)
Unknown		81	(11.25%)

DISCUSSION

Many studies from different parts of the world, including the Middle East, have discussed skin reactions induced by medications assessing their morphology, severity and causative medications. Up to our knowledge, this is the first study in Jordan to elicit the relation between drugs and skin rashes attributed to their use.

In this study, males were a little bit more affected than females; the ratio was (1.0:0.9). This difference is statistically insignificant. A study by Sharma R et al showed the ratio to be (1.7:1.2).[8] The females were out numbering males with variable ratios in different studies and that was attributed to differences in immunological responses and hormonal effects between the two sexes.[7,9,10]

The most affected age group in this study was between 41-50 years (33%), followed by the age group 51-60 years (28%). This might be explained by the changes in metabolism and pharmacodynamics that start at late aduldhood period. Also, many patients in these age groups are diagnosed to have chronic diseases and start combination of medications they were not exposed to before. In two different studies, the old age groups were found to be affected more.[3,9] While earlier age groups were reported to be affected more by different other studies.[6,11]

Fixed drug eruption was noted as the commonest clinical presentation of skin reactions to medications. Although this reaction is known to recur with the re-introduction of the offending drug or even a class of medications, some patients either forget to tell their treating physician about past events of allergy or they cannot recall the name of drug(s) they are allergic to. In addition to the fact that some patients use drugs offered by friends or people who are not medically oriented but they used the medication for some reason and start to spread their own experience with such a drug. Varieties of skin reactions to medications were reported as the most commonly observed by different studies as fixed drug eruption[12], exanthematous eruptions[1,6], urticarial.[3,13]

The most commonly incriminated group of medications was antibiotics. Co-trimoxazole was the on top of the list. In our country, this drug is still prescribed widely by general practitioners and some other specialists for different indications especially for urinary tract infections and also used by many patients even without physician prescriptions as it is sold as an over the counter medication.

In conclusion, cutaneous adverse drug reactions are common and widely encountered in daily practice. Patients and treating physicians should be aware of the possible skin reactions that might be induced by drugs. Patients need to know well the type of medicine they are allergic to in order to avoid more serious reactions.

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