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Serious drug toxidermia : a retrospective study

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ABSTRACT

The objective of this work is to describe the epidemiological and clinical characteristics of serious drug toxidermia. This is a retrospective study of 220 cases of serious drug toxidermia notified to the National center of pharmaovigilance of Morocco between 2010 and 2012. These toxidermia were registered with an average of 73 ± 27.17 cases /year. The average age of patients was 39 ± 1.62 years and the sex ratio (F / M) was 1.54. Adults aged between 16 and 69 years are most affected (78%). The most observed toxidermia are usually Rash with 26.5% of cases, with 11.1% Erythematous Rash, Stevens Johnson syndrome (8.9%), Acute Generalized exanthematous Pustulosis (6.8%). The mean time to onset of toxidermia was 15 ± 3.6 days and in 76% of cases, patients were hospitalized.

The most drugs are involved: Antibacterials for Systemic Use (18.1%), Antimycobacterials-Antituberculosis (15.1%), Antipyretic / Analgesics (6.6%). The WHO causal relationship between taking the drug and the onset of the adverse reaction, accountability was 69% of probable cases, 11% of possible cases, certain 11% of cases and 9% unclassified cases. The outcome was favorable in 82% of cases, 1% of cases recovered with sequelae, 12% of unknown cases and 5% died.

KEYWORDS

Toxidermia;
Drug;
Epidemiology.

INTRODUCTION

The drug is administered for curative, preventive or diagnostic, However, his action may exceed the desired aim. Many drugs are responsible for accidents, called adverse drug reactions, which by their frequency or severity represents a public health problem both in Morocco and in the world[1].

In France and in most Western countries, ADRs represent 10% of hospital patients[2]. The annual incidence of hospitalizations for adverse drug reactions between 3 and 5% of all hospital admissions[3-4].

Other hand, drug toxidermia are secondary mucocutaneous complications due to ingestion or injection of a drug systemically[5] ares among the most common adverse drug reactions with around 20% of notifications drug events[6].

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In Morocco, studies on toxidermia are very fragmentary, they are based on the description of clinical cases known. The aim of our study was to determine the frequency, the clinical aspects of serious toxidermia and therapeutic classes most involved reported to the National Center of Pharmaovigilance of Morocco during the period 2010-2012.

PATIENTS AND METHODS

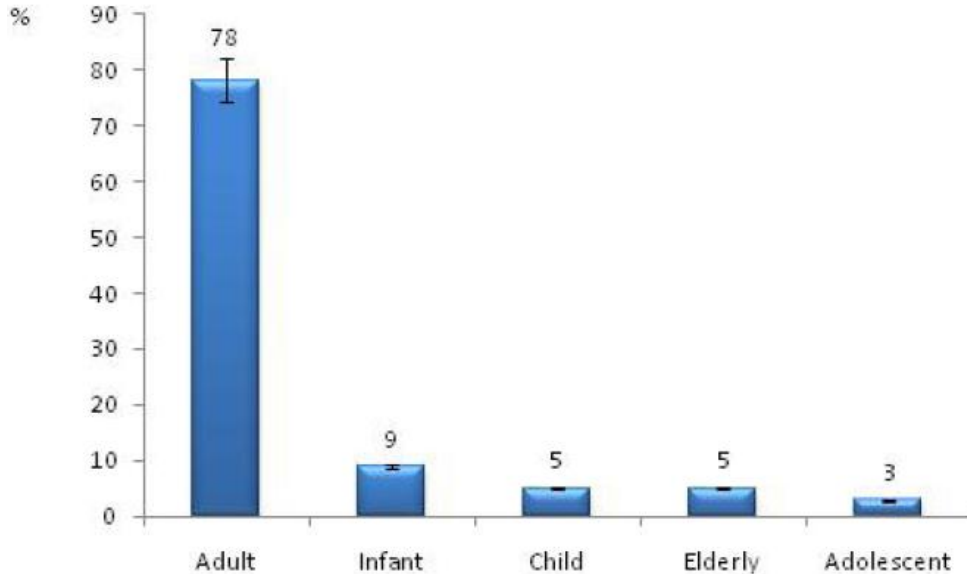
This is a retrospective study, cases of drug-induced serious toxidermia reported to the to the National center of pharmaovigilance of Morocco over a period of three years (2010-2012). This study is based on spontaneous reporting data from active and declarations sheets completed by healthcare professionals and the pharmaceutical industry. A patient may have one or more cutaneous adverse drug reactions following therapy.

The statistical methodology adopted was based on the calculation of frequencies or averages of each variable studied. The variables studied concern epidemiological characteristics of patients (age, sex), clinical (symptoms, severity, evolution, time of onset) and the most incriminated drugs. The chi-square test (χ^2) with 5% is used to calculate significant differences between the variables.

RESULTS

During the 2010-2012 study period, 220 cases of serious toxidermia were notified to the National center of pharmaovigilance of Morocco, averaging 73 ± 27.17 cases /year, representing 15.5% of all skin reactions collected. 75% of cases were collected by spontaneous way. The average age of patients was 39 ± 1.62 years, with ends ranging from one to 85 years. The sex ratio (F / M) was 1.54, with a highly significant difference (χ^2 = 8.29; P <0.001). The most affected age group was composed essentially of adults (78%) (χ^2 = 154.3, P <0.001), followed by that of infants (9% ; χ^2 = 134.1; P <0.001 and children (5% ; χ^2 = 164.9; P <0.001) (Figure 1).

The types of toxidermia are distributed according to the recommended terms and terms of inclusion we have recorded in TABLE 1. The most commonly observed toxidermia were: Rash (maculopapular rash papular, rash erythematous, purpuric rash, Photosensitive rash, Rash pruritic, vesiculobullous rash, Toxicoderma, Skin rash, Drug eruption) with 26.5% of cases, Erythematous rash (erythema, Erythroderma) with 11.1%, Stevens Johnson syndrome (8.9%), Acute Generalized exanthematous Pustulosis (6, 8%), urticaria (5.9%), Epidermal Necrolysis (Lyell Syndrome) and



Infant :1 month < to 4 year, Child : 4 ans to < 11 year, Adolescent : 11 year to < 16 year, Adult : 16 year to < à 69 year, Elderly :e+69 year.

Figure 1 : Distribution of toxidermia according to age groups

TABLE 1 : Distribution of toxidermia

Reaction (Prefered Terms)	Reaction (Inclused Terms)	n	%
Stevens Johnson syndrome	**Stevens Johnson syndrome**	**21**	**8,9**
Rash	Rash maculo-papular	18	7,6
	Rash	9	3,8
	Rash erythematous	8	3,4
	Rash purpuric	2	0,8
	Photosensitive rash	1	0,4
	Rash pruritic	5	2,1
	Vesiculobullous rash	4	1,7
	Toxicoderma	10	4,2
	Skin eruption	5	2,1
	Drug eruption	1	0,4
Rash pustular	Rash pustular	1	0,4
Rash erythematous	Erythema	15	6,4
	Erythroderma	11	4,7
Acute generalized exanthematous pustulosis	Acute generalized exanthematous pustulosis	16	6,8
Urticaria	Urticaria	14	5,9
Epidermal necrolysis	Lyell syndrome	13	5,5
Pruritus	Pruritus	13	5,5
Angioedema	Quincke's oedema	12	5,1
Epidermal necrolysis	Epidermal necrolysis	5	2,1
	Toxic epidermal necrolysis	1	0,4
Fixed eruption	Fixed eruption	5	2,1
Skin necrosis	Skin necrosis	5	2,1
Erythema multiforme	Erythema multiforme	4	1,7
Bullous eruption	Bullous eruption	3	1,3
Skin injury	Skin injury	3	1,3
Skin ulceration	Skin ulceration	3	1,3
Urticaria acute	Urticaria acute	3	1,3
Eczema	Dermatitis eczematoid	2	0,8
Dermatitis lichenoid	Lichen	2	0,8
	Dermatitis lichenoid	2	0,8
Psoriasis	Psoriasis	2	0,8
Sweet's syndrome	Sweet's syndrome	2	0,8
Alopecia	Alopecia	1	0,4
Angioedema	Quincke's oedema	1	0,4
	Angioneurotic oedema	1	0,4
Folliculitis	Folliculitis	1	0,4
Photosensitivity reaction	Photosensitivity reaction	1	0,4
Skin exfoliation	Red man syndrome	1	0,4
Skin disorder	Skin disorder	1	0,4
	Skin infection	1	0,4
Skin discolouration	Skin hyperpigmentation	1	0,4
Skin reaction localised	Skin reaction localised	1	0,4
Vitiligo	Vitiligo	1	0,4

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TABLE 2 : Distribution of the most implicated drugs

Therapeutic classes	International Nonproprietary Name	n	%
Antibacterials for Systemic Use	Amoxicillin sodium/Clavulanate potassium	2	0,6
	Amoxicillin/Clavulanic acid	7	2,1
	Ampicillin sodium/Sulbactam sodium	1	0,3
	Clavulanate potassium/Amoxicillin trihydrate	7	2,1
	Benzylpenicillin	4	1,2
	Terbinafine	4	1,2
	Amoxicillin	7	2,1
	Amoxicillin sodium	2	0,6
	Amoxicillin trihydrate	2	0,6
	Ampicillin trihydrate	3	0,9
	Cefixime	2	0,6
	Ceftriaxone sodium	8	2,4
	Sulfamethoxazole/Trimethoprim	7	2,1
	Metronidazole	4	1,2
Total		60	18,1
Antimycobacterials - Antituberculeux	Ethambutol dihydrochloride	2	0,6
	Ethambutol	6	1,8
	Pyrazinamide	12	3,6
	Isoniazid/Ethambutol/Pyrazinamide/Rifampicin	8	2,4
	Isoniazid/Rifampicin	3	0,9
	Isoniazid	7	2,1
	Rifampicin	12	3,6
Total		50	15,1
Antipyretic /analgesics	Paracetamol	18	5,4
	Acetylsalicylic acid	4	1,2
Total		22	6,6
Antiepileptic	Phenobarbital	12	3,6
	Carbamazepine	7	2,1
Total		19	5,7
Anti-viral	Peginterferon alfa-2a	3	0,9
	Interferon beta-1a	2	0,6
Total		5	1,5
Anti uremic	Allopurinol	15	4,5
Total		15	4,5
Antiacid	Omeprazole	4	1,2
Total		4	1,2
Antifungal for systemic use	Terbinafine hydrochloride	1	0,3
Total		1	0,3
General total		332	100

Prurirus with 5.5% for all of them, Angioedema (angioneurotic edema's) with 5.1% of cases. The mean time to onset of toxidermia was 15 ± 3.6 days.

Among the serious cases, hospitalization was made in 76% of cases. Most drugs implicated in the onset of toxidermia and therapeutic classes according to the International Nonproprietary Name are represented in TABLE 2.

According to the results of TABLE 2. The most incriminated drugs were: 18.1% Antibacterials for Systemic Use (Ceftriaxone Sodium, Amoxicillin / Clavulanic acid, sulfamethoxazole / trimethoprim, Amoxicillin), 15.1% Antimycobacterials-Antituberculeux (Pyrazinamide, Rifampicin, Isoniazid/ Ethambutol/Pyrazinamide/ Rifampicin, Ethambutol), 6.6% Antipyretic /Analgesics (Paracetamol, Acetylsalicylic acid), 5.1% Antiepileptic (Phenobarbital, Carbamazepine), 4.5% Anti uremic (Allopurinol).

According to the accountability of the World Health Organization method, the relationship of cause and effect between the medication and the occurrence of the adverse event was probable in 69% of cases, 11% of the possible cases, 11 % of cases and certain 9% of unclassified cases. The outcome was favorable in 82% of cases, 1% of cases recovered with sequelae, 12% of unknown cases and 5% are fatal.

DISCUSSION

Toxidermia drug can cause different types of lesions following administration by the enteral, intravenous, subcutaneous or intramuscular medication[5].

In most of cases, they are manifested by non-specific cutaneous signs. Only certain toxidermia have specific clinical aspect (fixed drug eruption) or quasi specific (toxic epidermal necrolysis, acute generalized exanthematous pustulosis)[7], are the most frequent adverse effects (1-3%) of drugs[8].

The work we have done describes the clinical and epidemiological aspects of toxidermia notified CAPM with a total of 220 recorded cases. The sex ratio (F / M) was 1.54. This result is comparable to that described in the literature[9-10]. It could be explained by the drug absorption mechanism, hormonal factors and increased consumption of drugs by self-medication among women than men.

Our results showed that all age groups are affected, but the greater frequency of toxidermia was observed in adults (78%), which is similar with the literature[11].

The prevalence of toxidermia in adults could be explained by self-medication and the increase of drug consumption[1].

The Antibacterials for Systemic Use were the most implicated drug class (18.1%), these results are similar to other studies[12], followed by the anti-tuberculosis drugs (15.1%), which are described by other authors in the onset of toxidermia[11-13-14-15].

Furthermore, in black Africa, given the prevalence of tuberculosis, toxidermia due Tuberculosis drug, including isoniazid, rifampicin are increasingly observed[16-17-18].

The most toxidermia were generally observed: Rash with 26.5% of cases, with 11.1% Erythematous Rash, Stevens Johnson syndrome (8.9%), Acute Generalized exanthematous Pustulosis (6.8%), urticaria (5.9%), Epidermal Necrolysis (5.5%), with 5.5% Prurirus, Angioedema (5.1%). In littérautre, severe forms of life-threatening patient are: acute generalized exanthematous pustulosis, syndrome, Stevens-Johnson epidermal necrolysis[14], which is similar with our results. The toxidermia are most often benign in 90%, but their evolution to reactions involving the vital prognosis is unpredictable[19].

CONCLUSION

The toxidermia are unpredictable event that could however be limited by the rational use of medicines. The diversity of their clinical manifestations, the difficulty of their diagnosis and the involvement of different mechanisms in their occurrence would require early treatment to prevent these accidents.

CONFLICTS OF INTEREST

None declared

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