Fixed Drug Eruptions (FDE) in an Urban Centre in South-South Nigeria

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Bolaji Ibiesa Otike-Odibi, Dasetima Dandeson Altraide, Christiana Olaitan Okunoye

Department of Internal Medicine, University of Port- Harcourt Teaching Hospital, Port Harcourt, Nigeria.

ABSTRACT

BACKGROUND

Fixed drug eruptions are adverse cutaneous reactions to ingested drugs, characterized by the formation of solitary or multiple erythematous patches, plaques, bullae or erosions that reoccur at an identical skin site within hours of re ingestion of the offending drug. The objective of this study was to describe the epidemiology of Fixed drug eruptions with the identification of common causative drugs among patients at the dermatology clinic of an urban tertiary hospital in the South-south region of Nigeria.

METHODS

All consecutive patients with a diagnosis of fixed drug eruptions seen at the dermatology clinic between January 2005 to January 2013 were included in the study. The diagnosis of fixed drug eruptions was made based on clinical findings of lesion (s) of the same form occurring twice or more at the same sites as a result of a readministration of a causative drug, and confirmation by a challenge test.

RESULTS

The diagnosis of fixed drug eruption was made in 99 out of 5106 (1.93%) patients, with a slight female dominance. FDE affected all age groups, the youngest presented at 9months of age andthe oldest at 86years. Majority of patients (66.7%) did not know the offending drug. The most implicated drugs were the sulphonamides (21.2%), followed by antibiotics made up of ampiclox, tetracycline and penicillin (4.04%) and Non steroidal anti inflammatory drugs (3.03%). The commonest site of presentation was the face (32%), especially the mucosa of the mouth, followed by generalized presentation (28%).The frequency of Lower limb presentation was (13%),followed by the upper limb (11%) and the trunk(7.1%).

CONCLUSION

Fixed drug eruptions are a cause for great concern to the patient. Consistent with some other studies sulphonamides, clotrimoxazole and fansidar were the most implicated drugs.

KEYWORDS

Fixed drug eruptions; Epidemiology: Out Patient clinic; Nigeria.

Correspondence: Dr B.I. Otike-Odibi
Email: otike_odibi@yahoo.co.uk

INTRODUCTION

Fixed drug eruptions are a cause for great concern in our environment because of the cosmetic embarrassment it causes. Fixed drug eruptions are characterized by well circumscribed hyper pigmented macules or patches, erosions or bullae, that reoccur at sites of initial presentation for unknown reasons. The most characteristic presentation of fixed drug eruption is a circumscribed lesion that heals with residual hyper pigmentation

and recur at the same anatomic site. Fixed drug eruption lesions initially appear when susceptible patients are sensitized to a particular drug. Such sensitization occurs more rapidly in patients intermittently receiving the causative drugs rather than those continuously receiving them.

Careful history taking about drug intake and a prior history of recurrent lesions in the same sites are essential for the precise diagnosis of fixed drug eruptions[2]. The lesion usually flares within 30minutes to 8hours after drug intake; mean length of time from drug intake to the onset of symptoms is approximately two hours. Sensation of burning often precede the appearance of lesions[2]. Guin[3] et al reported that FDE lesions appeared to migrate because some of the previously involved sites did not flare with each exposure whereas others flared.

The causes of Fixed drug eruptions differ from one place to the other and from one time to the other depending on the availability of drugs, socioeconomic status, literacy and application and adherence of drug control measures[4,5]. The diagnosis and management of FDEs can be compounded by non-identification of the causative drug. In Nigeria this is a major challenge as there is a high patronage of patent medicine stores and other unregulated outlets that dispense drugs to patients without labels.

There is a paucity of data on the epidemiology and pattern of fixed drug eruption in South-South Nigeria. Such data peculiar to the environment will be useful in planning for FDE care as well as provide information for patient education. It is on this basis that the purpose of this study is to describe the epidemiology of fixed drug eruptions and give list of causative drugs and body sites affected in the South-South region of Nigeria.

MATERIALS AND METHODS

All consecutive patients with a diagnosis of Fixed drug eruptions seen at the Dermatology clinic between January 2005 to January 2013, who gave informed consent were included in this retrospective study.

Data was obtained from the medical records of patients diagnosed with fixed drug eruptions. Inclusion criteria included informed consent, patients above the age of five years and non pregnant and lactating patients.

All institutional ethical protocol and guidelines were followed to protect patient's privacy and safety in the course of this retrospective study. Three Dermatology specialists validated the cases if they satisfied the following condition. Lesion(s) of the same form occurring twice or more at the same site as a result of re-administration of a causative drug. Confirmation by oral provocation tests was performed in an effort to confirm the history given by the patient. The patient's were given one tenth of the usual dose of the drug and it was considered positive. If previous FDE sites reactivated with marked erythema, burning and itching. This test was done with relative safety with a low risk of inducing systemic adverse reactions.

RESULTS

The diagnosis of FDE was made in 99 out of 5106 a prevalence of (1.93%). There was a slight female preponderance with 54(54.54%) of females and 45 (45.45%) of males. The age range was from 9months to 86years with a mean of 43.5years. More patients were seen in the third decade 37(42.05%).Table 1 shows the age distribution of the subjects.

Table1: Showing age distribution of patients.

Age distribution	Number (%)
0 -10	2 (2.02%)
11 -20	20 (2.02%)
21 -30	37 (42.05%)
31 -40	12 (12.1%)
41-50	8 (8.08%)
51-60	8 (8.08%)
61-70	7 (7.07%)
71-80	3 (3.03%)
81-90	2 (2.02%)

Out of the 99 patients with FDEs 33 (33.33%) could identify the implicatingdrugs and this was confirmed by oral provocation tests. The offending drug could not be identified in66 (66.67%) of patients.

Table 2, shows the frequency of drug involvement in FDEs using the oral provocation test. Oral provocation tests indicated that trimethoprim and sulfamethoxazole (co-trimoxazole) was the cause of FDE in 16(48%) of patients followed by fansidar 4 (12.12%),penicillin 2(6.06%).

The following had 1(3.03%) respectively: griseofulvin, metakelfin, piroxicam, naloxone, Ibuprofen, buscopan, ampiclox, tetracycline and quinine. Two patients gave a history of taking local herbs , this could not be verified by oral provocation tests.

Table 2: Showing list of implicated drugs with percentages.

Name of drug	Number	Percentages(%)
Co-trim oxazole	16	48
Fansidar	4	12.12
Penicillin	2	6.06
local herbs	2	6.06
Griseofulvin	1	3.03
metakelfin	1	3.03
Piroxicam	1	3.03
Naloxone	1	3.03
Ibuprofen	1	3.03
Buscopan	1	3.03
Ampiclox	1	3.03
Tetracycline	1	3.03
Quinine	1	3.03

Fixed drug eruptions most often involved the face and the lips in co-trimoxazole, with 16(37.5%) patients affected, and a male preponderance of 9(56.25%). The only case of genital affectation was in a female. Fansidar had 2 (50%) of patients with face and lip involvement and a male preponderance of 3(75%). The facial presentation was the commonest with 13 (39.4%) patients affected, followed by generalized presentation with 9(27.3%).

Two thirds of the patients with FDEs from non-steroidal anti-inflammatory drugs (naloxone and ibuprofen) showed limb presentations. Antibiotics (Ampicloxand tetracycline)had facial manifestations while the presentation with penicillin induced FDE was generalized. The distribution of the body sites involved in FDEs is shown in table 3.

Table 3: Showing drugs with sites of body involvement.

Drug	Male	Female	Face	Genital	Trunk	Limbs	Generalized
Co-trimoxazole	9	7	6	1	2	3	4
Fansidar	3	1	2	0	0	0	2
Penicillin	0	2	0	0	0	0	2
Local herbs	1	1	1	0	0	0	1
Griseofulvin	0	1	0	0	0	1	0
Metakelfin	0	1	0	0	1	0	0
Piroxicam	0	1	1	0	0	0	0
Naloxone	1	0	0	0	0	1	0
Ibuprofen	0	1	0	0	0	1	0
Buscopan	0	1	0	0	1	0	0
Ampiclox	1	0	1	0	0	0	0
Tetracycline	0	1	1	0	0	0	0
Quinine	1	0	1	0	0	0	0
Total	16	17	13	1	4	6	9

DISCUSSION

Fixed drug eruption is a cause of great concern to our patients because of the obvious residual hyper pigmentation it manifests with. It affects all ages 6 with a wide range from 9monthsto 86years reported in this study. More patients were in their third decade of life. This is coroborated by other studies that had patients between the ages of 20 to 40 years[7,8]. No specific explanation can be given for this age distribution of FDE reported in this study. More females were affected in this study 54(54.54%), with a ratio of 1.2:1, comparable with the study from Pakistan9 with a men to women ratio of 1:1.1, this is contrasted by the studies of Schgal6 and Nnoruka1 with male preponderance.9The female preponderance in this study does not appear to be significant.

The overall prevalence of FDE in this study was 1.93%. The prevalence of fixed drug

eruption in a study in Ibadan was 2.2%[10], while a study in Enugu reported a prevalence of 0.5%[1]. The prevalence of FDEs in studies outside Nigeria, in Pakistan documented a prevalence of 0.7%[9]. Fixed drug eruptions in a study in Cameroun[11], caused 60.7% of reported adverse cutaneous drug reactions. The results of the study in Ibadan10 is comparable to that of our study, while that of Enugu[1] and Pakistan[9] are lower (0.7%). The variations in this prevalence of the various studies may be due to better adherence and application of drug control measures and the pattern of drug prescriptions in these settings. It is known that some cases of recurrent exacerbations of FDE lesions without significant history of drug intake might be attributable to nonspecific exogenous factors. Non medical factors such as food and ultraviolet irradiation, have also been reported to precipitate exacerbations of FDE lesions[12,13,14]. This could explain the large number of patients with no history of drug intake in this study. In addition that high utilization of patent medicine stores in this region that dispense drugs to patients without a prescription and labelling also results in the inability of the patients to identify the causative drugs they used by name.

The finding of patients without knowledge of the causative drug in this study is similar to that of a study in Korea15 with 134 patients with FDE, that reported only 38(28.4%) with a clear documentation of causative drugs, comparable to the 33.33% reported in this study. This scenario poses a challenge for the confirmation of FDE diagnosis as the Oral provocation tests which is the most reliable way of testing for FDE16 is impossible to implement without a knowledge of the offending drug.

Co-trimoxazole accounted for 48.5% of fixed drug eruptions in this study and induced lesions mainly on the face and lips. This is consistent with the outcome of other studies that found co-trimoxazoleto be the most implicated drug[6,17,18,19]. Nnoruka, et allaslo reported that anti-malarials containing sulfadoxine and pyrimethamine were the commonest causes of FDEs in a study in Enugu, with the mucosa of the lips as the commonest site. The outcome of their study1is in line with our findings from this study and highlights the importance of sulfonamides as major cause of FDEs and other forms of adverse drug reactions.

The findings in our study of cotrimoxazole as the most frequent cause of FDE, is contrasted by Olumide[20] who found pyrazolone analgesics to be the most implicated. This difference in pattern may be due to the fact that at the time of this study pyrazoloneanalgesics are no longer commonly used. The trend of NSAIDS and analgesics as a predominant cause of FDEs is also reported by a Jung et al, in Korea who found Non-steroidal anti-inflammatorydrugs and acetaminophen to be the mostimplicated[15] in FDEs accounting for 71% of patients with accounted drug history. The large proportion of subjects (72.6%) in this study who had no knowledge of the offending drug in this study may be responsible for this outcome. As NSAIDs and acetaminophen may be sold over the counter and most people have a good knowledge of these drugs.

CONCLUSION

Sulphonamides are the commonest cause of FDE in this study. The commonest site of presentation of FDE lesions was the face, with a majority of patients not knowing the causative drug. It is recommended that the strict application and adherence of drug control measures be implemented to reduce the number of FDEs patients who cannot identify the causative drug. Better regulation of patent medicine stores and improved pharmacovigilance process are required to improve our knowledge and management of FDEs.

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