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CROSS SECTIONAL STUDY OF FIXED DRUG ERUPTIONS AMONG PATIENTS ATTENDING A TERTIARY CARE CENTER IN SOUTH GUJARAT

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ABSTRACT **Background:** Fixed drug eruption (FDE) is a cutaneous adverse drug reaction (CADR) characterized by well-defined round erythematous lesions as a result of systemic exposure to a drug. The main objective is to study epidemiological profile, clinical patterns of FDE and identify the culprit drugs.

Methods: A cross sectional, observational study was conducted between June 2019 to June 2020 at dermatology OPD. All patients presenting with clinical lesions of FDE were enrolled. Detailed history and clinical examination of the lesion and the drug was done. Naranjo ADR probability scale was used for determining causality with drug.

Results: 66 patients of Fixed drug eruptions [FDE] were enrolled. Most common age group was 41-50 years with mean age being 42.19 years with 60.60% males and 39.4% females. We could not suspect culprit in 17% cases. Commonest drugs were belonging to Antibiotics group-38% followed by NSAIDS-30%, antiepileptics-4.5%, antifungal-3% and others-7.5%. Pigmented FDE (68%) was the commonest clinical form followed by Bullous FDE (23%). Commonest site of occurrence was oral cavity (65%) followed by genitals (48%). 45.5% cases had past history of multiple episodes. 56% patients were developed lesions within 24 hours of drug intake. According to Naranjo ADR score, 45(68%) patients had definite cause and 10(15%) patients had probable cause.

Conclusions: Commonly used drugs (Antibiotics and NSAIDS) lead to maximum number of FDEs. Knowledge of these drug eruptions, causative drugs and clinical patterns are essential to prevent future episodes of cutaneous ADRs.

KEYWORDS : Fixed drug eruption, Pigmented FDE, Naranjo score.

INTRODUCTION

Fixed drug eruption (FDE) is a cutaneous adverse drug reaction characterized by recurrent well– defined lesions occurring at the same sites each time the offending drug is taken.[1] It was first described by Bourns in1889; five years later, it was termed by Brocq as "eruption erythemato-pigmentee fixe".[2] FDE accounts for 4-39% of all drug eruptions whose incidence has tended to increase in the recent years.[1,3] It is more common in females, particularly in the range of 40–80 year olds.[4] FDE usually develops 30 min to 8 h after drug exposure. Typically, FDE presents as a sharply– defined, round or oval erythematous and oedematous plaque which evolves to become dusky, violaceous and occasionally vesicular or bullous. The eruption may initially be morbilliform, scarlatiniform or erythema multiforme like; urticarial, nodular or eczematous lesions are less common. Lesions are usually solitary or few in number although multiple lesions may be present or may develop as a consequence of repeated challenges. Commonly affected sites include the lips, genitals, palms and soles; 5% of cases may have an exclusive mucosal involvement.[1,5]

Several variants of fixed drug eruption have been described, based on their clinical features and the distribution of the lesions. These includes Pigmented, Generalized or multiple, Linear, Wandering, Nonpigmenting,Bullous, Eczematous, Urticarial, Erythema dyschromicum perstans, Vulvitis , Oral eruption, and Psoriasiform FDE.[6]

The drugs most frequently associated with FDE include antibiotics (sulfonamides, tetracyclines, β-lactams, fluoroquinolones, macrolides), NSAIDs, acetaminophen, aspirin, barbiturates, dapsone, proton pump inhibitors, and azole antifungal drugs.[7]

Oral provocation of the implicated drug is the gold standard to confirm drug causality, however should not be done in case of Generalised Bullous FDE. Patch testing is an alternative diagnostic method.[1]

AIMS AND OBJECTIVES

To study epidemiological profile, morphological patterns of FDE and to identify the culprit drugs causing FDE.

METHODS

A cross sectional, observational study was conducted over a period of 1 year between June 2019 to June 2020 at dermatology OPD in a tertiary care hospital in South Gujarat. All patients presenting with cutaneous adverse drug reactions were examined. Only those having clinical lesions of FDE were enrolled irrespective of age and sex. Those who refused to give consent were excluded from the study. Thorough history pertaining to drug intake and detailed clinical examination of patients having FDE was done. Assessment about causality of drug was done using Naranjo ADR probability scale. [8] A prestructured proforma was used to collect the data. Exposure variables collected were socio-demographic profile like age, sex, co-morbidities etc. Outcome variables collected were clinical features, examination findings, etc. All data was entered using MS Excel software and analysis was done using MS Excel and SPSS software. Various statistics like proportions, percentage and ratio were calculated for above variables.

Naranjo score:-

>9	Definite
5-8	Probable
1-4	Possible
0	Doubtful

RESULTS

In our study, out of total 245 patients with cutaneous adverse drug reaction (CADR) examined, most common CADR was Maculopapular rash (34%) followed by Fixed Drug Eruption (FDE) in 27%.

A total of 66 patients of FDE were enrolled in this study fulfilling the inclusion and exclusion criteria. (Table 1) The age range of the patients was 11–65 years. Most common age group was 41-50 years with mean age being 42.19 years.

Out of total patients enrolled, 40(60.6%) were males and 26(39.4%) were females.

The commonest morphological variant found in our study was Pigmented FDE (68%) followed by Bullous FDE (23%).

Based on mucocutaneous involvement, half of the patients 34 (51%) had both cutaneous and mucosal involvement followed by cutaneous only in 23 (35%) and mucosal only in 9 (13%) patients.

Amongst all the sites, Oral mucosa was involved in 43 (65%) patients followed by genitalia in 32 (48%), trunk in 20 (30%), extremities in 15 (23%), and face & neck in 4 (6%) patients.

Single site involvement was seen in 45 (68%) patients whereas multiple sites simultaneously were involved in 21 (32%) patients.

Duration of onset of lesion after drug intake was less than 24 hours in 37 (56%) patients, between 24-48 hours in 23 (35%) patients while it was more than 48 hours in 6 (9%) patients.

History of First episode was noted in 36 (54.5%) patients whereas 30 (45.5%) patients gave history of recurrent episode.

Although involvement of multiple sites was noted, area of involvement was less than 5% in almost all the cases.

Causality association was found by Naranjo scale in the form of Definite or Probable score in 55 (83.33%). We couldn't find culprit in 11 (17%) cases.

Naranjo scale used for determining causality of culprit drugs showed Definite score in 45 (68%) patients, Probable score in 10 (15%), Possible score in 6 (9%) and Doubtful score in 5 (7.5%) patients.

The categories of causative drugs were Antibiotics (38%), NSAIDs (30%), Antiepileptics (4.5%), Antifungals (3%) and others (7.5%). The most common offending drugs were fluoroquinolones in 12 cases (18%), diclofenac in 8 cases (12%), cotrimoxazole in 7 cases (10%), ibuprofen in 5 cases (7.5%). (Table 2) Generalised FDE was seen in 2 cases; 1 with Phenytoin and other with metronidazole.

Table 1: Demographic data and clinical features of patients with FDE (n=66)

Variables	Number
Mean age (years)	42.19
Gender ratio (M:F)	1.54:1
Clinical variant	
Pigmented	45 (68%)
Bullous	15 (23%)
Mucosal	4 (6%)
Generalized	2 (3%)
Muco-cutaneous involvement	
Only mucosal	9 (13%)
Only cutaneous	23 (35%)
Both	34 (51%)
Location	
Oral mucosa	43 (65%)
Genitals	32 (48%)
Trunk	20 (30%)
Extremities	15 (23%)
Face & Neck	4 (6%)
No. of Site	
Single	45 (68%)
Multiple	21 (32%)
Time of Onset (after drug intake)	
<24 Hours	37 (56%)
24-48 Hours	23 (35%)
>48 Hours	6 (9%)
No. of episode	
1st episode	36 (54.5%)
Recurent episode	30 (45.5%)

Table 2: List of offending drugs (n=66)

Group of drug	No of patients (%)
ANTIBIOTICS	**25 (38%)**
Fluoroquinolones	12 (18%)
Ciprofloxacin	4 (6%)
Ofloxacin	2 (3%)
Ciprofloxacin-Tinidazole	3 (4.5%)
Ofloxacin-Ornidazole	3 (4.5%)
Cotrimoxazole	7 (11%)
Doxycycline	2 (3%)
Metronidazole	3 (4.5%)
Tinidazole	1 (1.5%)
NSAIDS	**20 (30%)**
Diclofenac	8 (12%)
Ibuprofen	6 (9%)
Aspirin	3 (4.5%)
Nimesulide	2 (3%)
Mefenamic Acid	1 (1.5%)
ANTI EPILEPTICS	**3 (4.5%)**
Phenytoin	2 (3%)
Carbamazepine	1 (1.5%)
ANTIFUNGALS	**2 (3%)**
Fluconazole	2 (3%)
OTHERS	**5 (7.5%)**
Pseudoephedrine	1 (1.5%)
Omeprazole	1 (1.5%)
Nifidepine	1 (1.5%)
Enalapril	1 (1.5%)
Over the counter medication	1 (1.5%)
UNKNOWN	**11 (17%)**

DISCUSSION

Jung et al.[9] and Ognongo-Ibiaho et al[10] reported a higher frequency of FDE for males in their fourth decade of life, but Mahboob et al[11] found equal rates in both sexes. FDE is more common after middle age because of increasing co-morbid conditions and simultaneous consumption of multiple medications.

Our study noted the most common site involved to be oral mucosa followed by genitalia which is comparable to Pai VV et al[12] study and in contrast to other studies having upper extremities as the most frequent site to be involved.[13]

We found 32% patients having FDE over multiple sites which is comparable to study done by Jae-Woo Jung et al (30.6%).[9]

The eruption occurred within the first 48 h of drug intake in 91% patients which was also seen to be high in study by Pai VV et al (73.6%).[12]

History of recurrence of FDE episode in our study (45.5%) was comparable to study by Pai VV et al (57.8%).[12]

FDE occurred within 24 hours of drug intake amongst patients having past history.

Although involvement of less than 5% area was seen in majority cases; due to involvement of oral and genital mucosa, it significantly affects the quality of life of the patient.

While we were able to identify culprit as a definitive cause in 68% patients and as a probable cause in 15% patients, we could not find culprit in 17% cases. Offending drug was not recognized by Lee et al[3] and Chen et al[14] in 71.6% and 23% of patients, respectively.

Concurrent intake of multiple drugs, multiple FDE, controversial usefulness of patch test, self-medication, and inaccurate past medical history reported by the patients are the most important impediments for determination of culprit drugs.[13]

Antibiotics were the commonest offending drugs followed by NSAIDS which is consistent with several other studies like Mahboob et al, Saka B et al, Sehgal VN et al and others[11,15–17]. But in contrast, analgesics medications have been frequently reported as offending drugs in some studies done by Jung JW et al,[9] Shukla SR et al[18] and Heng YK et al.[19]

CONCLUSION

In our study most of patients with FDE were middle aged males with involvement of oral mucosa, and antibiotic intake, especially ciprofloxacin and with pigmented variant.

FDE as a drug reaction has high chances of recurrence. This recurrence can be prevented by proper counseling regarding future drug intake.

Although involvement is less than 5% area in majority cases; due to involvement of oral and genital mucosa, it significantly affects the quality of life of the patient.

REFERENCES

1. Ardern-Jones MR, Lee HY. Benign Cutaneous Adverse Reactions to Drugs. In: Rook's textbook of dermatology. Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D, editors. 9th ed. Oxford: Blackwell Science; 2016. p. 118 .11-14.
2. Brocq L. Éruptionerythemato-pigmentée fixe due al'antipyrine. Ann Dermatol Venereol 1894;5:308-13.
3. Lee A-Y. Fixed Drug Eruptions. Am J Clin Dermatol. 2000 Sep;1(5):277–85.
4. Brahimi N, Routier E, Raison-Peyron N, Tronquoy A-F, Pouget-Jasson C, Amarger S, et al. A three-year-analysis of fixed drug eruptions in hospital settings in France. Eur J Dermatol. 2010;20(4):461–4.

5. Korkij W, Soltani K. Fixed drug eruption. A brief review. Arch Dermatol. 1984 Apr;120(4):520–4.
6. Pujara S, Shah B. Drug Reactions. In: Sacchidanand S, editor. IADVL Textbook of Dermatology. 4th ed. New Delhi: Bhalani Publishing House; 2018. p. 2344–95.
7. Valeyrie-Allanore L, Obeid G, Revuz J. Drug Reactions. In: Bolognia JL, Schaffer J V., Cerroni L, editors. Dermatology. 4th ed. China: Elsevier; 2018. p. 348–75.
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239–45.
9. Jung JW, Cho SH, Kim KH, Min KU, Kang HR. Clinical Features of Fixed Drug Eruption at a Tertiary Hospital in Korea. Allergy Asthma Immunol Res. 2014 Sep;6(5):415-420.
10. Ognongo-Ibiaho AN, Atanda HL. Epidemiological study of fixed drug eruption in Pointe-Noire. Int J Dermatol. 2012;51(SUPPL.1):30–1.
11. Mahboob A, Haroon TS. Drugs causing fixed eruptions: a study of 450 cases. Int J Dermatol. 1998 Nov;37(11):833–8.
12. Pai VV, Kikkeri NN, Athanikar SB, Shukla P, Bhandari P, Rai V. Retrospective analysis of fi xed drug eruptions among patients attending a tertiary care center in Southern India. Indian J Dermatol Venereol Leprol 2014;80:194.
13. Kavoussi H, Rezaei M, Derakhshandeh K, Moradi A, Ebrahimi A, Rashidian H, et al. Clinical Features and Drug Characteristics of Patients with Generalized Fixed Drug Eruption in the West of Iran (2005-2014). Dermatol Res Pract. 2015;2015:236703.
14. Lee C-H, Chen Y-C, Cho Y-T, Chang C-Y, Chu C-Y. Fixed-drug eruption: A retrospective study in a single referral center in northern Taiwan. Dermatologica Sin [Internet]. 2012;30(1):11–5. Available from: https://www. sciencedirect.com/ science/ article/pii/S1027811712000109
15. Saka B, Kombaté K, Médougou B-H, Akakpo S, Mouhari-Toure A, Boukari T, et al. [Fixed drug eruption in dermatology setting in Lomé (Togo): a retrospective study of 321 cases]. Bull Soc Pathol Exot. 2012 Dec;105(5):384–7.
16. Sehgal VN, Srivastava G. Fixed drug eruption (FDE): changing scenario of incriminating drugs. Int J Dermatol. 2006 Aug;45(8):897–908.
17. Sharma R, Dogra D, Dogra N. A study of cutaneous adverse drug reactions at a tertiary center in Jammu, India. Indian Dermatol Online J 2015;6:168-71.
18. Shukla SR. Drugs Causing Fixed Drug Eruptions. Dermatology [Internet]. 1981;163(2):160–3. Available from: https://www.karger.com/DOI/10.1159/000250153
19. Heng YK, Yew YW, Lim DSY, Lim YL. An update of fixed drug eruptions in Singapore. J Eur Acad Dermatol Venereol [Internet]. 2015;29(8):1539–44. Available from: http://dx.doi.org/10.1111/jdv.12919.