Pattern of fixed drug eruptions in a tertiary care teaching hospital Hi-tech medical college, Bhubaneswar, Odisha

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Abstract
Fixed drug eruption (FDE) is one of the common types of cutaneous adverse drug reaction. This study was conducted to study the common types of drugs causing FDE and to find the management pattern of FDE in a tertiary care teaching hospital. In this study we found that orindazole (24%) and co-trimoxazole (20%) had higher incidence of FDE. Sixty eight percent of patients developed post inflammatory pigmentation. The most common clinical presentations was black patch in 44%, followed by bulla with erythematous patch in 20% of pigmented patches. Topical steroids, antihistaminic and oral corticosteroids were the common drugs used in the management of fixed drugs eruptions. The most common affected site was lip in 33.3% followed by trunk in 21%. The most common age group was 11-20 year followed by 21-30 year, fifty-one cases were seen in male.

Keywords: Fixed drug eruption, Cutaneous Adverse drug reaction, Pigmentation.

Introduction
Fixed drug eruptions are characterized by one or more sharply demarcated, erythematous lesions which occur at the same site in the particular patient after rechallange.[1,2] Description of F.D.E. was first described by Brocq in 1894.[3-5] Although lesions can occur at any site, oral and genitalia are the most common sites. Common causative drugs are barbiturates, phenytoin, salicylate, sulphonamide phenolphthalein, tetracycline, griseofulvin, etc.[6] The mechanism of most drug induced eruptions are unknown. However, the proposed mechanism includes allergic reaction, other reaction caused by accumulation of drugs, pharmacological action of drugs or interaction with genetic factors.[7] Histopathology study shows that there will be hydropic degeneration of the basal cell layer leads to incontinentia pigmenti which is characterized by the presence of melanin within macrophages in the upper dermis. Scattered necrotic keratinocytes with eosinophilic cytoplasm and pyknotic nuclei (often referred to as Civatte bodies, colloid bodies, or dyskeratotic cells) are frequently seen in the epidermis and represent apoptosis. Bullae form by detachment of the epidermis from the underlying dermis.[2] There are some reports of FDE due to individual drugs in India, but the present study is carried out with the following objectives.

1. To study the demography of the patients experiencing FDE
2. To study the common types of drugs causing FDE
3. To study the histopathology of the FDE
4. To study the management pattern of FDE

Materials and Methods
FDE cases were identified from the dermatology OPD record. A retrospective analysis of data of patients diagnosed as FDE for a period of 5 years (from Aug 2012-Jul 2017) was made. We have included only those F.D.E. cases had been confirmed by provocation. In few cases histopathology had been written. The data recorded in patient profile form was analyzed using Microsoft Excel.

Results
75 patients were included in the study; 51 males (68%) and 24 females (32%). Age distribution revealed that maximum number of patient [n=21 (28%)] between age group 21-30, followed by age group between 31-40 [n=12 (16%)] and three patients were less than 10 years of age Table 1. There were different clinical presentation in Eighty percentage (n=60) of FDE cases. The type of pigmentation is listed in Table 2. Black pigmentation was the most common clinical presentation. Only two patients were in-patient and remaining 73 (97.3%) were out-patients. The reason behind the intake of suspected drugs causing FDEs include cough/cold [n=6 (8%)], loose motion [n=30(40%)], fever [n=5(6.7%)], headache [n=5(6.7%)], toothache [n=3(4%)], throat pain [n=3(4%)], vaginal discharge [n=3(4%)], vague complaints [n=3(4%)] and the reason was not mentioned in majority of patient [n=17(22.6%)]. The suspected drugs causing FDEs are listed below in Table 3. The most common sites affected were lip in 25 patients, limb in 15 patients, trunk in 16 patients, groin in 03 patients, genitals in 12 patients, one patient in oral cavity and 03 patients had multiple site involvement Table 4. Seventy-two (96%) out of 75 patients required topical or oral medication or combination of local and oral medication. The drugs used to treat the patients were given below in the Table 5. Chemical peeling with TCA 30% was done in three patient with good result.

Table 1: Case distribution in relation to age

Age	Number	Percentage
<10	03	04
11-20	11	14.6
21-30	21	28
31-40	12	16
41-50	10	13.4
51-60	09	12
>60	09	12

Table 2: Type of clinical presentation developed in patient

Pigment	Number of patients	Percentage
Violaceous	03	4
Dark Brown	09	12
Black	33	44
Erythematous	15	20
No pigmentation	15	20

Table 3: Suspected drugs causing fixed drug eruption

Drugs	Number	Percentage
Ibuprofen	6	8
Paracetamol	3	4
Orindazole	18	24
Cotrimoxazole	15	20
Tinidazole	3	4
Diclofenac	3	4
Aspirin	3	4
Cefixime	1	1.3
Ciprofloxacin	2	2.7
Amoxycillin	3	4
Metronidazole	9	12
Anticold &Cough Syrup	3	4
Unknown	6	8

Table 4: Site distribution in fixed drug eruption

Site	No of patients	Percentage
Limb	15	20
Oral cavity	01	01.4
Trunk	16	21.3
Lip	25	33.3
Groin	03	04
Genital	12	16
Multiple site	03	04

Table 5: Drug used for treatment of fixed drugs eruption

Drugs	Number	Percentage
Fluticasone Cream	17	22.5
Tab. Levocetirizin + Steroid cream	11	14.73
Tab. Prednisolone	5	6.7
Fusidic acid	8	10.5
+Steroid Cream		
Tab. Loratidin	7	9.4
Hydrocorticosone Cream	4	5.4
Tab. Fexofenadine	7	9.4
Inj. Dexamethasone	2	2.7
Inj Triamcinolone	2	2,7
No Drug	3	4
Aloe vera.and Vitamin E cream	9	12

There were hydropic degeneration (Fig. 2) in basal cell layer, thinned out epithelium (Fig. 1) and incontinentia pigmenti in upper dermis (Fig. 3) in histopathology study of patients. Most common clinical presentation was black (Fig. 4) followed by erythematous pigmentation (Fig. 5). Eight patients were associated with bullae. Fifteen patients were not presented with any pigmentation.

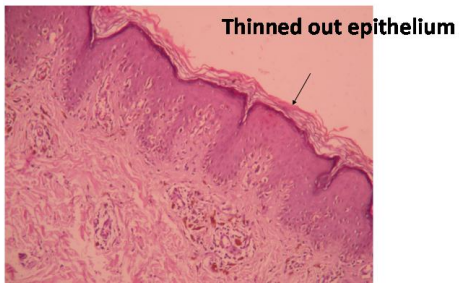

Fig. 1:

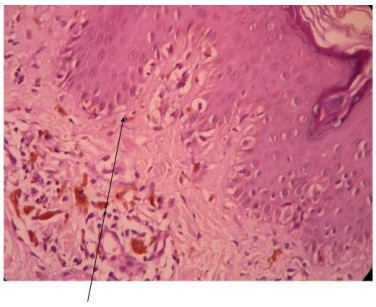

Fig. 2:

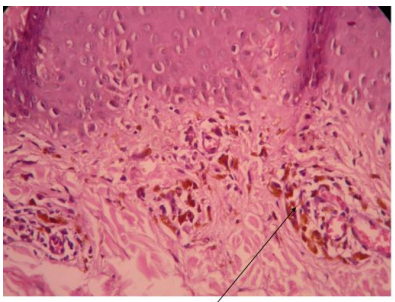

Fig. 3:

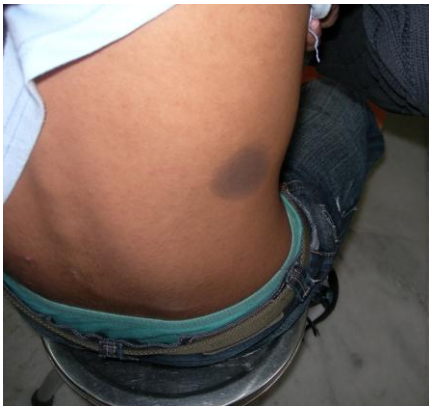

Fig. 4: Black pigmentation

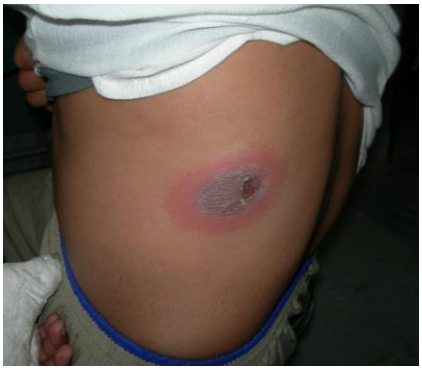

Fig. 5: Erythematous

Discussion

Cutaneous ADRs are the most common ADRs,[3] among which, FDE is one of the most common. The present study identified the pattern of fixed drug eruptions. We find that men to have a higher incidence of FDEs. In general, females are known to have high incidence of ADRs.[8,9] A study from Nnoruka EN study and Jung, J.-W et al also reported higher incidence in male.[10,11] Virendra N. Sehagal Indian study and Mahimanjan Saha et al suggests incidence is more in male.[12,16] Most common age group 21-30, followed by 31-40 age group. Mehta et al also observed in 11-40 age group.[13] In our study, most of patients were hospital outpatient. This suggests FDE to be a minor type of ADRs which can be managed on outpatient basis. In general, the patients with FDE present with usual morphology of intensively pruritic bright red macules and papules, symmetric on trunk and extremities; may become confluent.[1] In our study also most of the patients developed pigmentation and the most common was black pigmentation followed by erythematous type.

The most common drugs responsible for FDEs in our study are orindazole (24%) and co-trimoxazole (20%). In six patients there were history of unknown drug. The study from Nigeria noted maximum case of FDEs with cotrimoxazole[10] and similarly results was found in an Indian study where co-trimoxazole to be the major cause of drug eruption.[14] Now a days we are not using co-trimoxazole frequently, further day by day new drugs are coming and some older drugs are withdrawn from pharmaceutical market. In our study the most common site was lip. Gowri Thilagam T. et al Study and Mahimanjan Saha et al also noted oro genital were most common site.[15,16] Only one case we got intra oral lesion. R, Bihari et al also mentioned that intra oral lesion are very rare.[17] There were hydropic degeneration in basal cell layer, thinned out epithelium and incontinentia pigmenti in upper dermis in histopathology of patients.[2]

Treatment of a drug eruption depends on the specific type of reaction and management of FDE includes the use of first-generation antihistamines, mild topical steroids (e.g., hydrocortisone, desonide) and moisturizing lotions, especially during the late desquamative phase.[18] First step should be identification and discontinuation of the causative drugs but for immediate relief and better management local steroid and oral antihistamine can be given.[11] Similarly, in our study, topical steroid (e.g., Fluticasone) is used in the most of the case followed by the oral antihistamine (e.g., Levo Cetirizine) with local steroid and oral corticosteroids (e.g., Prednisolone). Two out of three multiple site F.D.E. patients were admitted and successfully treated with systemic steroid. Nine patients were treated with local application of Aloe vera and vitamin E cream with good result. More improvement was with combination of local steroid and oral antihistamine than only local steroid. Jung, J.-et al study also mentioned that there was improvement with local steroid or antihistamine.[11] Also with TCA (Trichloroacetic acid) chemical peeling there were improvement in pigmentation of F.D.E in three patients.

Conclusion

FDE is the most common cutaneous ADRs. Though the incidence of FDE is high with orindazole and co-trimoxazole, a large number of drugs can cause this reaction. So, the healthcare professional should be cautious while using these drugs.

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