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## Research Article

# STUDY OF FIXED DRUG ERUPTIONS IN TERTIARY CARE HOSPITAL, JAMNAGAR

<sup>1</sup>Margi Patel, <sup>2</sup>Nirav Dholaria and <sup>3</sup>Monika Chauhan

Department of Pharmacology, Shri M.P. Shah Government Medical College, Jamnagar-361008

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### ABSTRACT

**Introduction:** Fixed Drug Eruptions are dermatological manifestations of drug reactions which recurs in the same location after repeated exposure of same drug or related medications. They usually appear as round to oval erythematous plaque which evolves to become dusky and violaceous. So this study was conducted to observe the different drug which are responsible for fixed drug eruption. **Methods:** This was an observational study over a period of 2 years. In that period we have found 50 patients having fixed drug eruptions which were recruited according to selection criteria. After that proper history was taken in which demographic, clinical, time of start of reaction and drug intake information and were collected. **Results:** In this study, out of 50 patients, recognition of offending drugs were distinguished in 43 patients. Flouroquinolones (39.53%) were the most common agent for causing FDE followed by Nonsteroidal anti-inflammatory agents (18.60%), Amoxicillin (16.27%), Fluconazole (11.62%), Azithromycin (4.65%), Metronidazole(4.65%) and Doxycycline (4.65%). **Conclusion:** In this study, Flouroquinolones were the most common agent for causing FDE followed by Nonsteroidal anti-inflammatory agents. So with detailed history and Physical examination was made the diagnosis of fixed drug eruption

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### INTRODUCTION

Adverse drug reaction (ADR) is defined as "A noxious response to a drug which occurs at doses normally used for the prophylaxis, diagnosis and treatment of disease" [1].

Among the various adverse drug reactions, cutaneous drug reactions are the most common one. Various types of cutaneous adverse drug reactions are maculopapular rashes, steven Johnson Syndrome, fixed drug eruptions, pruritus, erythema, urticaria etc. [1]. Fixed drug eruption (FDE) was first described in 1889 by Bourns, and the term fixed drug eruption, or "éruption érythémato-pigmentée fixe" was coined by Brocq in 1895 [2]. Brocq described "round or oval apparently edematous plaques, which varied in size from that of a coin to that of a palm; and which recurred on various parts of the body" [2]. As the eruption faded, there remained in the affected areas, a pigmentation of variable shades and duration" [2]. So, fixed drug eruption(FDE) is defined as a reaction of specific drug which recurs in the same location after repeated exposure of same drug or related medications. Main pathology of recurrence is local reactivation of memory T cell lymphocytes in skin due to drugs. Morphology of FDE is sharply defined round to oval erythematous plaque which evolves to become dusky and violaceous [3]. Extensive FDE may sometimes present as bullous lesions known as Generalized Bullous FDE (GBFDE) [3]. Commonly present on lips, genitals, trunk, palms

and soles. There are many variants of FDE like pigmented and non-pigmented FDE, generalized FDE, linear FDE, wandering FDE, bullous FDE, eczematous and psoriasiform FDE, erythema dyschromicum perstans-like eruption [3]. The gold standard for diagnosing FDE is systemic provocation, while topical provocation testing offers a safer alternative method, and histopathologic examination helps to confirm the diagnosis [4]

Common agents causing FDE are Antibiotics (Tetracyclines, Doxycycline, Aminoglycosides like Streptomycin, Flouroquinolones like Ciprofloxacin, Cotrimaxazole, metronidazole, penicillins), Antifungals (Itraconazole, Amphotericin), Nonsteroidal anti-inflammatory drugs (Aspirin, Phenyl-butazone, Diclofenac, Naproxen), Anticonvulsant and drugs acting on CNS (Phenytoin, phenobarbitone, Barbiturates, Codeine), antihypertensive and antiarrhythmic (Quinidine), Anti TB and antileprosy (Dapsone) [3].

Consciousness regarding specific drug reaction by physician is necessary to stop repeated exposure of same or offending medications. A detailed history and physical examination can lead to prompt recognition after then discontinuation of the offending medication, which is the mainstay treatment for FDE [5].

The main purpose of this study was to observe the different drug which are responsible for fixed drug eruption over a

\*Corresponding author: Margi Patel

Department of Pharmacology, Shri M.P. Shah Government Medical College, Jamnagar-361008.

period of 2 years, so that awareness could be created regarding offending drugs for FDE.

**MATERIALS AND METHOD**

This was a single center, observational study conducted by department of pharmacology at tertiary care teaching hospital, Jamnagar over a period of 2 years from October 2020 to October 2022. Retrospective and prospective both type of data were collected. Total 50 patients were included in this study recruited according to selection criteria. Patients of both genders who were above 18 years of age were included in the study and other cutaneous eruptions caused by drugs (Steven Jonson Syndrome, Toxic epidermal necrolysis) were excluded from the study.

After the patients come in hospital, proper history was taken such as demographic data, history of drug intake, route of administration, reason for taking drugs, time of start of reaction, temporal correlation with drug intake, improvement of lesions on withdrawal of the drug and recurrence of the lesions on re-challenge were also recorded. The offending drugs were identified by taking proper history and affected area, nature of lesion like bullous/ non-bullous were recorded.

**RESULTS**

This study included total 50 patients, out of 50 patients 32 were males and 18 were females. Age of patients ranged between 20-55 years. Trunk involvement was most common followed by extremities among all patients who were diagnosed as fixed drug eruption. Non bullous variant (43 patients out of 50) was more compared to Bullous variant.

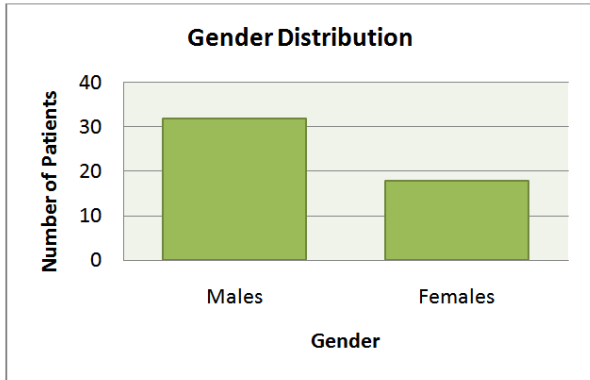


Figure I Gender Distribution

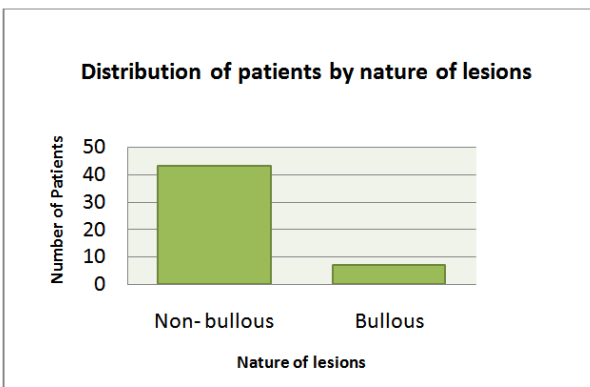


Figure II Distribution of patients by nature of lesions

Most of the drugs were taken orally (46 patients) followed by parenteral, among them 02 patients were taken intramuscularly and 02 patients were taken intravenously. In

this study, recognition of offending drugs were distinguished in 43 patients (86.00%) and offending drugs were not distinguished in 7 patients(14.00%). Out of 43 patients, Flouroquinolone antibiotics are more common as offending drug (39.53%) in which 7 cases of Ciprofloxacin (51.17%),5 cases of Ofloxacin (29.41%),3 cases of Norfloxacin (17.65%) and 2 cases of Levofloxacin (11.76%) were noted.

After Flouroquinolone , Nonsteroidal anti-inflammatory drugs (18.60%) and penicillin like Amoxicillin (16.27%) recognised as a common offending drugs in this study moreover . Five cases of FDE were noted in which fluconazole (11.62%) was recognised as offending drug. And also two cases of Azithromycin (4.65%), Metronidazole (4.65%) and Doxycycline(4.65%) were recorded.

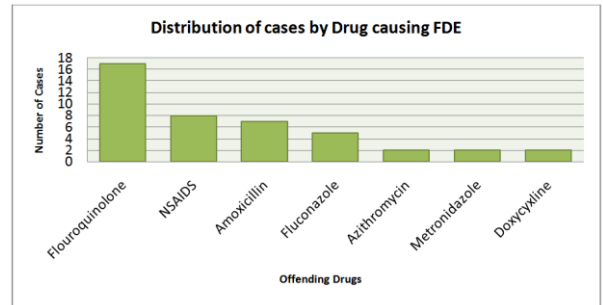


Figure III Distribution of cases by Drug causing FDE

**DISCUSSION**

Fixed Drug Eruption is one of the most specific Drug induced Muco-cutaneous reaction Pattern. The hallmark of the disease is the occurrence of the lesion(s) at the same site each time following administration of the causative drug(s) and the characteristic residual hyperpigmentation upon healing<sup>[6]</sup>.

FDE is a delayed type of hypersensitivity<sup>[3]</sup>. Tissue resident memory T cells (T<sub>RM</sub>) are memory T cells that reside in the tissue and are responsible for FDE<sup>[3]</sup>. Exposure of the drug everytime leads to reactivation of these TRM and release of interferon gamma (IFN-γ) leading to drug eruptions occurring at the same site<sup>[3]</sup>.

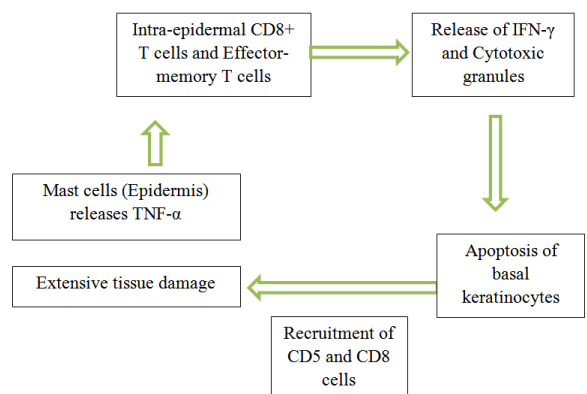


Figure IV Pathogenesis of fixed drug eruption<sup>[5]</sup>

Symptomatic treatment using anti-histaminics and topical corticosteroids usually given in patient of FDE. As the acute phase subsides, post-inflammatory and treatment-resistant residual hyperpigmentation remains<sup>[7]</sup>, causing cosmetic embarrassment to the patient. There are reports of cross-sensitivity<sup>[8]</sup> which means than an FDE can occur with other drugs similar in structure to the causative agent. Thus, patients need to be counselled and given a list of drugs to be avoided.

In present study fluoroquinolones (39.53%) were the most common agent for causing FDE followed by Nonsteroidal anti-inflammatory agents (18.60%), Amoxicillin (16.27%), Fluconazole (11.62%), Azithromycin (4.65%), Metronidazole (4.65%) and Doxycycline (4.65%). FDE have rarely been studied in children. According to one previous study which was done in 2021 by Babuna Kobaner G and Ozkaya E in Turkey<sup>[9]</sup>, The overall prevalence of pediatric FDE was 10.5 % (22/212). according to that study, cotrimoxazole was the leading cause of pediatric FDE in almost every location. Pediatric patients were excluded in present study.

Same study performed previously in 2016 by Saini R *et al.*<sup>[1]</sup>, according to that study, most common causative agent of FDE was fluoroquinolones (33.3%) which is similar to present study, followed by nitroimidazole antibiotics (26.6%), NSAIDs (25.5%), penicillin and antifungal (6.7%) and anti-tubercular drugs (2.2%). and in past study non bullous variant was more common than bullous variant which is also similar in present study. Another study which was done by Kavoussi H. *et al.* in west of Iran<sup>[10]</sup>, most common causative group of drug in that study was Antibiotics (60.9%) followed by analgesics (30.4%) and miscellaneous cases (8.7%). In antibiotics, cotrimoxazole (26.1%) was the most common offending drug followed by metronidazole (17.4%) which significantly differ from present study and in analgesic group, Ibuprofen was the common drug (13.0%) which is not similar to present study.

## CONCLUSION

Fixed Drug Eruptions are dermatological manifestations of a reaction which occur due to certain medications. In this study, fluoroquinolones were the most common agent for causing FDE followed by Nonsteroidal anti-inflammatory agents. So, detailed history and Physical examination typically derived to the diagnosis of fixed drug eruption, and also awareness of the variable presentations which will help for the prompt diagnosis. A past history of a similar reaction in the same location in the setting of recently starting a new medication can be helpful for the physician to diagnose FDEs.

### Limitations of Study

Lesser number of participants involved in this study which might not be the representation for population  
This was a single centre study, result can be more accurate if was done as multi centre study

### Conflict of Interest

No conflict of interest

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