



A FIXED DOSE COMBINATION OF FLUOROQUINOLONE AND NITROIMIDAZOLE INDUCED FIXED DRUG ERUPTIONS.

General Medicine

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ABSTRACT

Fixed drug eruptions (FDE) are a distinct type of drug eruptions which happens repeatedly at same location due to certain drugs. A 42 year old female developed FDE with the use of fixed dose combination of Ofloxacin and Ornidazole. On further scrutiny it was found she had developed similar rash with same drug in past. Patient condition improved after discontinuation of culprit drug. She was advised to avoid Ofloxacin and Ornidazole in future.

KEYWORDS

Fixed drug eruption, Ofloxacin, Ornidazole

INTRODUCTION

Fixed drug eruption (FDE) is a specific form of cutaneous adverse reaction due to certain drugs. Skin rash characterized by pruritic, single or multiple circumscribed, round shaped erythematous macule, edematous plaque or patches which reappear at same location of skin or mucous membrane after ingestion of offending drug. These unique rashes resolve spontaneously or with hyper pigmentation^[1]. FDE started within 30 minutes to several hours after administration of culprit drug^[2]. This cutaneous reaction accounts approximately 14%-32% of all drug induced eruptions^[3]. It is found in both gender at any age but predominantly at 3rd or 4th decade of life^[4-5].

Re-occurrence of FDE is controlled by CD8 + memory cell which are situated at epidermal basal layer of dormant fixed drug eruption lesion. After ingestion of culprit drug within a day these cells move upward in epidermis and generate cytokines and gain features of natural killer cells. Once acute phase of FDE passes, features of this natural killer cell diminish and these cells remain dormant at lesion till next introduction of trigger medicine occurs^[6]. One study suggested the most common site for FDE is upper extremity while others suggested lip^[4,7-8]. Multiple drugs are responsible for FDE such as Non steroidal anti-inflammatory drugs (NSAIDs), some antibiotics, antiepileptic agents, intravenous contrast agents^[7-11].

Ofloxacin is a fluorinated 4-quinolone antibiotic which targets bacterial DNA gyrase and topoisomerase IV and helps in inhibiting bacterial cell division by inhibiting replication. It has more potent activity against gram positive bacteria and has excellent bioavailability with a similar dose of 200-400 mg twice daily for intravenous and oral route^[12]. While ornidazole belongs to the nitro-imidazole group showing excellent effect against protozoa as well as anaerobic microorganisms^[13].

Diarrheal disorder is commonly observed in any age, most due to infective origin. Many fixed drug combinations are prescribed in treatment of diarrheal disorder such as antiprotozoal agents and antibacterial agents. Evidence to justify such treatment are not so common hence exposure to such FDC can cause adverse effects and rising of drug resistance^[14-15].

We are reporting FDE caused due to irrational use of Fluoroquinolones with nitroimidazole.

Case Presentation

On 4th May 2024, a 42-year-old female suffering with multiple episodes of loose, watery stool with bloating and mild abdominal cramps since 1 day visited private clinic in Tumkur. Physician diagnosed her diarrheal disorder and prescribed her fixed drug combination (FDC) containing

ofloxacin (200mg) and ornidazole (500 mg). Treatment prescribed twice a day for 5 days. After taking medication within 12 hours patient started complaining about macular rash, circle in nature at elbow joint flexor aspect of forearm and around the umbilical area. Rash was associated with intense itching and burning sensation. Patient was treated with Injection Pheniramine intramuscularly stat, tablet Hydroxyzine hydrochloride 25mg HS for 5 days and cream Hydrocortisone cream 1% locally 3 times a day for 5 days. Rash subsided gradually leaving behind hyperpigmented oval patch [figure 1], which persisted at the time of her follow up on 12th May 2024. During detailed history, patient informed experience of similar type of rash in the past when exposed to FDC containing fluoroquinolone and nitroimidazole.

In this case, temporal association between exposure to drug and occurrence of rash was found. She had no other history of allergy or bronchial asthma. Family history for any such illness was absent with no co-morbid condition. According to Naranjo's algorithm, causality assessment found to be possible^[16]. The patient was advised to avoid ofloxacin and ornidazole in the future.



Figure 1:

DISCUSSION

In 1889, the first case of fixed drug eruption was reported by Bourns. He described FDE when a patient ingested antipyridines and suffered with multiple hyperpigmented oval lesions over lips and on the tongue^[17]. FDE is most commonly observed when patient takes intermittent medication rather than taking continuously. FDC, which commonly causes fixed drug eruptions, are Angiotensin converting enzyme inhibitors (ACE), NSAIDs, Proton pump inhibitors (PPI), calcium channel blockers, some antibacterial agents^[18].

FDE is a kind of delayed type hypersensitivity reaction which is mediated by CD 8+ cells. FDE occurs due to mast cell activations which are present at the vicinity of epidermis layer of FDE lesion when exposed to causative agents^[19-20].

In our case, also patient had taken FDC of Fluoroquinolones and nitroimidazole. She also gave history of similar reaction in the past for similar drugs. Her hyperpigmented lesions were due to the culprit agent.

Same drugs or pharmacologically similar agents after re-exposure can cause similar type of lesion and cross-reaction^[21]. In our case patient declined further test hence we can only expect she might have sensitivity to FDC containing Fluroquinolone or nitro-imidazole or individual active components of FDC^[20-22].

Using FDC containing Ofloxacin and Ornidazole is inappropriate still in developing country like India it is prescribed as over the counter drug^[13,23-24]. Irrational rampant ingestion of such FDC causes drug - drug interaction, adverse drug reaction, mortality, drug resistance and increases financial burden to country^[25].

In our case, patient remains residual hyperpigmentation over forearm and umbilical area. We advised patient to avoid medication containing ofloxacin, ornidazole and FDC containing both. This case highlights physician or treating doctor must take detailed allergic history of patient prior prescribing any medication as well as patient must avoid self medication.

CONCLUSION

Fixed drug eruption due to fixed dose combination of ofloxacin and ornidazole are commonly observed in developing countries like India, where over the counter prescription of medication is practiced regularly. Such cutaneous adverse reactions are mostly unreported due to unawareness of pharmacovigilance to patient and physician. This combination has no added benefit but it increases financial burden, drug induced adverse reaction such FDE it is advised to avoid such combinations and treating physician must take detailed allergic history of patients. Patients and physician must educate regarding advantages and disadvantages of FDC. Wise use of FDC when there is dire necessity. Administrator, Policy maker must take action to minimize accessibility of such FDC.

Consent

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Conflict Of Interest:

None declared.

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