International Journal of Basic & Clinical Pharmacology
Halder D et al. Int J Basic Clin Pharmacol. 2025 Sep;14(5):860-862
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20252587

Case Report

Fluoroquinolone-nitro imidazole fixed-dose combination medication-induced fixed drug eruption with positive re-challenge

Debjyoti Halder[1]*, Indrani Dalal[1], Durbashree Das[2]

[1]Department of Pharmacology, Midnapore Medical College, West Bengal, India
[2]Department of Biochemistry, Institute of Postgraduate Medical Education and Research, West Bengal, India

Received: 29 May 2025
Accepted: 04 July 2025

***Correspondence:**
Dr. Debjyoti Halder,
Email: drdebjyotihalder@gmail.com

ABSTRACT

Fluoroquinolone-nitroimidazole fixed-dose combinations, such as ofloxacin-ornidazole and norfloxacin-tinidazole, are widely prescribed for gastrointestinal infections. However, fixed drug eruptions (FDEs) associated with these combinations are underreported. A 32-year-old female developed generalized itching and painful ulcerative lesions on the buccal mucosa shortly after taking an ofloxacin-ornidazole tablet. Upon discontinuation and substitution with norfloxacin-tinidazole by a physician, her symptoms worsened, indicating a positive rechallenge. Dermatological evaluation led to withdrawal of the drug and initiation of antihistamines and topical analgesics, resulting in symptom resolution. Her clinical course, including lesion recurrence at the same site upon re-exposure, confirmed the diagnosis of FDE, a delayed-type hypersensitivity reaction mediated by CD8+ T cells. Causality assessment using the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) scale classified the reaction as certain. This case highlights the need for thorough drug history taking and the importance of avoiding re-prescription of drugs from the same pharmacological class in patients with suspected drug allergies.

Keywords: Fixed drug eruption, Fixed dose combination, Adverse drug reaction

INTRODUCTION

Fluoroquinolones-nitroimidazole fixed-dose combinations like ofloxacin-ornidazole and norfloxacin-tinidazole are commonly prescribed antimicrobial combinations for the treatment of gastrointestinal disease (mixed infection).[1] But the fixed drug eruption (FDE) caused by these fixed dose combinations (FDCs) are underreported. FDEs are not only limited to a single drug, but also cross-sensitivity and poly-sensitivity [3] among different members of the same pharmacological class do present.[2-5]

CASE REPORT

A 32-year-old female presented with complaints of painful ulcerative lesions in the oral cavity, which developed following the intake of an antibiotic. She had initially taken a FDC tablet of ofloxacin and ornidazole for repeated episodes of loose motion. Within a few hours of ingesting a single tablet, she began experiencing itching predominantly over the trunk and upper limbs. This was soon followed by the appearance of 2-3 painful, polymorphic ulcerative lesions, each measuring approximately 0.5-1 cm in diameter. The lesions were located on the buccal mucosa along the inner side of the upper lip (Figure 1) and on the dorsal aspect of the tongue (Figure 2).

Recognizing the temporal association with the drug, the patient discontinued the ofloxacin-ornidazole combination and consulted a physician. In response, the physician advised her to stop the initial medication and started her on an alternative antimicrobial FDC containing norfloxacin and tinidazole.

However, shortly after initiating the new medication, the patient noticed a worsening of her symptoms. The number

of ulcerative lesions increased, and their severity intensified, leading to considerable discomfort and difficulty with oral intake. Concerned by the progression, she sought further medical attention and was referred to a dermatologist.

Upon dermatological evaluation, the norfloxacin-tinidazole combination was immediately withdrawn. She was managed conservatively with an oral antihistamine, cetirizine 10 mg once daily, to address the hypersensitivity reaction, along with a topical analgesic and anti-inflammatory gel (Zytee gel) applied to the affected oral mucosa. Following this treatment, her symptoms gradually subsided over the subsequent days.

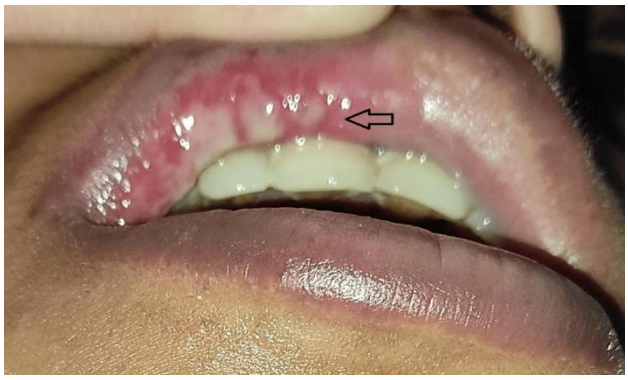

Figure 1: Polymorphic, ulcerative lesions on the inner aspect of the upper lip (buccal mucosa), appearing shortly after ingestion of ofloxacin-ornidazole fixed-dose combination.

Figure 2: Painful ulcerative lesions on the dorsal surface of the tongue observed following drug rechallenge with norfloxacin-tinidazole.

DISCUSSION

This ADR is reported in VigiFlow Software (Worldwide unique ID IN-IPC-300650406).

Her past treatment records confirmed accidental rechallenge. As eruptions occurred in the same site on re-exposure to the same drugs, it was diagnosed as fixed drug eruptions. FDE is a form of delayed-type hypersensitivity mediated by CD8+T cells.[6,7] According to the WHO-UMC causality assessment scale, the association between the drugs and the adverse drug reaction was found to be certain.

According to the WHO-UMC causality assessment scale, the association between the drugs and the adverse drug reaction was found to be certain (Table 1).

Table 1: Assessment of causality using the WHO-UMC criteria for adverse drug reaction.

Assessment criteria	Result
Temporal relationship	Present
Biological plausibility	Present
Present de-challenge	Positive
Rechallenge	Positive

The current case aligns with existing reports in several ways.

It confirms the individual capacity of both ornidazole and fluoroquinolones to cause FDE.

It demonstrates cross-reactivity across members of the same pharmacological classes, consistent with known mechanisms of class hypersensitivity.

It expands upon the literature by highlighting poly-sensitivity to two distinct pharmacological classes within combined formulations, a phenomenon that may be under recognized due to the widespread empirical use of FDCs in gastrointestinal infections.

CONCLUSION

FDEs due to FDCs of different fluoroquinolones and nitroimidazoles are uncommon, although both classes of drugs are individually well-documented triggers of FDEs. This case underscores the importance of recognizing the potential for cross-sensitivity and polysensitivity among structurally or pharmacologically related agents. In this patient, the recurrence of lesions at the same anatomical sites upon administration of a second, closely related FDC suggests a positive rechallenge and confirms the diagnosis of FDE. The case emphasizes the necessity for clinicians to conduct thorough drug histories and to exercise caution when prescribing medications from the same pharmacological group, particularly in patients with a known or suspected drug allergy. Proper documentation and patient counselling are essential to prevent future adverse drug reactions and improve pharmacovigilance.

Fixed drug eruptions due to FDCs of different fluoroquinolones and nitroimidazoles are rare, although they are individually notorious for causing FDEs. The importance of eliciting drug allergies is highlighted here. It shows that physicians should avoid prescribing the offending drugs or the same pharmacological group of drugs.

ACKNOWLEDGEMENTS

The authors would like to thank the patient for providing informed consent and for her cooperation throughout the evaluation and follow-up. They also acknowledge the support of the dermatology and pharmacovigilance teams involved in the management and reporting of this case.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Chakrabarti A. Prescription of fixed dose combination drugs for diarrhoea. Indian J Med Ethics. 2007;4:165-7.
2. Buffer DF. Fixed Drug Eruptions: Background, Pathophysiology, Etiology. Medscape. Available at: https://emedicine.medscape.com/article/1336702-overview. Accessed on 15 April 2025.
3. Pal A, Sen S, Das S, Biswas A, Tripathi SK. A Case of Self-treatment Induced Recurrent Fixed Drug Eruptions Associated with the Use of Different Fixed Dose Combinations of Fluoroquinolone-Nitroimidazole. Iran J Med Sci. 2014;39:584-8.
4. Sanmukhani J, Shah V, Baxi S, Tripathi C. Fixed drug eruption with ornidazole having cross-sensitivity to secnidazole but not to other nitro-imidazole compounds: a case report. Br J Clin Pharmacol. 2010;69:703-4.
5. Schmid DA, Depta JPH, Pichler WJ. T cell-mediated hypersensitivity to quinolones: mechanisms and cross-reactivity. Clin Exp Allergy J Br Soc Allergy Clin Immunol. 2006;36:59-69.
6. Shiohara T, Mizukawa Y. Fixed drug eruption: a disease mediated by self-inflicted responses of intraepidermal T cells. Eur J Dermatol EJD. 2007;17:201-8.
7. Gupta R. Fixed Drug Eruption Due to Ornidazole. Indian J Dermatol. 2014;59:635.

Cite this article as: Halder D, Dalal I, Das D. Fluoroquinolone-nitro imidazole fixed-dose combination medication-induced fixed drug eruption with positive re-challenge. Int J Basic Clin Pharmacol 2025;14:860-2