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OFLOXACIN AND ORNIDAZOLE - A FIXED DOSE COMBINATION INDUCED CUTANEOUS ADVERSE DRUG REACTION: A CASE REPORT

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ABSTRACT

A fixed dose combination (FDC) of ornidazole and ofloxacin is considered irrational as it increases the chances of occurrence of side effects and drug-drug interactions making its use inappropriate. Quinolones + nitroimidazole are known to be the highest suspected FDCs in Cutaneous adverse drug reactions (CADR). Present case report A 50 years old female patient who was prescribed Tab. Veil (Ofloxacin 200 mg + Ornidazole 500mg) BD who developed swelling, skin blisters, skin peeling and skin excoriation on right hand and right foot. According to modified Hartwig scale of preventability and severity of adverse drug reaction, this adverse drug reaction falls under level 4 (moderate) severity and was definitely preventable. Several studies show that the most common cause of cutaneous ADR is FDC of Ofloxacin and ornidazole. Combined preparation can be avoided by prescribing individual drugs Thus, the incidence of adverse drug reactions can be reduced. Measures must be taken to reduce the availability of such drugs. Judicious use of commercially available FDCs should be done

Key words: Fixed dose combination, ofloxacin, cutaneous adverse drug reaction, ornidazole

Introduction

Ornidazole has excellent activity against anaerobic bacteria and protozoa. It belongs to nitro-imidazole group of antibiotics. Ofloxacin is used against bacteria and belongs to second generation of fluoroquinolones. [1]

Fixed dose combination of two or more active drugs in a single dosage form is used frequently. However, a single drug has many disadvantages and thus, FDCs are considered twice as risky. Use of FDCs is a real challenge, and the Indian medicine market has become the world leader for FDCs with an estimated number of over 6000 FDCs in India.[2]

A fixed dose combination (FDC) of ornidazole and ofloxacin is considered irrational as it increases the chances of occurrence of side effects and drug-drug interactions making its use inappropriate. Quinolones + nitroimidazole are known to be the highest suspected FDCs in Cutaneous adverse drug reactions (CADR).[3]

Cutaneous drug reactions are common and cause 3% of all disability injuries during hospitalization.[4] The spectrum ranges from toxic epidermolysis necrosis (TEN), fixed drug eruptions (FDE), transient maculopapular rash, Steven Johnson syndrome.[5]

We are reporting a typical case of cutaneous adverse drug reaction induced by the irrational use of FDC of ofloxacin and ornidazole

Case presentation

A 50 years old female patient had bilateral knee pain and swelling since a month. Doctor prescribed Tab. Veil (Ofloxacin 200 mg + Ornidazole 500mg) BD and Tab Duloxetine 20mg OD from 25th November 2023.Few days after starting treatment, patient developed swelling, skin blisters, skin peeling and skin excoriation on right hand and right foot (figure 1-3). Patient was admitted to medicine ward for the same on 10th December 2023. Tab. Veil was withdrawn immediately and tab duloxetine was continued. cutaneous adverse drug reaction was treated with Clopad cream (0.05%) twice daily application, tab L-Dio, tab Atarax and rich moist cream Reactions subsided 48 hrs post the withdrawal of drug and no new lesions were seen. Following causality assessment, the reaction was graded as ‘probable’ as per Naranjo’s scale and WHO-UMC causality assessment scale. [6,7] According to Hartwig’s severity assessment scale this was a level 4 reaction and was definitely preventable as per modified Schumock and Thornton scale.[8]

Figure 1

Figure 2

Figure 3

Discussion

India accounts for the highest burden for antimicrobial resistance worldwide as it remains to be the top consumer of antimicrobials. [9,10] The biggest challenge being the highest market availability of FDCs of antimicrobials in the world.[11] The government banned 26 antimicrobial FDCs in September 2018 after a decade long battle with the pharmaceutical companies.[12] However, of all the antimicrobial FDCs available in the market the banned FDCs represent a very small fraction of it. There are at least 43 antimicrobial FDCs that are still available in market that are irrational.[13]

Although, ofloxacin + ornidazole injection and suspension formulation were banned, the combination tablet was not banned and was amongst the most sold FDC in India.

The exact mechanism for this kind of reaction is not known. Inflammatory process of the drug starts by binding with basal keratinocytes, which leads to release of inflammatory granules, interferon, and lymphokines. Repeated exposure results in stimulation of mast cells locally and inflammatory reaction occurs each time we expose the person to the suspected drug.

A study done in Odissa on Cutaneous adverse drug reactions (CADR) with fixed-dose combinations with fixed-dose combinations showed a high incidence of CADRs with use of FDCs. Majority of their cases were FDEs. The most common FDC implicated was antimicrobial-based FDCs, particularly fluoro-quinolones + nitroimidazoles combinations (42%) among which ofloxacin + ornidazole combinations were most common (25%). The next group to cause CADRs were NSAID-based FDCs (31%).[14] These study findings were nearly similar to the study of Radhika *et al*., in which they have shown FDE as the most common CADR and antimicrobial-based FDCs as the highest number.[15] Chakrabarti A. studied the proportion of physicians using the FDC of antiprotozoal and antibacterial agents for diarrhoeal disease from India. He found that out of 2163 physicians' prescriptions, 59% were prescribing FDC of the fixed-dose combinations of ofloxacin and ornidazole.[16,17,18,19]

Conclusions

As per the case report ADR caused by FDC of ofloxacin-ornidazole and other related compounds although underreported, are very common in developing countries. This combination increases the adverse effects like cutaneous ADRs rather than providing any added benefits and hence is considered as an irrational FDC. Combined preparation can be avoided by prescribing individual drugs separately as and when they are required. Thus, the incidence of adverse drug reactions can be reduced. Measures must be taken to reduce the availability of such drugs. Patients and physicians need to be educated regarding the advantages and disadvantages of such FDCs which, are commercially available and judicious use of these drugs should be done.

Additional Information

Disclosures

Participant was well informed and consent was taken for this study.

Conflict of interest: NIL

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