

Ocular Side Effect of Tinidazole: A Rare Case Report

Hina Kauser, Maniah Qadir, Waseem Anwar

Department of Ophthalmology, Hamdard Institute of Medical Sciences and Research, Jamia Hamdard University, Hamdard Nagar, New Delhi, India

ABSTRACT

Ocular side effects in the form of punctate epithelial erosions with the use of tinidazole – a 5-nitroimidazole group of drugs is very rare. A 32-year-old male was prescribed tablet tinidazole for the treatment of amoebiasis but developed adverse effects in the form of blisters on both upper and lower lips with itching and burning sensation, itching and burning on penile and anal area associated with punctate epithelial erosions of cornea of both the eyes. All these are rare manifestations but punctate epithelial erosions of cornea has never been reported in the literature so far. Punctate epithelial erosions of cornea have not previously been reported and should be added to the list of complications of tinidazole. Hence, this case is being reported.

Keywords: Adverse effects, punctate epithelial erosions, tinidazole

Introduction

Metronidazole, tinidazole, secnidazole and ornidazole – all belong to 5-nitroimidazole group of drugs and are believed to be safe, prescribed widely and are freely available in the market. Tinidazole, a synthetic imidazole derivative, is widely used in the oral treatment of several protozoal infections – giardiasis, trichomoniasis, and amoebiasis. The protozoal organisms inhibited by tinidazole are *Trichomonas vaginalis*, *Trichomonas foetus*, *Giardia duodenalis* (also termed as *Giardia lamblia*) and *Entamoeba histolytica*.^[1] Tinidazole is the most preferred choice of drug for intestinal amoebiasis. Tinidazole also has antibacterial activity; it is active *in vitro* against *Bacteroides* spp., *Gardnella vaginalis*, *Prevotella* spp that are associated with bacterial vaginosis. It is usually well tolerated. The most common side effects reported with tinidazole are upset stomach, bitter taste, diarrhea, and itchiness. Other side effects that occur are headache, physical fatigue, and dizziness. Drinking alcohol while taking tinidazole causes an unpleasant disulfiramlike reaction, which includes nausea, vomiting, headache, increased blood pressure, flushing, and shortness of breath. The punctate epithelial erosions secondary to the use of tinidazole has not been reported till date. The aim of reporting this rare case presentation is to awaken the medical fraternity about the occurrence of rarest manifestation of the punctate epithelial erosions with the use of tinidazole.

Case Report

A 32-year-old male reported to the eye outpatient department with complaints of redness, watering, and pain both eyes since morning. The patient had the history of frequent stools with blood and mucus accompanied by abdominal pain for last 1 week and was diagnosed a case of amoebiasis. He had no H/O fever. He was put on treatment with tinidazole. Five hundred milligram tablet was taken by the patient in the evening. He got up the next morning with itching, burning sensation of both upper and lower lips, external genitalia and there is pain, redness and excessive watering from both the eyes. There was no history of ocular disease or use of any eye drops. General examination was all normal.

Local examination showed blisters on both upper and lower lips [Figure 1]. There were no blisters on penis and anal area where the patient is having itching and burning sensation. There was no hyperpigmentation on the penis at the site of itching. Investigations showed hemoglobin, total leukocyte count, differential leucocyte count, erythrocyte sedimentation rate, blood sugar, liver function tests, and renal function tests to be within normal limits.

Her uncorrected visual acuity was 6/12 in both the eyes. Lids and lashes have no deformity.

Upon slit lamp examination, there was no conjunctival reaction. Cornea showed punctate epithelial erosions, well stained with fluorescein stain [Figure 2]. These erosions were diffuse throughout the cornea and have similar appearance in both the

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Address for correspondence:

Dr. Hina Kauser,
RZ 904/24, Flat 202, Gali-24, Tughlakabad Extension,
New Delhi - 19, India.
E-mail: hina3kauser@yahoo.co.in

corneas. There was no reaction in the anterior chamber. Lens was clear, no opacities were present. Tear film meniscus was elevated; there were no signs of dryness [Figure 3]. Corneal sensations were intact. Because tinidazole was considered to be the cause of this problem, tinidazole was discontinued. He was treated with antiallergics (Tablet levocetirizine 10 mg twice a day), vaseline, and diclofenac (Lipcy Gel containing diclofenac 10 mg/gm) locally three times a day on lips, lubricating drop (Refresh tears) instilled six times a day both the eyes. Patient came for follow up after 2 days with relief in symptoms. There was no itching and burning sensation. Crust formation was there on both the lips. Eye examination revealed healing of punctate epithelial erosions, no staining with fluorescein stain. Visual acuity was 6/6 in both the eyes. Fundus examination was normal.

Discussion

Punctate epithelial erosions are fine, faintly visible, depressed lesions of corneal epithelium. They can be missed easily unless stained with fluorescein. The location of corneal involvement is most helpful for etiological determination. Involvement of the upper one-third of cornea is seen in vernal keratoconjunctivitis, superior limbic keratoconjunctivitis, molluscum contagiosum, trachoma or a foreign body under the upper lid. Interpalpebral involvement is characteristic of neurotrophic keratitis, keratoconjunctivitis sicca and photokeratopathy. Lower portion of cornea is involved in staphylococcal blepharoconjunctivitis, exposure of cornea, rosacea, and entropion. Diffuse distribution occurs in drug toxicities, viral keratitis.^[2] In our case it was also diffuse distribution which confirms drug toxicity, corneal sensations were intact and not associated with viral systemic symptoms which means that there was no viral etiology, there is no dryness that is tear film meniscus was elevated in our case which confirms that it is due to toxicity and there was no history of usage of topical eye drops.

Not only the topical eye drops cause adverse ocular side effects but many systemic drugs also affect different segments of the eye as minor/insignificant or major/vision threatening adverse reactions. It is important to recognize early that the ocular findings are the adverse reaction to particular systemic drug and should appropriately intervene before irreversible damage sets in by modification of dose or use of alternative drug. Systemic drugs and their metabolites reach cornea and lens via the tear film, limbal vasculature, and the aqueous humor. Although corneal opacities secondary to drug therapy do not produce much of visual impairment, they may signal more permanent drug deposits in the lens and retina. Various systemic drugs such as amiodarone, atovaquone, tamoxifen, chlorpromazine, indomethacin, Isotretinoin, gold salts, crack cocaine, and chloroquine are reported to cause corneal adverse reactions, mostly in the form of whorl like corneal opacities.^[3] Amantadine can induce adverse corneal reactions in the form of superficial punctate keratitis, punctate subepithelial opacification, epithelial edema and stromal edema although ocular toxicity is extremely rare.^[4] But no adverse effects on cornea has been reported with tinidazole and other nitroimidazole drugs. The



Figure 1: Blisters on both upper and lower lips

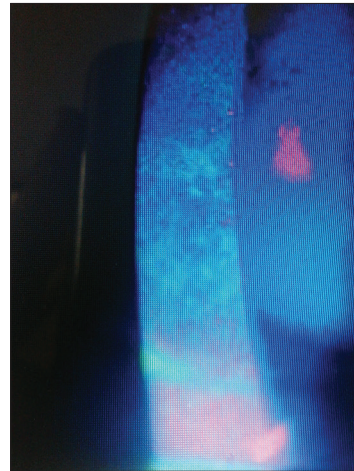


Figure 2: Cornea showing punctate epithelial erosions well stained with fluorescein stain on slit lamp examination



Figure 3: Elevated tear film meniscus

common side effects of the nitroimidazoles are symptoms from the gastrointestinal tract such as nausea, anorexia, vomiting, and metallic or bitter taste. Dizziness, ataxia, and headache have been reported.^[5]

Brownish-black hyperpigmentation of the angles of the mouth and medial canthus of both the eyes due to tinidazole was reported by Jose.^[6] They also report itching and burning sensation of lips and penis similar to our case. Acute visual loss following administration of metronidazole due to optic neuropathy was reported by Allroggen *et al.*^[7] McGrath *et al.* reported reversible optic neuropathy due to metronidazole use.^[8] Neurological complications in the form of peripheral neuropathy by metronidazole have also been reported.^[9] One patient with encephaloneuropathy with brain magnetic resonance imaging (MRI) changes due to harmful and chronic use of tinidazole was reported by Chacko *et al.*^[10] Sangma reported two cases of fixed drug eruption due to tinidazole.^[11] Six cases of anaphylactic reaction following a dose of 2 gm or more were reported in the literature,^[12] but Singbal reported severe anaphylactic reaction to 250 mg of tinidazole.^[13] To the best of our knowledge, corneal adverse reactions due to tinidazole has not been reported in the literature, and such immediate onset (within a day) is again, rare.

Conclusion

Nitroimidazoles are not only prescribed commonly by medical practitioners, but also available easily over the counter. Moreover, various combination preparations with other antimicrobials are readily available in the market and frequently used by people. Considering easy availability of nitroimidazoles, their range of activity and nonemergence of resistance to most organisms, adverse drug reactions (ADR) due to this group of drugs are very relevant. Although adverse corneal reactions are relatively rare with these drugs, but awareness of these reactions is important for early diagnosis and better management of such patients.

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