AN UNUSUAL ADVERSE EFFECT OF TINIDAZOLE

Tinidazole belongs to nitroimidazole group of drugs, which also include metronidazole, secnidazole, ornidazole and benznidazole\(^1\). These drugs have activity against Peptococcus, Peptostreptococcus, \textit{Gardnella vaginalis}, Clostridium, Propionibacterium, Eubacterium, Fusobacterium, Bacteroides, Helicobacterium, Campylobacter, Actinomyces and Spirochetes. It is effective against \textit{Entamoeba histolytica} and \textit{Trichomonas vaginalis} and useful in Crohn's disease and pseudomembraneous colitis. It also helps easy extraction of Guinea worm. It also sensitises hypoxic tumour cells to the effects of ionising radiation\(^1,2\).

Considering the range of activity and non-emergence of resistance to most organisms\(^1\), nitroimidazoles have become indispensable drugs in clinical practise. Hence adverse drug reactions (ADR) due to this group of drugs is very relevant. Here we report an unusual ADR that was observed with tinidazole.

A 27-year-old male medical personnel reported to the outpatient department with complaints of brownish-black hyperpigmentation of the angles of the mouth and medial canthus of both the eyes of 2 weeks duration.

The problem started on the second day following intake of tinidazole (Tablet Fasigyn 500mg by Pfizer) for the treatment of amoebiasis. Symptoms started as itching on both upper and lower lips which progressed to burning sensation, ulceration, oedema and ultimately resulted in hyperpigmentation of the lips. All these symptoms also involved the inner canthus of both the eyes. There was mild penile itching but it subsided in 3 days. After taking 4 tablets of tinidazole, on the second day, he stopped the drug following advice that the adverse effects may be due to the drug. He was treated with pheniramine maleate (Tablet Avil 25mg by Hoechst Marison Roussel) orally three times a day for a week, vaseline and diclofenac (Lipcy Gel containing diclofenac 10mg/gm by Comed chemicals) locally three times a day for two weeks, but without much change in hyperpigmentation.

He had taken 4 courses of tinidazole in the past. First course was taken one and half years back without any adverse effects. Second course of tinidazole was taken 6 months back, again without any adverse effects. Third course of tinidazole with ciprofloxacin (Tablet Ciplox-TZ containing ciprofloxacin 500mg and tinidazole 600mg by Cipla) was taken 3 months back following which he developed mild itching and swelling of the lips on the second day. The adverse effects that developed following the third course, were not considered serious by the patient since it was mild, occurred during the cold season and was not suspected as a drug reaction. After the fourth episode he has not taken any nitroimidazole group of drugs.

He had taken metronidazole before this episode, without any similar symptoms. There is no past history of drug allergy or phototoxicity. Diabetes, hypertension, asthma, metabolic disorders, skin diseases, endocrine disorders, autoimmune disorders, generalised hyperpigmentation and other chronic diseases were clinically ruled out. There is no similar history of allergy to tinidazole among the members of the family.

Examination showed normal blood pressure, pulse, temperature and respiratory rate. There was no evidence of pallor, cyanosis, jaundice, clubbing, generalised lymphadenopathy, pedal oedema or mucocutaneous involvement other than at the sites mentioned. Local examination showed hyperpigmentation of both the medial canthus and around the lips especially at the angle of the mouth. There was no hyperpigmentation on the penis at the site of itching. All other systems were with in normal limits.

Investigation revealed haemoglobin, total leucocyte count, differential leucocyte count, erythrocyte sedimentation rate, blood sugar, liver function tests and renal function tests to be with in normal limits.

The above-described clinical event showed time relation to drug administration, it could not be explained by concurrent diseases, drugs or chemicals and dechallenge improved the condition. Further rechallenge was not done fearing serious complication and ethical constrains. Hence this ADR can be labelled 'Probable/likely' as per causality assessment\(^3\). Since this ADR was not dose-dependent, it could be labelled as Type-B class of ADR\(^3\). Since pigmentation occurred only on the light exposed parts
like angle of mouth and inner canthus and not on the penis, phototoxicity component for the reaction cannot be totally ruled out. Different types of ADR's are described with tinidazole\textsuperscript{1,2,4}, but hyperpigmentation due to hypersensitivity, is rarely reported with tinidazole\textsuperscript{5}.

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\textbf{REFERENCES}


WORK STRESS DOUBLES RISK OF DEATH FROM HEART DISEASE

Work stress is associated with a doubling of the risk of death from heart disease, finds a study in BMJ.

Researchers followed 812 healthy employees (545 men, 267 women) of a company in Finland for an average of 25 years. They gathered data on stress, blood pressure, cholesterol levels, and body mass index by questionnaire, interviews, and clinical examinations. Cardiovascular deaths were calculated using the national mortality register.

They found that job strain (high work demands and low job control) and effort-reward imbalance (high demands, low security, few career opportunities) were each associated with a doubling of the risk of cardiovascular death among initially healthy employees. High job stress was also associated with increased cholesterol concentrations and body mass index.

In promoting cardiovascular health, the traditional advice has been for people to stop smoking, cut down drinking, eat less fat, and engage in physical activity. These findings suggest that attention should also be paid to the prevention of work stress, conclude the authors.

\textit{(Work stress and risk of cardiovascular mortality: prospective cohort study of industrial employees - http://bmj.com/cgi/content/full/325/7369/857)}