CONCENTRATION OF TINIDAZOLE IN VAGINAL FLUID AFTER ORAL ADMINISTRATION IN VAGINAL TRICHOMONIASIS*

(A Clinical and Pharmacokinetic Study)

By

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SUMMARY

Twenty-five patients suffering from Trichomonas vaginitis and 10 healthy volunteers were administered tinidazole orally in a single dose of 2 gms. Tinidazole concentrations were estimated in the vaginal discharge daily upto 4 days. Effect of tinidazole on free floating Trichomonas vaginalis was assessed by hanging drop preparation. Symptomatic and clinical improvement in the patients after tinidazole therapy was noted.

15 patients obtained symptomatic relief on the second day of therapy and 9 patients on the third day. In these patients hanging drop preparation revealed absence of Trichomonas vaginalis.

Tinidazole appeared in the vaginal fluid soon after administration and persisted in adequate concentrations upto 4th day. These concentrations were above the MIC of tinidazole against Trichomonas vaginalis.

Tinidazole was well tolerated in both, the patients and controls.

Introduction

Tinidazole is a nitroimidazole derivative. It is structurally related to Metronidazole and has been demonstrated to have superior pharmacotherapeutic effects than the latter. The chemical formula of Tinidazole is; 1-(2-ethylsulphonyl) ethyl-2 methyl-5-nitroimidazole.

After its synthesis in 1969, Tinidazole was shown to be highly effective against Trichomonas vaginalis (Howes *et al*, 1970). In addition to its anti-protozoal effect, Tinidazole is also effective in the treatment of anaerobic bacterial infections (Reynolds *et al*, 1975).

Results of a good number of clinical trials have established the therapeutic efficacy of a single 2 gm dose of tinidazole in the treatment of Trichomoniasis Forsgren and Wallin, 1974; Swarz, 1974; Ward, 1976. Lack of satisfactory response or relapse in a female patient denotes

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reinfection from the male partner (Goodman and Gilman, 1980).

It is now an established fact that both the sexual partners should be simultaneously treated for trichomoniasis. Single dose therapy with tinidazole has the advantage of being more acceptable to the patient and the partner (Weidenbach and Lax, 1974).

Trichomonads are not only burrowed in the vaginal mucosa but are also free floating in the vaginal secretions. In view of the efficacy of tinidazole in producing prompt symptomatic (Erb, 1975) as well as parasitological cure (Norgaard, 1975), the drug must be attaining Trichomonacidal concentrations in the vaginal secretions too. The present clinical study was undertaken in female patients with trichomoniasis to find out whether Tinidazole appeared in vaginal fluid and if so, in what concentrations, after a single oral dose of 2 grams. This study was also designed to correlate the clinical and parasitological cure with tinidazole therapy.

Material and Methods

Twenty five Female patients suffering from Trichomonas vaginitis were included in the study. 10 healthy women in the same age group were taken as control.

In the 25 patients the disease was confirmed by hanging drop examination of vaginal secretion for freely motile trichomonads.

Tiniba tablets (tinidazole 500 mg) were used for oral administration for the single dose therapy of 2 grams. Vaginal discharge was collected after 4 hours by a dropper from the posterior fornix. The patients were asked to report daily and vaginal discharge was collected every day for four days. On the fourth day hanging drop examination was repeated to find out presence of viable trichomonas vaginalis.

Both, subjective feelings of the patients and clinical evaluation of the disease were noted. Symptoms attributable to the disease or drug therapy were also recorded.

The control group was also administered tinidazole 2 gm in a single dose, clinical evaluation was done and the vaginal discharge was obtained for estimation of tinidazole.

Tinidazole was estimated in vaginal discharge by the chemical method described by Chaudhary *et al*, 1983.

Clinical Observations

All the 25 patients in the study group were in the child bearing age. 20 patients were between the age of 20 to 30 years. Five patients were parous and 2 were nulliparous.

All the patients had average built and 15 patients were adequately nourished. 10 patients were poorly nourished and had moderate degree of anaemia.

Presenting Symptoms

The onset of symptoms was sudden in 14 patients and gradual in 11 patients.

Vaginal Discharge

All the patients complained of vaginal discharge. The characteristics of which are as under:

Characteristics	*No. of Patients*
Profuse ..	16
Moderate ..	5
Scanty ..	4
Foul smelling ..	16

5 patients having leucorrhoea for more than a year gave the history of increase in discharge after menstruation.

Symptoms Related with Micturition

Symptoms	*No. of Patients*
Burning	17
Dysuria	9
Frequency	15

Other symptoms were headache, body-aches, nausea and giddiness. One patient had previous history of labial ulcer.

Local Examination

On local examination 1 patient had redness of the vulva. The characteristics of the discharge observed during examination were as under:

Characteristics	*No. of Patients*
Creamish	21
Whitish	4
Frothy	14

On internal examination the vagina appeared red in 9 patients, congestion was noted in 23 patients and there was local tenderness in 16 patients

Results

All the patients were given Tinidazole 2 gms. in a single dose. Subjective improvement was obtained as under:

No. of Pts. obtaining Relief	*Days after Therapy*
15	Second day
9	Third day

24 patients obtained symptomatic relief within 3 days of taking tinidazole. Trichomonas vaginalis was not seen in these patients when hanging drop examination was done on the 4th day. On local examination on the 4th day slight vaginal congestion was observed in 15 patients. 1 patient did not obtain symptomatic relief and the hanging drop preparation revealed the presence of T. Vaginalis. Another patient complained of pruritus and discharge on the 4th day.

Tinidazole concentrations were estimated in the vaginal discharge daily upto 4th day in both patients and control subjects. The average concentrations of tinidazole in the patients and controls are given in Table I.

TABLE I

Tinidazole Concentrations (mcg/ml)

Days	Patients	Control
1	3.29	3.08
2	2.32	2.99
3	1.79	1.76
4	1.19	1.02

Tinidazole appeared in vaginal secretions soon after oral administration in all the subjects included in the study. It was found in concentrations of 1.19 mcg/ml even on 4th day.

These findings indicate that tinidazole achieves effective concentrations in the vaginal secretions which persist for a long time.

Tinidazole was well tolerated by all the patients. It was devoid of any untoward effect. One patient complained of head-

ache and another complained of dryness of mouth.

Discussion

Tinidazole a newer nitroimidazole derivative is now widely prescribed for the treatment of various protozoal infections such as trichomoniasis, amoebiasis and giardiasis. (Khokhani *et al* 1977; Scragg and Proctor, 1977) (Farid *et al* 1974; Levi *et al* 1977). The clinical experience with its administration in single dose has added to its effectiveness and patient compliance. In India and other Asian countries, the single dose of tinidazole (2 grams) has been successfully used to treat trichomoniasis. However, the data regarding its concentrations in vaginal fluid in Asian females is not available. Our study was aimed at finding out the concentrations of tinidazole in vaginal fluid and its effects on free floating T. vaginalis.

As discussed in results, the symptomatic improvement was apparent within a day. The findings are in agreement with the results of other studies (Erb; 1975). High parasitological cure observed in other studies (Norgarrd, 1975; Sawyer, 1976; Apte, *et al* 1978; Kawamura, 1975) is substantiated by our findings.

The concentrations of tinidazole in the vaginal fluid soon after oral administration were in high therapeutic range (Table I) considering the minimum inhibitory concentration of tinidazole (1.25 mcg/ml) against trichomonas vaginalis (Forsgren and Wallin, 1974).

Persistence of tinidazole in vaginal fluid in adequate concentrations even upto 4 days after oral administration further proves the pharmacokinetic advantage of this drug in the treatment of trichomoniasis. Thus the satisfactory clinical and parasitological cure obtained with this drug reflects the effect of adequate concentrations at the site of infection.

The study further revealed that tinidazole was well tolerated in single dose of 2 grams. This is in accordance with the findings of other studies (Erb, 1975; Mati and Wallace, 1985).

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