ORAL SINGLE-DOSE THERAPY OF TRICHOMONAL VAGINITIS COMPARISON OF TINIDAZOLE AND METRONIDAZOLE

by

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Introduction

Trichomoniasis is a sexually transmitted disease. In spite of the availability of effective chemotherapeutic agents such as metronidazole, the incidence of the infection has been on the increase. One cause of failure is non-compliance of the patient taking the complete treatment as prescribed. Another cause of failure is reinfection from sexual partners who have not been simultaneously treated. In practice, therefore, successful treatment includes prevention of reinfection. If treatment could be administered simultaneously and in one session both to the patient and the consort, the problem of treatment could be considerably facilitated because its success would no longer depend on patient compliance. From this point of view a single dose treatment has much to be recommended. Recently we came across the report (Swarz, 1974) of clinical trials of a new imidazole compound, tinidazole (Fasigyn, Pfizer), in which a single oral dose of 2 grams cured trichomoniasis in over 95% of cases. In view of this encouraging report we decided to undertake a comparative study of this drug with metronidazole in our own patient population.

Material and Methods

Patients attending the outpatient department with a complaint of leucorrhoea were screened for trichomoniasis. The diagnosis was established by demonstrating the organism in vaginal discharge collected from posterior fornix of vagina, both microscopically (hanging drop preparation and stained smear) and by culture (Feinberg-Whittington medium).

Patients with gross dysfunction of vital organs were excluded, and so were those who had received any specific anti-trichomonal treatment during the previous 2 weeks. The qualifying patients were randomly allocated to receive either tinidazole or metronidazole, both as a single dose of 2 grams by mouth under direct supervision. In most cases the consorts were treated in the same manner. Further, the patients were advised to abstain from sexual intercourse during the study period.

Clinical and parasitological examinations were done before initiating therapy,

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and then on 7th, 14th and 21st post-treatment days. Side effects were noted only if volunteered by the patient.

Results were analysed, both parasitologically and clinically. The criterion of successful treatment was (a) parasitological—disappearance of the parasite from vaginal secretion; (b) clinical—complete or marked relief of signs and symptoms.

Results

Of 250 patients of leucorrhoea that were screened, 108 were suffering from trichomoniasis and 90 qualified for inclusion in the present trial.

Of the 90 patients treated, 66 completed a 3 weeks follow-up as per protocol, 36 on tinidazole and 30 on metronidazole. Rest of the patients defaulted and, since they could not be traced, nothing could be known of their response to treatment. Table I shows the important features and initial comparability of 2 treatment groups.

The therapeutic response is shown in Table II. In the tinidazole group clinical

TABLE I
Comparison of Treatment Groups

Item	Tinidazole	Metronidazole
Age		
Range	19—50 yrs.	20—60 yrs.
Mean	31.1	34.3
S.E.M.	± 1.3	± 1.7
Previous *Treatment*		
Metronidazole	2*	0
Consorts		
Treated	28 (77.8%)	24 (80%)
Not treated**	8 (22.2%)	6 (20%)

* Both the patients responded to tinidazole.

** These patients were either unmarried, or widows or separated, and their history of sexual contact was negative.

TABLE II
Comparison of Therapeutic Response

Response	Tinidazole N	Tinidazole %	Metronidazole N	Metronidazole %	Significance of difference
Parasitological					
Cure	35	97.2	24	80	$X^2 = 5.1$ ($P < 0.05$)
Failure	01	02.8	06	20	
Clinical					
Cure/Marked Improvement	35	97.2	24	80	$X^2 = 5.1$ ($P < 0.05$)
No improvement	01	02.8	06	20	

and parasitological cure was observed in 97.2% of patients. In this series, 2 patients who had previously shown poor therapeutic response to standard, divided dosage therapy of metronidazole responded effectively to tinidazole therapy. In metronidazole group, 80% of patients demonstrated clinical and parasitological cure. Thie difference was statistically significant ($P. < 0.05$).

In the tinidazole group, 8 of 36 patients (22.2%) complained of nausea, vomiting and giddiness. In the metronidazole group, 9 patients out of 30 (30%) had similar side effects; one of the patients had severe vomiting, requiring hospitalization and treatment with parenteral prochlorperazine.

Discussion

Human nature being what it is, noncompliance with the prescribed drug therapy becomes a problem, as the number of doses per day increases and the duration of treatment is prolonged. In the case of sexually transmitted diseases, the consort is often asymptomatic and therefore unwilling to accept treatment. These factors contribute not only to failure of treatment in the patient but, even if the treatment is successful, to reinfection by the sexual partner. It is therefore desirable to treat the patient and her consort simultaneously under direct supervision, which can be done if the prescribed therapy consists of a single dose to be given at one time. Such treatment can have a tremendous influence not only on the management of individual patient but also on the epidemiological control of the disease.

We observed that tinidazole in a single oral dose of 2 g. gave a cure rate of 97.2% vis-a-vis 80% with metronidazole on a similar regime, establishing that under comparable conditions tinidazole is more effective than metronidazole. These results agree closely with results of noncomparative studies reported elsewhere. Swarz (1974) has reported a cure rate of 97.6% with tinidazole in 251 patients with a single 2 g. dose. On the other hand, Csonka (1971) and Woodcock (1972) have reported cure rates of 82 and 86%, respectively, with a 2 g. single dose of metronidazole.

The higher efficacy of tinidazole over metronidazole reflected in the foregoing study may be due to its pharmacologic properties. A blood level study by Monro (1974) showed that when these drugs are given orally in a dose of 2 g., tinidazole produces higher blood levels than metronidazole; further, the levels of tinidazole decline more slowly than those of metronidazole. Thus, tinidazole is able to achieve a higher in vivo concentration and to persist longer in the system. Besides, the in vitro antitrichomonal activity of tinidazole is twofold higher than that of metronidazole (Forsgren and Wallin, 1974).

With respect to side effects, the severity was generally less with tinidazole than with metronidazole, although the effects were qualitatively similar. On account of this difference, tinidazole can be expected to be more acceptable to patients than metronidazole.

On the basis of this study, it is our opinion that tinidazole is a definite improvement over metronidazole and can contribute significantly to the treatment and control of trichomoniasis.

Summary

In a randomised comparative clinical study, 36 patients suffering from trichomonal vaginitis were treated with tinidazole, and 30 patients with metronidazole. Both the drugs were administered as a single dose of 2 grams by oral route; both

the patient and the consort were treated in a majority of cases. Tinidazole produced clinical and parasitological cure in 97.2% of patients, whereas metronidazole did so in 80% of patients ($P < 0.05$). Gastrointestinal side effects were milder with tinidazole than with metronidazole.

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