

Metronidazole and tinidazole in a single large dose for treating urogenital infections with *Trichomonas vaginalis* in men

NOBUO KAWAMURA

From the Department of Urology, Tokai University School of Medicine, Kanagawa, Japan

SUMMARY Seventy-three men with urogenital trichomonal infection were treated with a single daily dose of 1 g tinidazole or 1.5 g metronidazole. Both treatments gave satisfactory results. Wives who were also infected with *Trichomonas vaginalis*, were less likely to have a recurrence of the infection after their husbands had been given either drug.

Introduction

It has been pointed out by many investigators that more men would be found to have urogenital infection with *Trichomonas vaginalis* than actually reported if thorough examinations were performed (Strain, 1945; Bedoya *et al.*, 1958a, b; Schuppis, 1958; Catterall and Nicol, 1960; Ohmura, 1960; Hoffman *et al.*, 1961; Catterall, 1965; Kimura, 1965; Perl *et al.*, 1965; Schmor, 1974; Weidenbach and Leix, 1974). *T. vaginalis* is found in a little over 2% of normal male urine samples and in 8 to 11% of urine samples after prostatic massage. This detection rate rises to 10 to 13% when the spouses are infected with *T. vaginalis* (Nittono, 1959; Kawamura, 1969).

Male patients with trichomonal urogenital infections are usually asymptomatic or present only mild symptoms of urethritis or prostatitis (Freed, 1948; Keutel, 1959; Yamamoto, 1963; Wallin, 1974). Asymptomatic patients should be treated to prevent spread of pathogenic protozoa, particularly if the spouse suffers from trichomoniasis. In such cases it is evident (Sylvestre *et al.*, 1960; Mizuno, 1963) that both partners have to be treated simultaneously to prevent possible recurrence of the wife's infection.

Trichomonal infections respond to drugs much more effectively in men than in women (Kawamura, 1969, 1973a, b). Oral trichomonocides may cause gastrointestinal disturbances and it is difficult to persuade men to take oral treatment for 7 to 10 days; this is particularly so if there are no symptoms or they are mild, or if the infection is

present only in the wife. These factors may result in inadequate treatment.

The American Medical Association, Drug Evaluation, warns that metronidazole has not been completely cleared from carcinogenicity and its use should be limited to a maximum total dosage of 5.25 g. Prolonged use should therefore be avoided. Hitherto we have treated men with urogenital trichomonal infections with a 7 to 10-day oral course of nitrofurantoin, acetylfurazirine, trichomycin, or metronidazole. However because of these problems, we compared a single oral dose of either metronidazole or tinidazole with the normal 7 to 10-day course.

Literature published in the USA and Europe shows that for single doses either 750 mg tinidazole or 2 g metronidazole is generally used (Csonka, 1971; Campbell, 1972; Morton, 1972; Ozaki, 1972; Woodcock, 1972; Dellenbach and Muller, 1974; Forsgren and Wallin, 1974; Wallin and Forsgren, 1974; Hayward and Roy, 1976). In view of the average body weight of the Japanese, however, either 1 g tinidazole or 1.5 g metronidazole was given.

Materials and method

Male outpatients from the departments of urology in Tokai University Hospital, Keio University Hospital, Nerima General Hospital, Saiseikai Kanagawa Prefecture Hospital, and Kawasaki City Hospital were selected during 1974-76. They had presented with symptoms of urethritis or prostatitis, were incidentally found to be infected with *T. vaginalis*, or had wives with trichomoniasis.

Address for reprints: N. Kawamura, Department of Urology, Tokai University School of Medicine, Kanagawa, Japan

Received for publication 23 June 1977

The patients who were selected in 1974 and at the beginning of 1975 were treated with tinidazole. After June 1975, patients were treated with metronidazole.

Examinations were carried out on morning urine, the first glass of Thompson's two-glass test, mid-stream urine, prostatic fluid, urethral secretion, and urine after prostatic massage. If the patient was married, the wife was investigated in the gynaecological or the urological department.

Cultures for *T. vaginalis* were done using mainly the Asami culture medium (Asami, 1952; Kawamura, 1969), and also the commercial Vaginal Trichomonas-Candida culture medium (product of Nissui Seiyaku Co. Ltd). In each case, urine sediment or secretion smear was examined microscopically. Some cases were detected only by microscopical examination.

T. vaginalis detection rates vary considerably according to the medium employed. Although the relevant data are not presented here, we believe the Asami culture medium is most suitable for the examination of trichomonal infection in men (Iijima, 1959; Nakabayashi, 1959; Matsuda, 1969, unpublished; Kawamura, 1976, unpublished). This is because trichomoniasis in men is characterised by a relatively small number of protozoa and this medium is capable of culturing even a single protozoon.

Altogether 73 patients were found to have trichomoniasis (Table 1). 1 g tinidazole or 1 g metronidazole was administered as a single oral dose.

Table 1 Total and *T. vaginalis* positive findings (73 patients)

	Total specimens	<i>T. vaginalis</i> positive specimens
Morning urine	12	3
First-glass urine	60	46
Midstream urine	58	23
Prostatic fluid	3	2
Urethral secretion	4	1
Urine after prostatic massage	46	32

As more than one specimen was tested for each patient and more than one specimen in many patients was found to be *T. vaginalis* positive the two columns do not add up to 73.

Drug evaluation was made by culturing between 7 and 14 days after treatment the same specimens that had been found to contain trichomonads before treatment. If *T. vaginalis* was not detected, the cases were judged as cured. In cases where the wives had been infected with trichomoniasis the husbands were asked to undergo investigation on two occasions during the 14-30-day period and a cure was judged if trichomonads were absent in all the specimens.

Results

The results are summarised in Table 2. All 73 men with trichomonal infection (tinidazole-treated group 39; metronidazole-treated group 34) were cured and there were no relapses.

Table 2 Results of treatment in 73 patients with *T. vaginalis*

Treatment	No. treated	No. cured
Tinidazole	39	39
Metronidazole	34	34

Six cases in the tinidazole-treated group and four cases of the metronidazole-treated group complained of gastrointestinal disturbances. These disappeared naturally within a few days. No marked difference in severity of these side effects was observed between the two drugs and no serious side effects were seen.

Nine patients in the metronidazole group had liver function tests and blood urea nitrogen was measured before and 7 to 14 days after treatment and a sperm count was taken. No abnormal values were found in any of the biochemical tests. In three cases the sperm count was reduced by more than 10 million and in a fourth case by 30 million.

Discussion

The dosage and method of administration of tinidazole and metronidazole can be considered adequate, judging by the results obtained in this study. No particular difference in efficacy was seen between the two drugs.

In view of the minor side effects, the dosage could safely be increased. The results of Hoffman *et al.* (1961) and Kawamura (1973a) suggest that the dosage might even be reduced with equally effective results. Clinical trials are under way to assess this point. Minimum inhibitory concentrations of these two drugs for *T. vaginalis* were determined (Kawamura, 1973b, 1974) using MSF medium; these were 0.6 to 1.2 mg/ml for tinidazole and 0.8 to 1.2 mg/ml for metronidazole. Bearing this in mind, as well as the blood levels for these two drugs (Ozaki, 1975; Wood and Monro, 1975; Seiga, 1976, unpublished), administration of metronidazole in a single dose of 0.75-1 g should be sufficient.

The results presented here are better than those reported by Morton (1972) and are in approximate agreement with those of Rodin *et al.* (1960) and Schapira (1965). The data are also compatible with the report of Perl (Perl *et al.*, 1965) that 98.2% of patients treated with 0.75 g metronidazole daily for 10 days were cured.

Trichomonal infections of the female genital tract may recur (Jones, 1972), but it is known that the cure rate improves if the husband is treated simultaneously (Schuppius, 1958; Perl and Ragazzoni, 1963; Campbell, 1972; Woodcock, 1972). As trichomonal infection in men can easily be controlled, as demonstrated in this study, treatment with a single dose large enough to be effective is advocated.

Neither tinidazole nor metronidazole is a safe drug. It is possible that as nitro-compounds they may have an adverse effect on spermatogenic function and they are not recommended for heavy drinkers or for prolonged medication. Treatment with a single, large dose eliminates these disadvantages.

The sample size of the present study (73 patients with urogenital trichomoniasis) is larger than in similar studies, and can perhaps serve as a useful reference on the clinical application of this treatment in the future.

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