Treatment of trichomoniasis in females with and without gonorrhoea

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Summary

46 women with trichomoniasis and gonorrhoea were treated with nimorazole (300 mg twice daily for 7 days) and a trichomonal cure rate of 90.2 per cent. was noted.

In addition, 53 of 112 patients with trichomoniasis but without gonorrhoea, were treated with metronidazole (200 mg three times a day for 7 days) and 59 with nimorazole (300 mg twice daily for 7 days) in a randomized trial. The cure rates were 96 and 90.5 per cent. respectively. There was no significant difference in the results noted in the two groups.

Neither the trichomonal infection itself nor the result of antitrichomonal therapy was affected by antigenococcal therapy (one-day treatment with ampicillin or single-dose therapy with doxycycline).

No increase was noted in the frequency of candidiasis after antitrichomonal therapy (in patients without gonorrhoea) or after antigenococcal therapy, but there was substantial variation between consecutive specimens in the prevalence of *C. albicans*.

Introduction

In a one-year study of female patients attending a venereal disease clinic, the frequency of *Trichomonas vaginalis* was found to be 20 per cent. (Eriksson and Wanger, 1975).

Good results in the treatment of trichomoniasis have been obtained with metronidazole. During the last few years other potent antitrichomonal agents have been produced, one of these being nimorazole. In our investigation of women with *T. vaginalis*, we have studied (a) the effect of treatment with nimorazole, (b) the comparative effect of metronidazole and nimorazole, and (c) the effect, if any, of the treatment of *T. vaginalis* on *Neisseria gonorrhoeae* and *Candida albicans*.

Patients and methods

All women attending the clinic were examined at all visits for the presence of *N. gonorrhoeae*, *T. vaginalis*, and *C. albicans* during the period November, 1971, to October, 1972.

Diagnosis

N. gonorrhoeae was detected by direct microscopy and/or culture. Specimens were taken from the urethra, cervix, and rectum, and were cultured on Thayer-Martin medium. *T. vaginalis* was identified by direct microscopy and/or culture during the first half of the investigation, and by culture alone during the second half. Cultures were done by the method of Diamond (1957).

C. albicans was identified by culture on Sabouraud agar plates. Eriksson and Wanger (1975) have described the diagnostic procedures in detail.

Treatment

Patients with uncomplicated gonorrhoea were treated either with 2 g ampicillin (Doktacillin®, Astra Läkemedel AB, Sweden) administered orally in two doses with a 5-hour interval or with 0.3 g doxycycline (Vibramycin®, Pfizer AB, Sweden) in a single oral dose.

Patients with *T. vaginalis* were treated differently depending on the presence or absence of *N. gonorrhoeae*.

(a) *Patients with trichomoniasis and gonorrhoea* Trichomoniasis was treated with nimorazole 300 mg twice daily for 7 days. Every third patient was excluded from treatment.

(b) *Patients with trichomoniasis alone* These patients were treated in randomized series with metronidazole (Flagyl®, AB Leo, Sweden) 200 mg three times a day for 7 days or, alternatively, with nimorazole 300 mg twice daily for 7 days. The randomization was carried out in groups of ten patients, five being treated with metronidazole and five with nimorazole. The investigator did not know which preparation each patient received.

Treatment for trichomoniasis was not given until gonorrhoea was diagnosed or excluded. In patients in whom both gonorrhoea and trichomoniasis were diagnosed and treated at the same visit, antitrichomonal treatment was started the day after the antigenococcal treatment.

Patients in whom trichomonal cultures became positive during the follow-up period, after antitrichomonal therapy, were not treated again.

All pregnant patients were excluded from the study, and it was not usually possible to treat the sexual partners

of the patients with trichomonal infestation. Blood specimens were collected for white blood cell counts and liver function tests before and immediately after treatment.

Patients with candidiasis Patients with candidiasis were not treated until other therapeutic procedures and follow-up examinations had been completed.

Follow-up

Patients were asked to return for follow-up examinations at weekly intervals. Our aim was to recall patients treated for trichomoniasis for at least three visits. At these visits the patients were asked about subjective symptoms and complaints, and any side-effects of the drugs.

Results

During the period of investigation specimens were collected from 1,347 women, and at the first visit *N. gonorrhoeae* was found in 506 cases (38 per cent.), *T. vaginalis* in 272 (20 per cent.), and *C. albicans* in 233 (17 per cent.).

The frequency of infection, the relationships of the different pathogens, and their symptomatological significance have already been reported (Eriksson and Wanger, 1975), as well as the results of the antigenococcal treatment (Enfors and Eriksson, 1975).

Patients with trichomoniasis and gonorrhoea

In this group, 46 patients were treated with nimorazole (Table). Among the patients in whom antitrichomonal treatment failed, three were noted at the first follow-up visit and one at the second.

In 26 patients the gonorrhoea was treated with ampicillin and in twenty with doxycycline. Neither ampicillin nor doxycycline therapy affected the results of the antitrichomonal therapy, nor was any difference noted in the therapeutic results if the antitrichomonal therapy was initiated at the same time as the antigenococcal therapy or later.

Patients with trichomoniasis alone

In this group, 112 patients were treated—53 with metronidazole and 59 with nimorazole (Table).

Among the patients registered as failures, two, treated with metronidazole, were noted at the first follow-up, and four, treated with nimorazole, at the

second follow-up. One patient treated with nimorazole was noted as a failure at the third follow-up.

The results of the *tests of cure* are presented in the Table. In the group of patients with trichomoniasis but without gonorrhoea who were treated with metronidazole, 48 out of 50 (96 per cent.) were cured, while 48 of 53 (90.5 per cent.) treated with nimorazole were cured. Thus there was no significant difference ($\chi^2_1=0.49$; $P=0.5$). In the group of patients with trichomoniasis and gonorrhoea, 37 out of 41 (90.2 per cent.) were cured. There was no difference in the results of treatment with nimorazole in patients with or without gonorrhoea.

Side-effects of antitrichomonal therapy

Four patients treated with metronidazole developed raised S-GOT and S-GPT. (The rise was slight in two, two-fold in one, who was an alcoholic, and marked in one, who proved to have hepatitis). Two patients treated with metronidazole complained of nausea. One patient treated with nimorazole complained of dizziness, one (treated for gonorrhoea one week before antitrichomonal therapy) of nausea, and one developed a rash. None of the patients in the study had to discontinue treatment because of side-effects.

Correlation between antitrichomonal therapy and the prevalence of candidiasis

The prevalence of *C. albicans* was studied at visits before and at the first follow-up examination after antitrichomonal therapy (in patients without gonorrhoea). Out of a total of 103 patients, two who had been previously negative had positive results to *C. albicans* cultures after therapy; both had been treated with metronidazole.

Correlation between antigenococcal therapy and the prevalence of other pathogens

To provide a control group for the study of the effect, if any, of antigenococcal therapy on *T. vaginalis* and *vice versa*, every third patient (a total of 22) was excluded from treatment when antitrichomonal therapy was started. However other patients were left untreated during the period of investigation for various reasons, such as lack of co-operation, and the control group eventually contained fifty patients.

TABLE Results of antitrichomonal treatment

Treatment group	Drug	Patients treated		Patients cured				
		No.	Defaulted	No.	Percentage of those followed	No. of negative examinations		
						1	2	3
Patients without gonorrhoea	Metronidazole	53	3	48	96	10	16	22
	Nimorazole	59	6	48	90.5	10	17	21
Patients with gonorrhoea	Nimorazole	46	5	37	90.2	6	12	19

During the follow-up of the gonococcal infection all of these showed persistence of *T. vaginalis*.

The treatment for trichomoniasis had no demonstrable effect on the results of the antigonococcal therapy, but the number of failures in the treatment of gonorrhoea, with both ampicillin and doxycycline, was very low (Enfors and Eriksson, 1975), so that a very large series would have been required to demonstrate any such effect.

No increase in the frequency of *C. albicans* was observed after the antigonococcal therapy.

In 552 patients without any treatment, 404 had no finding of *C. albicans* at the first and second visit, thirty had negative findings at the first visit and positive at the second, and in 29 patients the opposite results were obtained.

Discussion

A trichomoniasis cure rate of about 90 per cent after one week of treatment with metronidazole has been reported by Rodin, King, Nicol, and Barrow (1960) and Csonka (1963). Similar good therapeutic results have been reported for nimorazole (Cohen, 1971; Moffet, McGill, Schofield, and Masterton, 1971). In a comparative study of randomized treatments, McClean (1972) obtained equivalent results with both preparations (cure rate 82 per cent.) whereas Evans and Catterall (1971) and McCann, Mahony, and Harris (1972) obtained less satisfactory results with nimorazole than with metronidazole.

In our study we found no difference in the results of treatment with metronidazole and nimorazole (cure rates of 96 and 90 per cent. respectively), and both can be regarded as very good. The number of defaulters was comparatively low, but the observation period was fairly short.

Possible causes of therapeutic failure in the treatment of trichomoniasis

The risk of re-infection is high as the patients who attend a venereal clinic are sexually active and the possibility of re-infection will increase during long observation periods.

Patients may not complete the prescribed course of treatment. A demonstration of the significance of these factors was provided by Keighley (1971), who obtained a cure rate of 98 per cent among patients in prison with supervised medication.

Poor absorption of the drug, conversion into inactive metabolites, and inactivation of the vaginal flora have been suggested as causes of therapeutic failure (Kane, McFadzean, and Squires, 1961; Cohen, 1971; Nicol, Evans, McFadzean, and Squires, 1966). McFadzean, Pugh, Squires, and Whelan (1969) found no evidence of primary or acquired resistance after 8 years of treatment with metronidazole. According to de Carneri (1970),

experimentally produced metronidazole-resistant strains were still sensitive to nimorazole, whereas Benazet and Guillaume (1972) demonstrated cross-resistance. The good therapeutic results with metronidazole provide evidence that no clinically important resistance develops. In assessing cure, cultures have proved to be superior to microscopy, particularly in cases with occasional trichomonads (Eriksson and Wanger, 1975).

Correlation between antitrichomonal therapy and the prevalence of C. albicans

Antitrichomonal therapy has been considered to be one of the contributory factors in the increasing frequency of *C. albicans* (Csonka, 1963; Catterall, 1971; Keighley, 1971; Ross, 1973), but we have not observed any such increase in the prevalence of *C. albicans* after antitrichomonal therapy in our series.

Correlation between antigonococcal therapy and the prevalence of C. albicans

Antibiotic therapy has also been cited as a cause of the higher frequency of candidiasis (Catterall, 1971). In the present series antigonococcal therapy did not affect the prevalence of *C. albicans*. The period of treatment was probably too short to have any major effect on the microbial environment apart from the disappearance of the gonococci.

The variation in the prevalence of *C. albicans* between consecutive specimens was substantial, however, and this must be taken into consideration when analysing the frequency of this organism.

References

- BENAZET, F., and GUILLAUME, L. (1972) *Lancet*, **1**, 597
- DE CARNERI, I. (1970) *J. Parasit.*, **56**, part 1, 69
- CATTERALL, R. D. (1971) *Brit. J. vener. Dis.*, **47**, 45
- COHEN, L. (1971) *Ibid.*, **47**, 177
- CSONKA, G. W. (1963) *Ibid.*, **39**, 258
- DIAMOND, L. S. (1957) *J. Parasit.*, **43**, 488
- ENFORS, W., and ERIKSSON, G. (1975) *Brit. J. vener. Dis.*, **51**, 99
- ERIKSSON, G., and WANGER, L. (1975) *Ibid.*, **51**, 192
- EVANS, B. A. and CATTERALL, R. D. (1971) *Brit. med. J.*, **4**, 146
- KANE, P. O., MCFADZEAN, J. A., and SQUIRES, S. L. (1961) *Brit. J. vener. Dis.*, **37**, 276
- KEIGHLEY, E. E. (1971) *Brit. med. J.*, **1**, 207
- MCCANN, J. S., MAHONY, J. D. H., and HARRIS, J. R. W. (1972) *Brit. J. vener. Dis.*, **48**, 387
- MCCLEAN, A. N. (1972) *Ibid.*, **48**, 69
- MCFADZEAN, J. A., PUGH, I. M., SQUIRES, S. L., and WHELAN, J. P. F. (1969) *Ibid.*, **45**, 161
- MOFFET, M., MCGILL, M. I., SCHOFIELD, C. B. S., and MASTERTON, G. (1971) *Ibid.*, **47**, 173
- NICOL, C. S., EVANS, A. J., MCFADZEAN, J. A., and SQUIRES, S. L. (1966) *Lancet*, **2**, 441
- RODIN, P., KING, A. J., NICOL, C. S., and BARROW, J. (1960) *Brit. J. vener. Dis.*, **36**, 147
- ROSS, S. M. (1973) *Ibid.*, **49**, 310