Trichomonal vaginitis
A 24-hr regimen of nimorazole compared with a 7-day regimen of metronidazole

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Several studies have been made comparing the relative efficacy of metronidazole and nimorazole in the treatment of trichomonal vaginitis (Evans and Catterall, 1971; McClean, 1972; McCann, Mahony, and Harris, 1972; Tinkler, 1974).

Results have been disparate as between one trial and another, but generally speaking it would seem that these two drugs, being of similar structure, not surprisingly vie with one another with an equal claim for a place in routine treatment. For some time the recommended dosage of metronidazole by the manufacturers of 'Flagyl' (May and Baker) has been one 200 mg. tablet three times daily for 7 days, totalling 4:2 g. The recommended dosage of nimorazole by the manufacturers of 'Naxogin' (Carlo Erba) used to be one 250 mg. tablet twice daily for 6 days, totalling 3:0 g. With a higher dose per tablet but a smaller dosage per course of treatment, coupled with less frequent administration and a shorter course, the suggestion was made that an equally efficacious and more convenient treatment could be provided by nimorazole at less cost per patient than with metronidazole.

The almost completely innocuous nature of the two drugs, and our awareness of the well-attested fact that patients are not to be wholly relied upon to take their tablets regularly for more than a few days, led to shortened courses of treatment being tried. Published results of the clinical evaluation of various short courses with both metronidazole (Csonka, 1971; Woodcock, 1972; Morton, 1972; Ross, 1973b; Davidson, 1973) and nimorazole (Jelinek and Jones, 1971; McCann and others, 1972; Campbell, 1972; Jones, 1972; Ross, 1973a,b) confirm that shortened courses are as efficacious as standard courses. With nimorazole in particular, a dosage of 1 g. at 12-hrly intervals for three doses, over a period of 24 hrs, gave highly satisfactory results (97:1 per cent. cure rate) with very rare side-effects (Campbell, 1972). Only one of the above published trials (Ross, 1973b) compared the two drugs.

It was decided to evaluate nimorazole in the '24-hr' treatment of vaginal trichomoniasis administering 3 g. (two 500 mg. tablets 12-hrly for three doses), and to compare the results with those obtained with metronidazole using the manufacturer's standard dosage of 4:2 g. (one 200 mg. tablet three times daily for 7 consecutive days).

Patients

The trial took place between June 1, 1972, and June 18, 1973, and included patients with trichomonal vaginitis diagnosed by positive darkground microscopy showing motile trichomonads. Excluded from the trial were patients known to be pregnant or who reported an overdue menstrual period. 99 persons (100 cases) were treated with metronidazole, one patient becoming re-infected and being re-treated on the same schedule. 100 persons were treated with nimorazole. At first the patients were advised to ask their consorts to attend for examination and therapeutic or epidemiological treatment. After the first fifty cases in each schedule had been recorded, the practice of asking consorts to attend was discontinued as being unproductive.

Methods

The two treatment schedules were given to alternate patients. Treatment was commenced upon diagnosis except that the patients taking nimorazole were told to time their three doses so that they were taken at precisely 12-hr intervals without the necessity for waking up at night. Thus, patients diagnosed in the afternoon delayed their first dose until the evening. All patients were instructed to take their tablets after meals and to avoid both alcohol and sexual intercourse. Patients found to have concomitant gonorrhoea were treated with a combination of probenecid, penicillin, and cotrimoxazole; patients with vaginal candidiasis were treated with amphotericin B vaginal pessaries and oral tablets. All patients were asked to return on completion of treatment and thereafter at weekly intervals for three further tests including one after their next menstrual period, which in many cases occurred after their third attendance but which in some occurred earlier than this. At follow-up attendances all patients were
examined clinically and specimens of the vaginal secretions were subjected to microscopy and culture using Feinberg-Whittington medium. To assess the efficacy of the latter, material from 22 Trichomonas-positive patients was cultured before treatment and all these cultures were likewise positive.

Results

The Table shows that there were no observed failures. The ratio of single to married patients was 3:1. Double infections with gonococi or Candida (84) amounted to three-quarters of those with trichomonal vaginitis alone (116). 43 patients (23 and 20 respectively) from the two schedules defaulted immediately and completely. Cases are shown as having been subsequently tested one, two, three, or four times, one of which tests was postmenstrual. From these figures it can be calculated that 203 follow-up tests were performed on patients treated with metronidazole and 236 on those treated with nimorazole. There was one re-infection in the metronidazole series as judged by positive smear and culture in a patient who, at the second week, admitted fresh coitus. She was re-treated successfully by the same treatment. Two patients on nimorazole confessed to some nausea without vomiting but this did not preclude the full dose being taken.

Half way through the trial only seventeen consorts had been sought. Five attended for examination; all were negative and all took epidemiological treatment with the same schedule as that prescribed for their partners.

Although the official follow-up ceased after the fourth test and did not extend to a 3-month surveillance, no case, other than the one recorded, returned within the following 2 months with a fresh trichomonal vaginitis.

Discussion

The number of cases involved in this trial is rather small for statistical conviction concerning the results but confidence can be placed in both forms of treatment. The way seems open for considerable shortening of routine treatment which may yet contract down to a single 'once-for-all' dosage. This could lead to trichomonal vaginitis being the first sexually-transmissible disease to be treated out of existence.

Provided concomitant infections are appropriately treated, their presence appears to have no adverse effect on the treatment for trichomoniiasis, but their very existence in over half the cases deserves close attention.

A 100 per cent. success rate calls for some comment, for such cannot be lightly claimed without engendering doubt or scepticism. Both metronidazole and nimorazole are very effective drugs and the reasons why no clinical trial had previously produced the theoretically possible cure rate of 100 per cent, are the probable inclusion among patients of the inevitable 'tablet defaulter' and the possible inclusion of patients in whom absorption was defective or in whom metabolism of the drugs into inactive products occurred before they reached the vagina. According to Cohen (1971), the incidence of patients not responding to trichomonicidal drugs in his clinic in 10 years has been about 1 in 150.

Cure rates near to 100 per cent. have been reported with both drugs. With metronidazole, Keighley (1971) reported 98 per cent. and Davidson (1973) 98.6 per cent. success. With nimorazole, Cohen (1971) reported 98 per cent., Ross (1973a) 96 per cent., and Campbell (1972) 97.1 per cent. success. So mere fortune may have smiled upon the present trial.

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Results of comparative trial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schedule</strong></td>
<td><strong>No. of follow-up smears and cultures at intervals of approximately 1 week</strong></td>
</tr>
<tr>
<td></td>
<td><strong>No. treated</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Diagnosis</strong></td>
</tr>
<tr>
<td>Metronidazole tabs, 1 (200 mg.) three times a day for 7 days (Total 4.2 g.)</td>
<td>T.V. only</td>
</tr>
<tr>
<td></td>
<td>T.V. + GC.</td>
</tr>
<tr>
<td></td>
<td>T.V. + Candida</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
</tr>
<tr>
<td>Nimorazole tabs, 2 (500 mg. each) 12-hrly for three doses (Total 3 g.)</td>
<td>T.V. only</td>
</tr>
<tr>
<td></td>
<td>T.V. + GC.</td>
</tr>
<tr>
<td></td>
<td>T.V. + Candida</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
</tr>
</tbody>
</table>
On the other hand, patient co-operation and understanding was particularly stressed in this trial, and the suggestion is here made that, except where some complication might be responsible for recalcitrant trichomoniasis, the majority of other workers’ cases of re-infection might well have been misconstrued as treatment failures, and modestly recorded as such.

Summary
A 24-hr regimen of nimorazole (1 g. orally at 12-hrly intervals for three doses) was compared with metronidazole (200 mg. three times daily for 7 days) in the treatment of trichomonal vaginitis. The two treatment schedules were given to alternate patients, pregnant women being excluded. One hundred cases were treated on each schedule; roughly one-fifth of the patients in each group defaulted. There were no observed failures with either schedule. The reasons for these exceptionally good results are discussed.

The author wishes to thank Messrs. Carlo Erba Ltd. for a free supply of nimorazole (Naxogin) for this trial and a generous contribution to the cost of the culture medium. Gratitude is also due to the female nursing staff of Ward 34, Newcastle General Hospital, for their co-operation and meticulous keeping of records.

References
COHEN, L. (1971) Ibid., 47, 177
CSONKA, G. W. (1971) Ibid., 47, 456
McCLEAN, A. N. (1972) Ibid., 48, 69
MORTON, R. S. (1972) Ibid., 48, 525
ROSS, S. M. (1972a) Ibid., 49, 310
— (1972b) Ibid., 49, 475

Vaginite à trichomonas. Prescription d’un traitement de 24 heures par le nimorazole comparé à un traitement de 7 heures par le métronidazole

SOMMAIRE
Un traitement de 24 heures par le nimorazole (3 doses orales de 1 g à 12 heures d’intervalle) fut comparé au métronidazole (200 mg trois fois par jour pendant 7 jours) dans le traitement de la vaginite à trichomonas. Les deux traitements étaient prescrits alternativement à une malade sur deux, femmes enceinte exclues. Cent cas furent traités dans chaque groupe; à peu près un cinquième des malades ne revinrent pas dans chaque groupe. On n’observa aucun échec avec l’un ou l’autre schéma. On discute les raisons de ces résultats exceptionnellement bons.
Trichomonal vaginitis. A 24-hr regimen of nimorazole compared with a 7-day regimen of metronidazole.

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*Br J Vener Dis* 1975 51: 54-56
doi: 10.1136/sti.51.1.54

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