THE TREATMENT OF TRICHOMONIASIS WITH NIMORAZOLE-A COMPARISON OF SINGLE DOSE AND 24 HOUR THERAPY

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Summary

A study of the efficacy of short-term high-dose therapy of nimorazole for trichomoniasis in the female is reported. Patients in one group received a single dose of 2 g. each, while those in the other group were given 1 g. twelve hourly for 3 doses. The results of treatment were equally good with both regimes. Side effects, too, were remarkably few on both regimes. Since single-dose therapy has considerable advantages over longer courses it is concluded that when nimorazole is used the most suitable treatment for trichomoniasis is a single dose of 2 g.

Trichomoniasis is a disease which occurs all over the world. It is one of the commonest infections transmitted by sexual intercourse and is estimated to occur in 10 to 20% of women of child-bearing age.

Due to the presence of the causative organism, Trichomonas vaginalis in vaginal and extra-vaginal sites like the urethra, Skeine's and Bartholin's glands, vaginal treatment alone was not very satisfactory and remained so until Durel, et al [1,2] reported excellent results with the systemic trichomonacide, Flagyl (metronidazole), both orally and vaginally. Rodin, et al[3] using the drug only orally in a dosage of 200 mg. three times daily for 7 days obtained an immediate success rate of 95% which fell to 83% by 3 months. This regime soon became the standard treatment for trichomoniasis and has continued to give good results to the present day.

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The failure of a certain proportion of patients to respond to this treatment stimulated further research into related compounds and ten years later De Carneri et al[4] introduced a new compound, Nitrimidazine (now known as Nimorazole). After oral administration of this drug to humans the blood levels of the active substance were somewhat higher than, and the urine levels twice as high as, those produced by metronidazole[5]. In view of this, a dosage level lower than that commonly used for metronidazole was tried by Rognoni and Sideri[6]. They recorded a cure rate of nearly 94% using a dose of 250 mg. twice daily for 5 days. Many studies have since then confirmed the efficacy of Nimorazole the treatment of trichomoniasis[7-11].

Because patients cannot be relied upon to take tablets regularly as prescribed, short regimes of treatment would be preferable, a single dose administered at the clinic itself being the best. Csonka[12], Woodcock[13] and Morton[14] have shown that a single dose 2 g. of metronidazole was adequate

treatment for trichomoniasis, while Jelinek and Jones[19], and Jones[15] found that a single dose of 2 g. nimorazole was very effective. Campbell[16] obtained excellent results using 1 g. of nimorazole twice a day for 3 doses as did McCann, et al[17], who used a 2-day course of 1.25 g. in the morning and 0.75 g. at night.

The present study was designed to compare the efficacy of two dosage regimes of nimorazole, one being a single dose of 2 g. (Group A) and the other 1 g. twelve hourly for 3 doses (Group B).

Material and Methods

Diagnosis was established by immediate direct microscopy of vaginal secretions as well as by culture on Feinberg-Whittington medium though, unfortunately, this was not done on every case. Cervical cytology was done as a routine unless the patient had such a test done within the previous year, but the presence of trichomonads in such smears was not used as a diagnostic criterion. In addition, routine smears and cultures for gonorrhoea as well as vaginal smears and cultures for candidiasis were taken. Serological tests for syphilis were performed on all cases on the first visit and again after 3 months unless indicated earlier.

Follow-up genital tests were essentially the same as described above and were arranged for 1 week, 2 weeks, 4 weeks, 2 months and 3 months after treatment. However, some patients did not attend at all these times. Letters were sent and sometimes visits made by the Social Health Worker when patients defaulted and a fair proportion of them returned for further tests as a result.

Patients seen by 2 of the doctors in the clinic were given 2 g. (4 tablets) of nimorazole (Naxogin 500 each) orally on diagnosis while those seen by the other 2 doctors were given 1 g. (2 tablets) each orally immediately, and prescribed a further 4 tablets, 2 of which were to be taken 12 and 24 hours later. Sex contacts were given a single dose of 2 g. nimorazole whenever possible.

Results

Positive smears for T. vaginalis were obtained in 218 (87.9%) of the 248 patients examined. Positive cultures were found in 57 (27.8%) of 205 patients and cervical cytology showed trichomonads in 79 (67.5%) of 117 patients. Immediate microscopy of wet films thus gave the best results with cervical cytology being rather less efficient. The poor culture results were probably due to loss during transit from the clinic to the laboratory which was situated 2 miles away, the organism being sensitive to temperature change.

Table 1 shows the distribution of patients in the 2 groups by age. There were 119 patients in Group A and 129 in Group B initially, but 23 of the former and 19 of the latter defaulted after the first visit, leaving 96 patients in Group A and 110 patients in Group B for assessment. The youngest was 13 years old and the oldest 62. One patient in Group B was 10 weeks pregnant, but she had already arranged for a termination by the time she attended the clinic. None of the other patients in either group was pregnant.

TABLE 1

Distribution of patients by age-groups

	15–19 years	20–24 years	25–29 years	30 years and above	Total
Nimorazole 2 g.	42[a](8)	2[c](6)	21(3)	30(6)	119(23)
Nimorazole 1 g. x 3	34[b](4)	39(11)	26(3)	30(1)	129(19)

a – includes 1 of 14 years

b – includes 2 of 13 and 1 of 14 years

The figures within brackets indicate the number of patients who failed to return to the clinic after the initial visit.

The response to treatment of patients given a single dose of 2 g. of nimorazole is shown in Table 2. The failure rate was 7.3% at the end of the 1st week and rose through 11.2% at 4 weeks to 17.3% between 2 and 3 months after treatment; there was no further failure among the 19 patients seen for over 3 months after treatment. 2 of the failures at the end of the 1st week and both between 1 and 2 months admitted to re-exposure to infection.

TABLE 2

Nimorazole 2 g. stat regime

Last seen	No. followed	Successful	Failure	Failure Rate Percentage	Admitted further for infection
0	119	—	—	—	—
1 week	96	7	7	7.3	2
2 weeks	82	11	2	9.7	—
3 weeks	69	5	—	9.7	—
4 weeks	64	8	1	11.2	—
1-2 months	55	12	2	14.9	2
2-3 months	41	21	1	17.3	—
Over 3 months	19	19	—	17.3	—
Total	96	83	13		4

Table 3 shows the results of treatment with 1 g. nimorazole given 12 hourly for 3 doses. The failure rate in this group was 1.8% at the end of the 1st week, rising through 8.5% at 4 weeks and 24 per cent 2 to 3 months after treatment. 1 of the 2 failures at 4 weeks, all 4 between 1 and 2 months, and 3 of the 5 failures between 2 and 3 months admitted to further exposure to infection.

TABLE 3

Nimorazole 1 g. x 3 regime

Last seen	No. followed	Successful	Failure	Failure Rate Percentage	Admitted further for infection
0	129	—	—	—	—
1 week	110	11	2	1.8	—
2 weeks	97	8	3	4.9	—
3 weeks	86	3	1	6.1	—
4 weeks	82	9	2	8.5	1
1-2 months	71	16	4	14.2	4
2-3 months	51	28	5	24.0	3
Over 3 months	18	18	—	24.0	—
Total	110	93	17		8

Trichomonads were found by immediate microscopy in the uretarhl discharges of 2 of 56 contacts of Group A patients and 5 of 63 contacts of Group B patients.

Associated Conditions

Gonorrhoea was found in 49 (20%) of the 248 patients and Candidiasis in 45 (18%). Other conditions present were secondary Syphilis 1, early latent Syphills 2, latent treponemal disease, presumably Yaws, 4, and Genital warts 4. The frequent association of gonorrhoea with trichomoniasis demands the performance of full tests for gonorrhoea whenever a patient is treated for trichomoniasis. While this procedure is adopted in all V. D. clinics, it is not always so in other departments or in general practice.

Side effects

Patients were asked about side-effects at the time of the second visit. In common with previous reports they were remarkably few in both groups of patients. Nausea was the commonest side-effect, occurring in 3 patients in Group A and one patient in Group B. It was associated with sleepiness in one, dizziness in another and loss of appetite in a third. Vomiting occurred in one patient in each group. The two patients who vomited after treatment had negative tests at 1 week. One of them defaulted thereafter, while the other had a recurrence at 2 weeks. One patient in Group B had a skin reaction.

Discussion

It would appear that both schedules of treatment gave cure rates comparable with those recorded by previous authors.

Nimorazole, in the schedules used here, also appeared to be equally effective as Metronidazole given either as 200 mg. three times a day for 7 days or as a single dose of 2 g. Ross[18], too, found short-term high-dose therapy with metronidazole or nimorazole to be quite as effective as longer courses, though the incidence of side effects were probably higher.

In this study tolerance with either regime was good, there being little to choose between the two with regard to side-effects. One patient developed a skin reaction which was most probably due to the drug as the patient had not been on any other medication at the time,

The cure rate of the 1 g. x 3 schedule appeared to be better than that of the 2 g. schedule both in the immediate follow-up period and up to 1 month after treatment. It fell thereafter but a fair comparison cannot be made after that time because of the difficulty in assessing the frequency of re-infection, a difficulty which increases as the period of follow-up lengthens. Statistical analysis, however, showed no significant difference between the results of the 2 schedules of treatment, initially as well as one month later. Single dose therapy is certainly better than a course of 6 or 7 days or even 3 doses in 24 hours. Such treatment can be administered in the clinic itself, thus removing the necessity of relying on the patient to complete a longer course. Since the results of treatment with both schedules in this study were equally good and the incidence of side effects no different, it is felt that if nimorazole is used a single dose of 2 g. is the most suitable treatment for trichomoniasis in the female.

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Final Diagnosis :

Anaplastic squamous cell carcinoma with metastasis.

Repeated smears from all the lesions failed to reveal Donovan's organism. A biopsy from the edge of inguinal ulcer showed anaplastic squamous cell carcinoma. X-ray chest revealed miliary shadows bilaterally. Miliary Tuberculosis was ruled out by negative sputum and gastric juice for AFB. Radiological findings in lungs could represent a rare blood borne metastasis.