The treatment of *Trichomonas vaginalis* vaginitis

An open controlled prospective study comparing a single dose of metronidazole tablets, benzoyl metronidazole suspension and tinidazole tablets

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Summary

Metronidazole tablets, benzoyl metronidazole suspension and tinidazole tablets each given as a single 2 g bolus dose in an open controlled prospective study were found to be effective forms of treatment for *Trichomonas vaginalis* vaginitis. The cure rates on wet smear preparations were 100%, 100% and 94,8% respectively, and symptomatic and observed improvements were excellent. There was a statistically significant difference between the response rates associated with both metronidazole preparations and tinidazole. The results of this study indicate that single-dosage bolus therapy can confidently be recommended in trichomonal infections and that it has a number of advantages.

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It has become evident in recent years that patient compliance with regard to medication is improved by single-dose therapy. This is particularly the case in troublesome conditions which improve rapidly on commencement of therapy and where minor side-effects may occur, prompting discontinuation as soon as symptomatic relief is achieved. *Trichomonas vaginalis* infections are an excellent example of this situation, and in order to evaluate and compare patient compliance with and the safety and efficacy of metronidazole and tinidazole, an open controlled randomized prospective study was performed. The objective of the study was to compare oral metronidazole tablets, benzoyl metronidazole suspension 50 ml, and tinidazole tablets, each given as a single 2 g dose to patients with proved *T. vaginalis* vaginitis. In addition, the incidence of reinfection was studied.

Patients and methods

A total of 161 women were admitted to this randomized prospective open study. Informed consent was obtained from all patients, and thereafter the patients were randomly allocated to three groups: group A (58 patients) — metronidazole tablets (2 g); group B (44) — benzoyl metronidazole suspension (2 g); and group C (59) — tinidazole tablets (2 g).

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Because of the categorial nature of the data or skewed distribution, the chi-square and van der Waerden distribution-free tests were used to analyse baseline comparability, examination comparability, and results obtained in the three treatment groups.

The diagnosis of *T. vaginalis* infection was made on the basis of typical clinical findings and by the demonstration of active forms of the organism in a wet smear preparation by a specially trained clinical research sister-technician. Associated infections and in particular monilial vaginitis were excluded by performing confirmatory cultures and examining a cytological smear. Only after bacteriological diagnosis had been confirmed and randomization performed was treatment with the therapeutic agent started. No concomitant local intravaginal medication was permitted to be used and preselection evaluation included the taking of a medical and coital history, physical examination including a blood pressure estimation, and urinary dipstick examination to exclude glycosuria.

The patients were asked to take the trial drug in the presence of the investigator or research assistant and an identical quantity of the same drug was given to each patient for consumption by her consort.

The patients were re-examined 7 days after treatment and if they were still found to have a trichomonal infection they were questioned as to coital events and the treatment was repeated with the same drug at the same dosage level. Examination was repeated 7 days thereafter (14 days after initial treatment), and if testing was still positive treatment was changed to the alternative drug, which was repeated 7 days later if required. Failure after this led to withdrawal from the trial. In all cases requiring treatment the consort was also supplied with the identical drug.

A patient was regarded as cured only when two consecutive wet smears taken at weekly intervals were negative.

Side-effects and adverse reactions were evaluated and documented on specially designed case-report forms.

Criteria for exclusion were age 50 years or over, associated pelvic lesions, diabetes mellitus, concomitant monilial infections, a past history of adverse reactions to a 5-nitro-imidazole drug or the ingestion of a 5-nitro-imidazole drug within 10 days of diagnosis, more than one consort or refusal to give medication to the consort, and pregnancy (first trimester).

Results

The three treatment groups were statistically similar as regards all parameters except marital status; more patients were married in group C and more had regular consorts in group A ($P = 0{,}032$) (Table I).

There were no statistically significant differences between the three groups for the characteristics recorded (Table II).

TABLE I. PATIENT CHARACTERISTICS — HISTORY*

	Group		
	A ($N = 58$)	B ($N = 44$)	C ($N = 59$)
Age (yrs)	**31,1**	**29,6**	**30,4**
Weight (kg)	**51,8**	**62,4**	**63,5**
Age at first coitus	**18,5**	**18,2**	**18,2**
Parity	**1,5**	**1,6**	**1,9**
Marital status			
Married	**31,0%**	**43,2%**	**55,9%**
Single — no regular consort	**27,6%**	**25,0%**	**27,1%**
Single — regular consort	**41,4%**	**31,8%**	**16,9%**
Coitus regular	**29,3%**	**29,5%**	**42,4%**
Previous pelvic infection	**0**	**0**	**0**
Glycosuria	**0**	**0**	**0**
Previous vaginal infection	**36,2%**	**50,0%**	**57,6%**
Previous imidazole therapy	**17,2%**	**11,4%**	**16,9%**
Successful consort medication	**81,0%**	**84,1%**	**84,7%**

*Comparison of mean values for baseline data.

TABLE II. PATIENT CHARACTERISTICS — INITIAL EXAMINATION*

	Group		
	A ($N = 58$)	B ($N = 44$)	C ($N = 59$)
Vaginal discharge	**100**	**100**	**100**
Pain	**0**	**0**	**0**
Dyspareunia	**13,8**	**15,9**	**10,2**
Dysuria	**25,9**	**38,6**	**27,1**
Other findings	**1,7**	**6,8**	**3,4**
***Monilia*-positive**	**0**	**0**	**0**
***Trichomonas*-positive**	**100**	**100**	**100**
Abnormal urine labstick results	**0**	**2,3**	**0**
Vaginal pH	**5,8**	**5,8**	**5,7**

*Comparison of mean values for baseline data (%).

The only variable for which the three groups were not statistically similar was the incidence of trichomonal positivity at the visit on day 14; 5,1% of patients in group C, who had taken tinidazole, were found to be positive as against a zero incidence in groups A and B ($P = 0,05$) (Table III).

It is evident from Table III that although no patient was admitted to the study with a positive smear or culture for moniliasis this pathogen was present on days 7 and 14 in 6,9%, 9,1% and 3,4% of cases in groups A, B and C respectively. This may be due to the monilial infection becoming evident and active after elimination of *T. vaginalis* or possibly (but less likely) due to a new infection.

Even though the trichomonal infection was no longer evident in the vast majority of cases in all three groups, a vaginal discharge persisted in an appreciable percentage (43,1 — group A; 34,1 — group B; and 42,4 — group C). There is no obvious explanation for this finding since the incidence of monilial infection was very much lower than that of persistent discharge, and it may be that associated infections with organisms such as *Chlamydia trachomatis or Gardnerella vaginalis* were not identified. There was, however, a much higher incidence of improvement in the amount of discharge and its effects in all three groups — 70,7%, 68,2% and 76,3% respectively in groups A, B and C (Table III).

Table IV, a summary of the side-effects, patient observations and observer perceptions of improvement, shows there was no statistically significant difference between the three treatment groups except regarding observed improvement on day 14 in group C, where improvement was recorded in only 88,3% of

TABLE III. RESULTS OF TREATMENT (%) AT DAYS 7 AND 14

	Group					
	A ($N = 58$)		B ($N = 44$)		C ($N = 59$)	
	P	I	P	I	P	I
Vaginal discharge						
IPE	**100**	**—**	**100**	**—**	**100**	**—**
Day 7	**93,1**	**100**	**86,4**	**93,2**	**84,7**	**94,9**
Day 14	**43,1**	**70,7**	**34,1**	**68,2**	**42,4**	**76,3**
***Trichomonas*-positive**						
IPE	**100**		**100**		**100**	
Day 7	**1,7**		**4,5**		**1,7**	
Day 14	**0**		**0**		**5,1**	
***Monilia*-positive**						
IPE	**0**		**0**		**0**	
Day 7	**6,9**		**9,1**		**3,4**	
Day 14	**6,9**		**9,1**		**3,4**	

P = present or persistent; I = improved; IPE = initial pretreatment examination.

TABLE IV. RESULTS OF TREATMENT (%) — ALL VISITS

	Group		
	A ($N = 58$)	B ($N = 44$)	C ($N = 59$)
Side-effects	**22,4**	**7,5**	**13,3**
Symptomatic improvement			
Day 7	**100**	**95,5**	**98,3**
Day 14	**74,1**	**70,5**	**71,7**
Observed improvement			
Day 7	**98,3**	**93,2**	**96,7**
Day 14	**100**	**90,9**	**88,3**

patients compared with 100% in group A and 90,9% in group B ($P = 0{,}0062$).

Side-effects were mild, the commonest being nausea, flatulence, indigestion and gastric upsets. Although not achieving statistical significance ($P = 0{,}06$), there appeared to be a lower incidence of side-effects in group B, who took metronidazole suspension.

Repeat medication was necessary in 1 patient and a consort in group A, 2 patients in group B and 3 patients in group C. In all these patients the repeated identical medication resulted in a negative smear when seen 7 days later. Only 1 patient in group C required a switch in medication to that used in group B. This resulted in a negative smear when she was seen 14 days later. It was only necessary for 6 patients to attend for a visit on day 28, and no significant findings were recorded.

Discussion

Numerous non-randomized clinical trials have shown that a cure of vaginal trichomoniasis is as likely after a 'day treatment' regimen with metronidazole 2 g as with the long recommended regimen of 200 mg 3 times daily for 7 days.[1,2] This randomized study once again confirms this finding; cure rates in the three groups studied were 100% in groups A and B and 94,9% in group C at day 14. These excellent results were certainly due to the ease of administration and good patient compliance as well as the fact that medication was successfully administered to consorts in 81,0%, 84,1% and 84,7% of cases in groups A, B and C respectively.

Not all patients with trichomoniasis are cured by either metronidazole or tinidazole and the reasons for this are probably multiple and varied:[3] reinfection from a partner, overgrowth of suppressed pathogens, poor absorption of the compound, or inactivation of the drug by other vaginal organisms. The question of drug resistance arises and there have been isolated reports of strains of *T. vaginalis* resistant to 10 - 15 times the concentration of metronidazole required for the killing of strains isolated elsewhere.[4]

An additional factor which has apparently not been explored is the question of lowering the dose in the single-dose technique, and with the cure rates obtained by a single 2 g dose of these drugs it may be that a 1 g or 1,5 g bolus would be equally clinically effective and more cost-effective and produce fewer side-effects.

It can be concluded from this study that metronidazole tablets, benzoyl metronidazole suspension and tinidazole tablets in a 2 g bolus dose are effective methods of treating *T. vaginitis*, the metronidazole in both forms being slightly more active and the suspension causing fewer side-effects.

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