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The Comparison of the Efficacy among Three Different Nimorazole Regimens in the Treatment of Bacterial Vaginosis

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Abstract

The efficacy of 3 different nimorazole regimens in treating bacterial vaginosis in women was evaluated. The regimens consisted of: Nimorazole 2 g single dose (Group I), 1 g per day for 3 days (Group II), and 1 g per day for 7 days (Group III) orally. In a simple randomized trial of 90 cases (30 cases in each group) with demonstrated clinical bacterial vaginosis on the presence of 3 of 5 of the following signs: (1) Characteristic thin homogenous discharge; (2) vaginal pH>4.5; (3) release of a fishy amine odor from vaginal fluid mixed with 10% KOH; (4) presence of clue cells (usually representing at least 20% of vaginal epithelial cells); and (5) vaginal fluid contains few or no lactobacilli. Cure rates for bacterial vaginosis by nimorazole were 70.0% (21/30), 83.3% (25/30), and 90.0% (27/30) in Group I, II, and III, respectively. Thus nimorazole is another effective drug for the treatment of bacterial vaginosis.

Key words: nimorazole, bacterial vaginosis

Introduction

Bacterial vaginosis in association with positive culture of *Gardnerella vaginalis* is a common condition accounting for approximately half of patients with all cases of symptomatic vaginal discharges encountered in outpatient practice.[1–5] From previous investigations it was found that treatment of bacterial vaginosis with metronidazole, 500 mg given twice daily for 7 days, had a significantly higher cure rate than with other agents.[3–6]

Nimorazole, the 5-nitroimidazole derivative, had antitrichomonal activity property *in vitro* similar to that of metronidazole.[7] Both have been used successfully in treatment of trichomoniasis. With a reduction in both daily dose and the treatment period, the results of treatment of bacterial vaginosis with nimorazole were comparable with low incidence of side effects.[8,9] Considering the low adverse drug reaction and well tolerance, the authors thought it would be worthwhile to carry out a study to compare the efficacy of different dose-duration nimorazole regimens in the treatment of bacterial vaginosis.

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Table 1. Demographic characteristics of study patients

	Group I	Group II	Group III
Mean age	35.5±8.3	34.3±6.9	35.5±8.3
Contraceptive method			
Tubal sterilization	10	9	14
Pills	3	0	3
DMPA	1	1	2
Condom	2	1	0
IUCD	1	5	0
Other	4	4	0
None	9	10	11

Table 2. Characteristics of vaginal discharge

Findings	Group I		Group II		Group III	
	Pre No. (%)	Post No. (%)	Pre No. (%)	Post No. (%)	Pre No. (%)	Post No. (%)
pH >4.5	29 (96.6)	14 (46.6)	30 (100)	12 (40.0)	27 (90.0)	11 (36.6)
Thin, homogeneous	25 (83.3)	9 (30.0)	25 (83.3)	4 (13.3)	25 (83.3)	5 (16.6)
Amine test positive	25 (83.3)	7 (23.3)	27 (90.0)	3 (10.0)	27 (90.0)	1 (3.3)
Clue cell >20%	25 (83.3)	7 (23.3)	22 (73.3)	6 (20.0)	23 (76.6)	2 (6.6)
Few or absent lactobacilli	28 (93.3)	17 (56.6)	30 (100)	17 (56.6)	29 (96.6)	17 (56.6)

Material and Methods

The study was carried out at Sexually Transmitted Diseases Clinic, Songklanagarind Hospital from November, 1988 to June, 1989 among women with hypervaginal secretion but not associated with menses, offensive discharge, or yellowish discharge. The women diagnosed as having bacterial vaginosis were included in the study. Women at pregnant and lactating period, prostitutes or those having a history of using antibiotic or vaginal suppository during the last 2 weeks, were excluded.

The diagnostic criteria of bacterial vaginosis (at least 3 of the following) are: (1) pH above 4.5 (2) thin, homogenous (3) fishy odor or amine test positive (4) clue cell at least 20% of total vaginal epithelial cells and (5) few or no lactobacilli.

Data on age, contraceptive method, and obstetric history were recorded. Tests for sexually transmitted diseases were carried out as a routine procedure, using standard methods for the diagnosis or exclusion of gonorrhea, trichomoniasis, and candidiasis.

Recruited patients were randomly selected into 3 groups:

Group I: 30 patients treated with nimorazole 2.0 g single dose

Group II: 30 patients treated with nimorazole 1.0 g per day for 3 days in dividing dose, twice daily

Group III: 30 patients treated with nimorazole 1.0 g per day for 7 days in dividing dose, twice daily.

Patients were advised to abstain from sexual intercourse until at the end of the first follow-up 1–2 weeks after completing treatment.

Patients were assessed as cure if the symptoms totally disappeared with the absence of both abnormal vaginal discharge and microscopic characteristics described above or having less than 3 criteria on examination of vaginal discharge.

For statistical analysis, the Chi-square test and the Student's *t*-test were employed.

Table 3. The organisms identified before and after treatment

Organism	Group I		Group II		Group III	
	Pre No. (%)	Post No. (%)	Pre No. (%)	Post No. (%)	Pre No. (%)	Post No. (%)
G. vaginalis	19 (63.3)	18 (60.0)	18 (60.0)	12 (40.0)	18 (60.0)	3 (10.0)
B. melaninogenicus	4 (13.3)	6 (20.0)	7 (23.3)	5 (16.6)	9 (30.0)	2 (6.6)
B. fragilis or mixed anaerobes	3 (10.0)	2 (6.6)	—	—	2 (6.6)	—

Table 4. Results of the treatment

Result	Group I (N=30) No. (%)	Group II (N=30) No. (%)	Group III (N=30) No. (%)
Cure	21 (70.0)	25 (83.3)	27 (90.0)
Not cure	9 (30.0)	5 (16.6)	3 (10.0)

Results

The demographic and contraceptive characteristics of the 90 patients enrolled in the study were shown in Table 1. These showed no significant differences among patients assigned to the various treatment regimens.

The characteristics of vaginal discharge are shown in Table 2. With regards to the cure results employing the laboratory criteria, there were no difference among 3 groups of treatment. However, there are statistical difference of positive result of amine test among the groups of patient.

Table 3 shows the micro-organism identified by culture before and after treatment. *G. vaginalis* is by far the most commonly organism encountered while *B. melaninogenicus* ranked second.

The results of treatment are shown in Table 4.

The adverse drug reactions such as nausea, vomiting, and dizziness occurred in 7 of the 30 patients (23.3%) in Group I, 2 of the 30 patients (6.6%) in Group II, and 1 of the 30 patients (3.3%) in Group III, respectively. But none of the symptoms was so severe that the medication had to be withdrawn.

Discussion

Pheifer *et al.* noticed that women with both trichomoniasis and bacterial vaginosis who were treated with metronidazole were cured of both infections.[6] However, *G. vaginalis* is not particularly sensitive to metronidazole *in vitro*.[10] Thus the process of metronidazole between the sensitivity *in vitro* and the efficacy *in vivo* was different. The anaerobic vaginal environment may potentiate the efficacy of metronidazole. Because bacterial vaginosis is a mixed infection of both *G. vaginalis* and anaerobic bacteria, the efficacy of metronidazole may be related to its activity against anaerobic bacteria. Anaerobic bacteria may provide certain undefined factors that support *G. vaginalis* growth, and inhibition of anaerobic may in itself decrease the concentration of *G. vaginalis*.[3] The activity of nimorazole *in vitro* on *T. vaginalis* is as active as metronidazole (0.8–3.0 μg/ml). In addition, it is well absorbed after oral administration.[8] The serum level after administration of 2 g nimorazole reaches 32 μg/ml after 2 hours and falls to 1.9 μg/ml in 24 hours in a subject weighing 62 kg.[9]

A recent study has also reported that the cure rate of a single 2 g dose of nimorazole was 88%.[11] So nimorazole, the 5-nitroimidazole derivative, may be in the selection for treatment of bacterial vaginosis. This study showed that the 3 different regimens of nimorazole were unequally effective in the treatment of bacterial vaginosis. Although the 7-day regimen had higher cure rate than the 3-day regimen, there was no statistical sig-

nificant ($p>0.05$), whereas the 7-day and 3-day regimens were superior to the single-dose regimen, and had statistical significance ($p<0.05$). The relative efficacy of several 5-nitroimidazole derivative might appear in the concerning of dose-duration therapy.

Its high dose of 2.0 g single dose increased the adverse drug reactions (23.3%), when compared with low dose of 1.0 g per day (3.3–6.6%). It is possible in view of the pharmacokinetic profile that a higher dose gives the higher serum level. The incidence of side effects may not relate to duration of therapy.

Metronidazole and other 5-nitroimidazole derivatives (tinidazole, nimorazole, etc.) are selectively active against *T. vaginalis* and other anaerobic protozoa (*Entamoeba histolytica*, *Giardia lamblia*) and bacteria (*Bacteroides* and *Clostridium* species). Recent study correlated this selectivity with characteristic metabolic differences between anaerobes and aerobes.[12] And in this study, nimorazole as well as other 5-nitroimidazole derivatives showed the similar efficacy against bacterial vaginosis. The cure rate of 90% for the 7-day nimorazole regimen was satisfactory result compared with dose achieved in the standard 7-day course of metronidazole.

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