

The Effectiveness of Single-Dose Metronidazole Therapy for Patients and Their Partners With Bacterial Vaginosis

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A randomized, placebo-controlled, double-blind clinical trial was performed to test the hypothesis that a 2-g single dose of metronidazole for male partners of women with bacterial vaginosis was more effective than placebo in improving cure rate and decreasing recurrence rate. In addition, the effectiveness of a 2-g single dose of metronidazole was compared with a seven-day course of 500 mg of metronidazole twice a day in patients with bacterial vaginosis.

Statistically significant benefits of partner treatment were noted in the initial cure rate by Gram-stained smear criteria ($P < .01$) and in percentage of women with symptoms eight weeks after initiating therapy ($P < .05$). The seven-day course of metronidazole was superior to the single-dose regimen in the percentage of patients with clue cells and the percentage of patients with a positive "sniff" test at the first follow-up visit; however, differences in the initial cure rate assessed by clinical criteria and Gram-stained smear criteria were not statistically significant between the two patient treatment regimens. Recurrence rates by Gram-stained smear criteria between patient and partner treatment groups at five and eight weeks after initiation of treatment were also not significantly different between the two patient regimens.

Single-dose metronidazole treatment of the sexual partner of women with bacterial vaginosis improves initial bacterial vaginosis cure rates. The seven-day course of metronidazole was not found by statistical analysis to be significantly superior to single-dose therapy when considering initial cure rates by clinical or Gram-stained smear criteria or recurrence rates. Thus, single-dose metronidazole therapy appears to represent an effective treatment option for both patients and their partners who have bacterial vaginosis.

Bacterial vaginosis is a superficial vaginal infection, formerly known as nonspecific vaginitis, caused by a mixture of anaerobic bacteria associated with *Gardnerella vaginalis*.¹ In the late 1970s several treatment trials demonstrated the superiority of a seven-day course of

metronidazole (500 mg twice a day) over general existing bacterial vaginosis treatments.²⁻⁴ Considerations of cost, compliance, and side effects, as well as the demonstrated effectiveness of single-dose metronidazole therapy for vaginitis resulting from a *Trichomonas* infection, stimulated the development of several clinical trials comparing a 2-g single dose of metronidazole with the traditional seven-day course. In general, these trials showed the seven-day course to be slightly superior to single-dose therapy in some outcomes, but not all.⁵⁻⁷ Unfortunately, high dropout rates, failure to control for male sexual partner treatment, and low statistical power in many of these trials clouded conclusions even further.

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Epidemiologic evidence suggests that bacterial vaginosis can be spread through sexual contact.⁸⁻¹⁰ Conclusions, however, from a recent treatment trial and a statement in a leading textbook on sexually transmitted diseases, based on unpublished data, did not support male sexual partner treatment to improve cure rates or reduce recurrence rates in women with bacterial vaginosis.^{7,11} Confusion also clouds these conclusions, as both the published and unpublished trials did not have enough statistical power to show adequately a significant difference, if it indeed existed.¹²

Because of the confusion surrounding single-dose metronidazole treatment for patients with bacterial vaginosis, and the contradiction between epidemiologic evidence and the results of male sexual partner treatment trials, a randomized, placebo-controlled, double-blind clinical trial was designed to test the effectiveness of (1) single-dose metronidazole therapy for sexual partners of patients with bacterial vaginosis, and (2) single-dose metronidazole therapy compared with the now-standard seven-day course in patients with bacterial vaginosis.

METHODS

Women between the ages of 18 and 40 years who complained of genitourinary symptoms were admitted to the study if their vaginal discharge fulfilled three of the four following criteria:

1. Gray homogeneous discharge adherent to the vaginal walls
2. pH greater than 4.5
3. Positive clue cells on wet mount
4. Release of a fishy amine odor on addition of 10 percent potassium hydroxide (KOH)

Patients were excluded from the study if they were pregnant, menopausal, had used oral antibiotics or vaginal medications in the previous month, had clinical evidence of a mucopurulent cervical discharge or genital herpes, or had *Trichomonas vaginalis* or *Candida albicans* on wet mounts or KOH preparations of their vaginal discharge.

Patients were also excluded if they had a contraindication to metronidazole, including prior allergy to metronidazole, seizure disorder, peripheral neuropathy, cancer, and liver disease, or if currently taking warfarin, phenytoin, or phenobarbital. In addition, to participate, patients were required to have a telephone and only one current sexual partner.

Determination of eligibility was performed by study physicians (the Bacterial Vaginosis Study Group) who were recruited from the Seattle area by the principal in-

TABLE 1. TREATMENT GROUPS

Group	Patient		Partner
	Single Dose (2 g)	7 Days (500 mg twice a day)	Single Dose (2 g)
1 (7D + SP)	Placebo	Active	Active
2 (7D only)	Placebo	Active	Placebo
3 (SD + SP)	Active	Placebo	Active
4 (SD only)	Active	Placebo	Placebo

7D + SP—7-day treatment for the patient and single-dose therapy for the sexual partner
7D only—7-day therapy for the patient and no therapy for the sexual partner
SD + SP—Single-dose therapy for both the patient and the sexual partner
SD only—Single-dose therapy for the patient and no therapy for the sexual partner

vestigator. Study physicians performed a vaginal examination on potentially eligible women in which the presence of a gray homogeneous discharge was determined. Samples of the vaginal discharge were collected from the posterior fornix using cotton-tipped swabs and placed on pH paper and three glass slides. The vaginal discharge on one of the three glass slides was mixed with normal saline and examined under a light microscope for the presence of clue cells and *Trichomonas vaginalis*; the next sample was mixed with 10 percent KOH to determine whether a fishy odor was present (positive sniff test) and then examined under light microscopy for the presence of hyphae consistent with *Candida albicans*; and the third sample was allowed to air dry for Gram staining.

All patients meeting eligibility requirements were asked to participate in the study. After obtaining informed consent, women were randomized into one of four treatment groups (Table 1). Randomization was accomplished by blocks of varying sizes (4, 8, or 12) so that an equal number of women in each block entered each of the four treatment groups. Placebo was used to ensure that both subjects and physicians did not know the subject's treatment.

Patients were then asked to fill out a questionnaire on sociodemographic factors, reproductive history, and bacterial vaginosis risk factors. They were asked to take a single dose of medication in the clinic and to deliver a consent form, a questionnaire on symptoms and bacterial vaginosis risk factors, and medication to their sexual partner. The sexual partner was contacted by a study investigator that night by telephone to obtain informed consent, answer questions, and be given instructions. Partners who consented were asked to return their questionnaire by mail and to take the single dose of medication provided by the patient.

Patients returned to their study physician two weeks after entry to assess cure. At the follow-up visit, patients

completed a questionnaire on symptoms and medication side effects, returned their pill bottles for a pill count, and underwent a pelvic examination in which the four clinical criteria were measured and a slide of their vaginal discharge was obtained and Gram stained. If the patient was not cured (ie, three or more of the four clinical criteria being present), she received a seven-day course of metronidazole for herself and her partner.

Patients were then followed for six more weeks to assess recurrence rate. At five and eight weeks after induction into the study, patients were contacted by telephone and asked whether they had any symptoms of bacterial vaginosis, whether they had taken any antibiotics since their last visit, and whether they had engaged in sexual intercourse with any partners not involved in the study. Patients were also asked to obtain a slide of their vaginal fluid using materials provided at the first follow-up visit. Collection of vaginal fluid samples by patients has been shown to be a valid and reliable technique, yielding results virtually identical to physician-collected samples.¹³ Slides were then mailed to the study using envelopes provided. Those slides were Gram stained and interpreted to determine whether a recurrence of bacterial vaginosis had developed. Patients with symptoms of a bacterial vaginosis infection were asked to return to their physician for further evaluation and treatment.

Interpretation of all Gram-stained smears of the patient's vaginal fluid was performed by an experienced laboratory technician (V.H.) who did not know the patient's treatment group.

Laboratory Methods

The Gram-stained smear of a patient's vaginal discharge is a very sensitive and specific test for bacterial vaginosis.¹⁴ Using criteria developed by Spiegel et al,¹⁴ the Gram-stained smear was interpreted as normal if more than six large gram-positive rods (*Lactobacillus* morphotypes) were present per oil immersion field. Gram-stained slides of vaginal discharge were interpreted as consistent with bacterial vaginosis if fewer than six *Lactobacillus* morphotypes per oil immersion field were present with an increase in gram-negative to gram-variable rods (*Gardnerella* morphotypes) and other morphotypes.

As the study progressed, a few Gram-stained smear interpretations did not fulfill the criteria for bacterial vaginosis but also were not normal. These smears were placed into a category labeled "other." Hillier (S. L. Hillier, PhD, personal communication, May 24, 1985) describes "other" as a Gram-stained smear containing *Lactobacillus* and *Gardnerella vaginalis* morphotypes in low quantities, together with a quantity of mixed facultative and anaerobic morphotypes, especially streptococci and coliform bacteria.

Statistical Methods

To compare the four treatment groups with regard to potential confounders, chi-squared analysis was used for categorical variables and analysis of variance for continuous variables. Log-linear modeling was used to test for an interaction effect between patient and partner treatment regimens and was used to test the significance of the main effects of patient and partner treatment on cure rates and other outcome variables.¹⁵ Log-linear modeling was also used to test for treatment effects while controlling for confounding variables.

RESULTS

One hundred sixty-one women fulfilled study criteria and were enrolled in the study from the first of May 1985 until the end of December 1986. Of these 161 women, 21 were dropped from the study for the following reasons: 15 did not return for their first follow-up visits, four did not have proper information collected at their first follow-up visit, one had a positive *Neisseria gonorrhoeae* culture, and one received recurrence medicine instead of initial randomized therapy. The 21 patients dropped from the study were distributed evenly among the four treatment groups. This left 140 patients (87 percent) for further analysis.

Patients in the four treatment groups were similar with regard to race, marital status, number of pregnancies, method of birth control, and past history of sexually transmitted diseases (Table 2). Differences approaching statistical significance did exist in number of women who had undergone a bilateral tubal ligation and number of women with an abnormal result on a Papanicolaou smear. Controlling for these differences in subsequent analysis did not materially alter results.

Ninety-eight of 140 partners (70 percent) consented to participate in the study. The differences in partner consent rate did not reach statistical significance among the four treatment groups. Partner age, race, marital status, and past history of sexually transmitted diseases were also similar among the four treatment groups (Table 2).

Patient symptoms and signs at the initial visit in the four treatment groups did not differ statistically to a significant degree (Table 3). There was a difference approaching significance in percentage of women with bacterial vaginosis by Gram-stained smear; however, excluding those women without bacterial vaginosis by initial Gram-stained smear produced little change in the subsequent analysis and results.

Using log-linear modeling, no significant interaction effect between patient and partner treatment was noted in outcome measures at the follow-up, five-week, or eight-week visits. Accordingly, only the statistical significance

TABLE 2. COMPARISON OF BACTERIAL VAGINOSIS PATIENTS AND PARTNERS IN THE FOUR TREATMENT GROUPS ON LISTED CHARACTERISTICS*

Characteristics	Treatment Group				P**
	1 7D + SP	2 7D Only	3 SD + SP	4 SD Only	
Patient					
Number	33	34	34	37	
Age (years, mean ± standard deviation)	30 ± 7	28 ± 7	30 ± 8	28 ± 7	.20
Black	9	3	3	11	.38
Single	36	29	51	46	.21
Never pregnant	18	14	26	30	.38
Method of birth control					
Birth control pills	18	40	20	24	.14
Foam	9	3	6	0	.27
Condoms	9	5	11	14	.72
Diaphragm	15	6	6	6	.37
Intrauterine device	6	9	11	8	.88
Sponge	12	9	9	11	.95
Bilateral tubal ligation	18	0	17	16	.07
Vasectomy	12	17	20	14	.80
None	6	14	6	11	.55
Past history of sexually transmitted diseases					
Candida vaginitis	83	83	72	76	.61
Trichomonas vaginitis	17	24	31	43	.21
Bacterial vaginosis	54	61	61	69	.71
Gonorrhea	13	14	13	15	.98
Syphilis	0	0	3	3	.58
Pelvic inflammatory disease	16	24	21	18	.89
Abnormal Papanicolaou smear	17	44	37	26	.10
Partner					
Number	23	24	26	25	.86
Age (years, mean ± standard deviation)	33 ± 7	32 ± 6	35 ± 11	31 ± 8	.24
Black	6	3	9	8	.75
Single	24	29	34	32	.81
Past history of sexually transmitted diseases in partners					
Gonorrhea	9	4	17	4	.34
Syphilis	0	0	4	0	.38

* Percentage with characteristic unless otherwise indicated
** From test of statistical significance of differences among all four treatment groups based on chi-square (for categorical variables) or analysis of variance (for continuous variables)
7D + SP—7-day treatment for the patient and single-dose therapy for the sexual partner
7D only—7-day therapy for the patient and no therapy for the sexual partner
SD + SP—Single-dose therapy for both the patient and the sexual partner
SD only—Single-dose therapy for the patient and no therapy for the sexual partner

of the main effects of patient and partner treatment are reported.

Symptoms

While the percentage of women with any symptom—discharge, odor, itching, dyspareunia, and dysuria—decreased in all treatment groups after treatment was completed, there was no significant difference among the four treatment groups in any of the above symptoms, except in the percentage of women with any symptom at eight

weeks (less if the partner was treated, $P < .05$, Figure 1), and percentage of women with vaginal odor at five and eight weeks (less if the patient received single-dose therapy, $P < .05$, Figure 2).

Signs

At the first follow-up visit, women who received a seven-day course of metronidazole had significantly fewer clue cells and less odor detected by their physicians (Figure 3). The percentage of women with a gray discharge and pH

TABLE 3. PERCENTAGE OF PATIENTS WITH INITIAL VISIT SYMPTOMS, SIGNS, AND GRAM-STAINED SMEAR RESULTS IN THE FOUR TREATMENT GROUPS*

Symptoms and Signs	Treatment Group				P**
	1 7D + SP	2 7D Only	3 SD + SP	4 SD Only	
Symptoms					
Discharge	94	83	93	95	.22
Odor	85	71	74	78	.58
Itching	47	40	43	47	.91
Dyspareunia	29	34	20	26	.64
Dysuria	16	24	21	14	.68
Signs					
Gray discharge	88	80	83	81	.85
pH > 4.5	89	100	90	86	.24
Clue cells	100	100	100	97	.42
Odor	90	80	71	83	.26
Gram-stained slide					.07
Bacterial vaginosis	72	91	63	58	
Other	15	6	20	28	
Normal	13	3	17	14	

* Percentage with characteristic unless indicated

** From test of statistical significance of differences among all four treatment groups based on chi-square (for categorical variables) or analysis of variance (for continuous variables)

> 4.5 were similar among the four treatment groups. There was no difference in percentage of women among the four groups who achieved a clinical cure as judged by lack of three of four clinical criteria being present (Figure 4).

There was a significant association between clinical criteria and Gram-stained smear interpretation at the first follow-up visit (Table 4). Despite that significant association, however, only eight of 25 women with bacterial vaginosis by Gram-stained smear had three or more clinical criteria positive at the follow-up visit.

Gram-Stained Smear

Women whose sexual partners were treated were found by statistical analysis to have significantly less bacterial vaginosis by Gram-stained smear at the first follow-up visit ($P < .05$, Figure 5). The effect of partner treatment was almost significant at five weeks, $P = .12$, as well. The effect of patient treatment was not significant at any of the visits. Eighty-nine of 140 (64 percent) and 96 of 140 (69 percent) patients returned slides at five and eight weeks, respectively.

Using a computer simulation to model what was felt to be a clinically significant difference (25 percent) in bacterial vaginosis cure rates by Gram-stained smear criteria between seven-day and single-dose patient therapy at the first follow-up visit, the power of this study to detect such a 25 percent difference was estimated to be 85 percent.

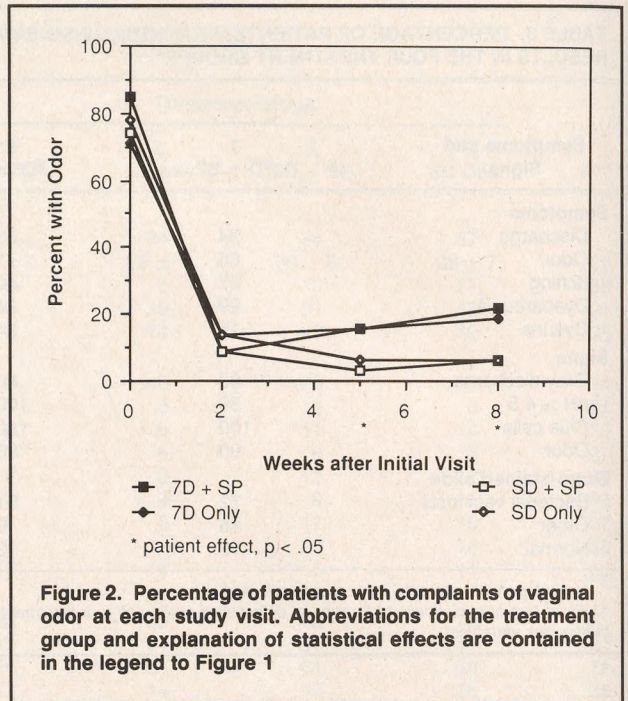
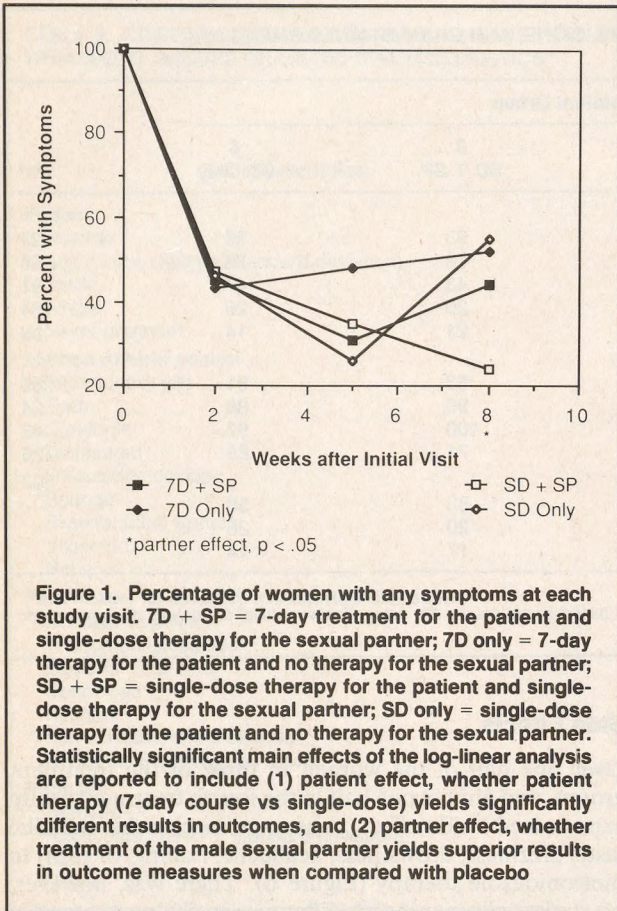
Side Effects

Over one half of the women in three of the treatment groups, and almost one half in the fourth treatment group experienced a side effect (nausea, stomach ache, metallic taste, dizziness, drowsiness, headache, itching, or rash) to metronidazole therapy (Figure 6). There was, however, no statistically significant difference in the percentage of women with a particular side effect that could be attributed to patient treatment between the four treatment groups, although women who were randomized to the seven-day treatment probably experienced their side effects for a longer period of time.

Partners who took metronidazole experienced more side effects ($P < .05$), more stomach aches ($P < .05$), more metallic taste ($P < .01$), and more dizziness ($P < .05$) (Figure 7). There were no statistically significant differences in the percentage of partners with nausea, drowsiness, headache, itching, or rash among the four groups.

Return Visits

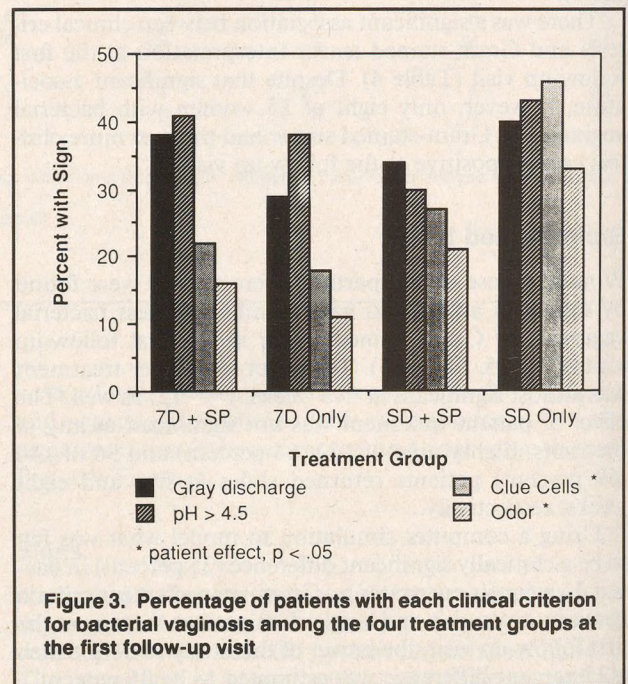
Twenty-seven women returned to their physicians with recurrent symptoms. Nineteen of the 27 were considered to have bacterial vaginosis by clinical criteria, but only four of those 19 had bacterial vaginosis determined by Gram-stained smear. There were no significant differences among the four treatment groups in number of patients with visits for recurrent symptoms, clinical diagnosis of



bacterial vaginosis, or Gram-stained smear diagnosis of bacterial vaginosis.

Potential Confounders

The percentage of women who had a new untreated partner, were noncompliant (took less than 80 percent of their medicine), or could guess correctly their treatment group did not differ significantly among the four groups at the first follow-up visit. Likewise, the percentage of women at five and eight weeks who had a new untreated partner, who had been treated with metronidazole after the first follow-up visit, or who had additional antibiotics during the follow-up period did not differ significantly among the four treatment groups. Excluding women with potential confounders from the appropriate step in the analysis did not materially alter the results.



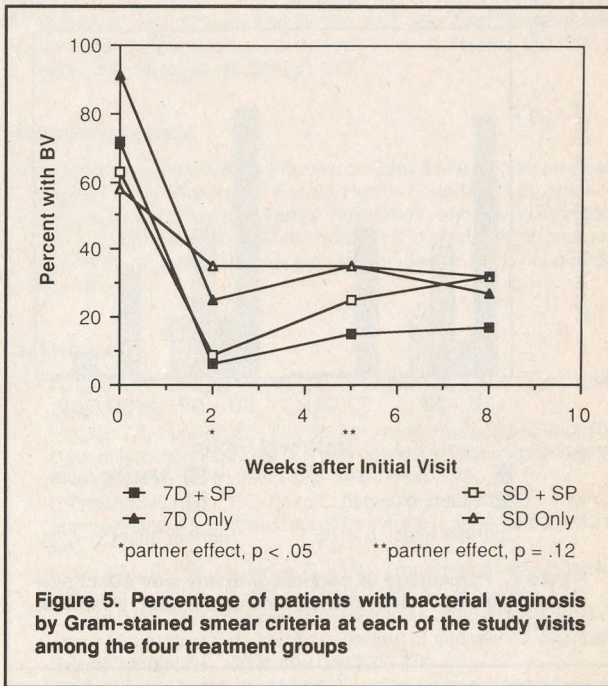
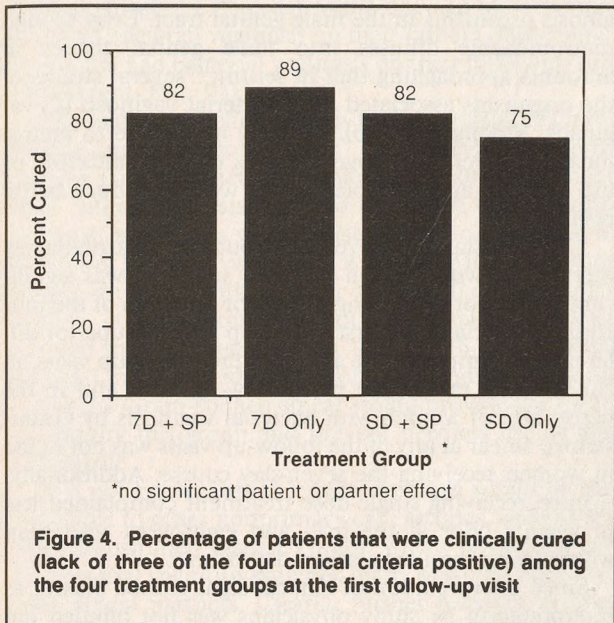


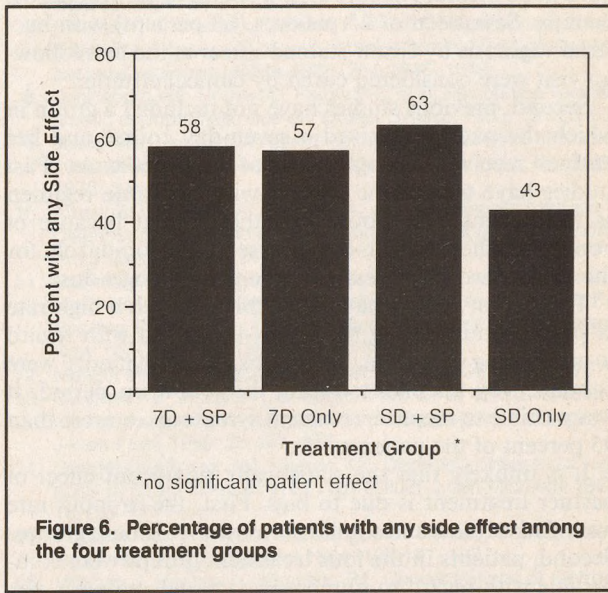
TABLE 4. ABILITY OF CLINICAL CRITERIA TO ASSESS CURE AS JUDGED BY GRAM-STAINED SMEAR RESULTS AT THE FOLLOW-UP VISIT*

Number of Criteria Positive	Number of Patients with Follow-up Gram-Stained Smear Results		
	Bacterial Vaginosis	Other	Normal
3 or 4 (+bacterial vaginosis)	8	6	5
0, 1, or 2 (-bacterial vaginosis)	17	14	62
Total	25	20	67

* $P < .01$

DISCUSSION

Unlike previous studies showing no significant effect when the patient's sexual partner is treated, this study showed a statistically significant improvement in two outcome measures and an improvement approaching significance in a third when the partner was treated. Specifically, women whose sexual partners were treated showed less bacterial vaginosis by Gram-stained smear at the follow-up and five-week visit and fewer symptoms suggestive of bacterial vaginosis at eight weeks.



Several factors may account for the different conclusion reached in this study. First, past studies have relied upon G vaginalis cultures and clinical criteria to determine cure. G vaginalis cultures are a poor indication of cure, as they do not reliably indicate the presence of bacterial vaginosis.¹⁰ Also, as shown in this study, clinical criteria are

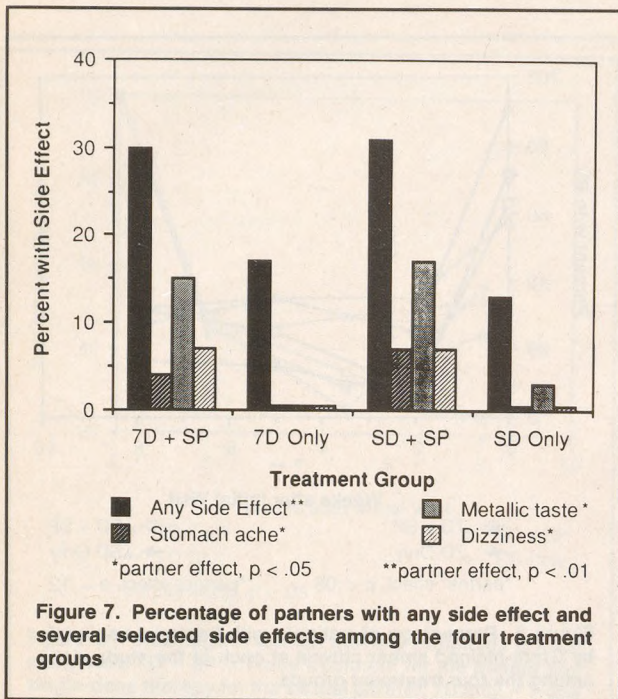


Figure 7. Percentage of partners with any side effect and several selected side effects among the four treatment groups

not a good measure of cure after a course of metronidazole therapy. Seventeen of 25 patients (68 percent) with bacterial vaginosis by Gram-stained smear at the first follow-up visit were considered cured by clinical criteria.

Second, previous studies have not included a group in which the patient received a seven-day course and her partner received a single dose of metronidazole. Past studies have treated the partner with the same regimen as the patient. One could hypothesize that because of noncompliance a seven-day course of metronidazole for the partner would be less effective than a single dose.

Third, past studies have not achieved such a high rate of participation during the follow-up period with regard to measuring recurrent symptoms. Since patients were contacted by telephone during the follow-up period, it was possible to measure recurrent symptoms in more than 95 percent of the patients.

It is unlikely that the statistically significant effect of partner treatment is due to bias. First, the dropout rate was relatively low and similar across the treatment groups. Second, patients in the four treatment groups were comparable with regard to numerous bacterial vaginosis risk factors. Third, although most patients were able to guess which regimen they were taking, physicians performing examinations and the laboratory technician interpreting the Gram-stained smears were blinded to patient and partner regimen.

Unfortunately, partner treatment with a single dose of metronidazole does not appear to confer a long-lasting

effect, perhaps as a result of a resurgence of bacterial vaginosis organisms in the male genital tract. Even though metronidazole diffuses into male genital tissues in amounts approaching that in serum,¹⁶ several strains of the organisms associated with bacterial vaginosis (*G vaginalis*, *Mobiluncus* spp) are fairly insensitive to metronidazole.¹⁷ Perhaps longer courses of metronidazole or use of other antimicrobial agents would produce better results.

The now-standard seven-day course of metronidazole therapy for women with bacterial vaginosis was significantly superior to the single dose for only two of the four clinical criteria at the first follow-up visit. A superior difference in symptom rate at any of the follow-up visits, in clinical cure rate at the first follow-up visit, and in the percentage of women with bacterial vaginosis by Gram-stained smear at any of the follow-up visits was not noted in women receiving the seven-day course. Additionally, women receiving single-dose treatment complained less of vaginal odor at the five- and eight-week visit than women who received a seven-day course.

Since interpretation of clinical signs can be biased, as interpretation by study physicians was not blinded but took place after a history and physician examination, and since cure was not adequately indicated by clinical criteria, the lack of other significant outcomes indicates that the two treatment regimens are similarly effective. Also, the two patient regimens showed no significant difference in cure rates or recurrence rates as determined by Gram-stained smear criteria.

The Gram-stained smear is emerging as the best objective indicator of bacterial vaginosis infection.¹⁸ Thus, conclusions as to the effectiveness of single-dose treatment when compared with a seven-day course should be heavily influenced by the Gram-stained smear outcome measure rather than more subjective and possibly biased clinical signs and symptoms.

Finally, it is unlikely that this study would miss a clinically significant difference (25 percent) in cure rates because of its high power (85 percent). Therefore, shortening the course of metronidazole therapy to a single 2-g dose does not seem to impair effectiveness in treating women with bacterial vaginosis in the primary care setting and has the potential advantages of lowering cost, improving compliance, decreasing recurrent vaginal odor symptoms, and shortening the duration of side effects.

No conclusion about the cause of the Gram-stained category "other" emerged from this research. That patients with "other" present with exactly the same clinical symptoms and signs as bacterial vaginosis led to the idea that the Gram-stained smear category "other" might be a "prebacterial vaginosis" or transition state. Patients with "other" were not cured by metronidazole, however. Of 21 patients with "other" on their initial Gram-stained smear, 11 still had "other" on their follow-up visit Gram-

stained smear (52 percent), while only 22 of 91 women who had bacterial vaginosis on their initial Gram-stained smear still had bacterial vaginosis on their follow-up slide (24 percent, $P < .05$).

The inability of clinical signs to distinguish the Gram-stained smear category "other" from bacterial vaginosis and the failure of metronidazole therapy to cure patients with "other" suggests the need to use the Gram-stained smear of a patient's vaginal discharge to confirm the diagnosis of bacterial vaginosis. Of the 140 patients enrolled in this study, all with three or more of the four clinical criteria, 40 (29 percent) did not have bacterial vaginosis (24 had smears categorized as "other," 16 were normal) on the Gram-stained smears of their vaginal discharge. Using the Gram-stained smear would provide the means to identify this group and prevent needless use of metronidazole.

It is not known whether these findings would be generalizable to other nonprimary care settings, such as sexually transmitted disease clinics, where physicians care for bacterial vaginosis patients, many of whom have multiple sexual partners. Clearly, further research in other settings should be done before treatment of the male sexual partner of women with bacterial vaginosis can be advocated in all settings and circumstances.

In conclusion, this study demonstrates the effectiveness of treatment of the male sexual partner of women with bacterial vaginosis who present in the primary care setting. In addition, single-dose therapy for patients with bacterial vaginosis appears as effective as the currently accepted seven-day course. Single-dose therapy with 2 g of metronidazole for both the patient with bacterial vaginosis and her sexual partner is emerging as an additional bacterial vaginosis treatment option for the primary care physician.

The Bacterial Vaginosis Study Group

The Bacterial Vaginosis Study Group consists of 12 primary care group practices in the Seattle area who enrolled patients into the study. The following physicians, physician assistants, and nurse practitioners participated in the study:

Ballard Family Medicine: Cynthia B. Johnson, MD, Gary D. Rosen, MD, Nancy K. White, MD; *Bellevue Family Medicine Associates:* Barbara Perez, CRN, Peter B. Schock, MD; *Eastside Family Medicine Clinic:* Janine R. Cooley, MD, Denise S. Kraft, MD; *Greenwood Family Medicine:* Linda J. Clark, MD, Chris Leininger, MD, Kristen T. Vittone, PA; *Highland Clinic:* Sandra K. Borg, MD, Donald M. Keith, MD, Laura C. Lippman, MD, Richard E. Rust, MD; *Lakewood Family Medicine:* Adrian Call, MD; *The Mason Clinic—Mountlake Terrace:* Christine Adams, MD, Judith Bowen, MD, Patricia L. Clayton, MD, David Huntington, MD, Dave Yonkers, MD; *Monroe Medical Associates:* Martha Bennett, MD, Sam Cullison, MD, Hans Dankers, MD, Jeff Hambleton, MD, Liz Herseth, MD, James Reppnick, MD, Charles Strub, MD, Deborah Riedesel, PA, Vera Reynolds, CRN, Joyce Lingerfelt, CRN; *Northwest Family Medicine:* William R. Phillips, MD, MPH, G. Scott Stevens, MD; *Ranier Family Medical Group:* Robert Crittendon, MD, David Goldman, MD, Shou-ling Leong, MD, E. Yumi Shitama, MD,

Brian Wong MD; *Seattle Family Medicine:* Cici B. Asplund, MD, Pamela H. McDonald, MD, Charles Lee Wilson, MD; and *West Seattle Family Health Care:* Debbie Kearnes, CRN, FNP, Holly W. Hadley, MD, Winnie L. Mann, MD, Peter M. McGough, MD.

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