

Treatment of Recurrent Bacterial Vaginosis With Tinidazole

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BACKGROUND: Recurrent bacterial vaginosis is a difficult clinical condition. In women with recurrent bacterial vaginosis, relapses are common, even after prolonged courses of maintenance therapy. Because of its spectrum of activity, tinidazole was used in a patient with recurrent bacterial vaginosis.

CASE: A 23-year-old woman taking oral contraceptives had a single sexual partner. She was treated for recurrent bacterial vaginosis with multiple courses of metronidazole gel 0.75%, including regimens of maintenance therapy. The patient experienced repeated recurrences shortly after stopping treatment. A single course of oral tinidazole resulted in a prolonged period where she was free of bacterial vaginosis.

CONCLUSION: Treatment options for recurrent bacterial vaginosis are currently limited. Tinidazole may be a useful option in women with recurrent bacterial vaginosis. (*Obstet Gynecol* 2004;104:931-2. © 2004 by The American College of Obstetricians and Gynecologists.)

Bacterial vaginosis is the most common cause of vaginitis in women of childbearing age. Approximately 30% of patients who are treated for a diagnosis of bacterial vaginosis experience a recurrence within 3 months.¹ Over a longer period of time, recurrence may even be more common. Women with recurrent bacterial vaginosis are often frustrated by the chronicity of their symptoms and the lack of effective treatment alternatives. Tinidazole, a nitroimidazole closely related to metronidazole, may be an effective alternative in refractory cases of bacterial vaginosis.

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CASE

A 23-year-old nulligravida presented in December 2000 with a history of symptomatic recurrent bacterial vaginosis. She had been taking oral contraceptives and had the same sexual partner for several years. Previous treatments included numerous courses with topical clindamycin and oral and topical metronidazole. Intermittently, her symptoms had seemed to resolve without treatment. At her first visit, her symptoms included a copious thin discharge and a fishy odor. Physical examination confirmed the diagnosis of bacterial vaginosis, with an elevated vaginal pH (> 4.5), an amine odor on application of 10% potassium hydroxide (KOH) to a sample of vaginal discharge, and saline microscopy revealing the presence of clue cells. The patient was placed on metronidazole gel twice daily for 10 days, with the plan to continue maintenance therapy 3 times per week for 3 months.

When the patient returned 2 weeks later, signs and symptoms of bacterial vaginosis had resolved. However, hyphae were noted on the KOH mount, and a fungal culture was positive for *Candida albicans*. Over the next 18 months, the patient had recurrent episodes of bacterial vaginosis, despite repeated attempts at acute therapy and maintenance. While on therapy, all evidence of bacterial vaginosis resolved, but her infection would recur each time within a month of discontinuing medication. The patient was also treated for recurrent vulvovaginal candidiasis with fluconazole, and she was diagnosed with cervical intraepithelial neoplasia (CIN 1), which resolved on subsequent visits. She has had the same sexual partner throughout this time. Use or nonuse of condoms had no impact on her episodes of bacterial vaginosis.

In October 2002, because of the refractory nature of her infection, she was offered a course of tinidazole, 500 mg twice daily for 2 weeks, as a different approach to therapy. The patient responded well to tinidazole and remained asymptomatic for 10 months. During this time, several follow-up visits revealed normal findings, including a low vaginal pH, negative amine test, and absence of clue cells on saline microscopy. In August 2003, she developed another episode of bacterial vaginosis. She was again treated with a 2-week course of tinidazole and, 7 months later, has thus far remained free of infection.

COMMENT

Bacterial vaginosis is the most frequent vaginal infection in women of reproductive age. The pathogenesis of



recurrent bacterial vaginosis is unclear. Evidence suggests that recurrent bacterial vaginosis is not due to a reinfection but rather a relapse of a previous infection. Treatment of the sexual partners of individuals with recurrent bacterial vaginosis has not been shown to decrease recurrences and is not currently recommended.^{1,2} It has been suggested that a lack of re-establishment of the normal vaginal flora, particularly hydrogen peroxide-producing lactobacilli, may lead to recurrent episodes of bacterial vaginosis.³ In addition, the vaginal pH of women with recurrent bacterial vaginosis may fail to decrease despite adequate treatment, which could potentially lead to more frequent relapses.⁴ The persistence after treatment of an organism or organisms that trigger bacterial vaginosis could also account for the relatively high rate of recurrences.

The Centers for Disease Control and Prevention currently recommend 3 treatment protocols for bacterial vaginosis: metronidazole, 500 mg orally twice a day for 7 days; metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days; or clindamycin cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days. Clindamycin cream can weaken latex condoms and diaphragms and may be less effective than metronidazole.⁵ In the case of recurrent bacterial vaginosis, these treatment options can quickly be exhausted, and no options are offered for women failing these described regimens. In a pilot, prospective, controlled trial of maintenance therapy with metronidazole gel, twice weekly for 3 months, 5 of 6 patients in the treatment group, as opposed to 4 of 6 in the placebo group, remained free of infection.⁶ However, as in our patient, recurrence after stopping therapy was frequent. Furthermore, episodes of recurrent vulvovaginal candidiasis, also experienced by our patient, can complicate long-term antibiotic therapy.

Tinidazole is a nitroimidazole derivative that is structurally similar to metronidazole but has a different pharmacokinetic profile. Tinidazole has a higher peak serum concentration, longer half-life, and less variation in blood levels than metronidazole. Tinidazole has also been shown to be equally or more effective in vitro than metronidazole as an antibacterial agent.² Recently, tinidazole has been used with a great deal of success in cases of metronidazole-resistant trichomoniasis.⁷ Tinidazole in a 2-g dose on a single occasion has been shown to be an effective treatment for nonrecurrent bacterial vaginosis.⁴ For these reasons and because of this woman's frequent and rapid recurrences following maintenance therapy

and prior failures with clindamycin, tinidazole was offered as an option for treatment. She did very well, with an extended disease-free period of time. Following relapse, another course with tinidazole was met with similar success. Her response suggests that, in her case, recurrences may have been secondary to the persistence of triggering organisms that may have been treated more effectively by tinidazole. On a final note, tinidazole may also cause less nausea, vomiting, and dizziness than metronidazole;⁸ our patient had no adverse effects with her 2 courses of therapy.

Clinical management of recurrent bacterial vaginosis can be frustrating for health care providers because of the limited therapeutic options. Given our success with this patient, we feel that tinidazole represents a viable treatment alternative and deserves further study in women with recurrent bacterial vaginosis.

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