# Recurrent Bacterial Vaginosis Unresponsive To Metronidazole: Successful Treatment With Oral Clindamycin

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Bacterial vaginosis is known to be a polymicrobial condition that can include infections with *Gardnerella vaginalis*, *Mycoplasma hominis*, *Mobiluncus*, *Bacteroides*, and *Peptococcus*.[1] Currently, many physicians consider oral metronidazole to be the drug of choice for the treatment of bacterial vaginosis. Cure rates of up to 91 percent have been reported after 7 days of pharmacotherapy[2]; however, it is common and often frustrating for the clinician to see a lack of response after this standard treatment regimen. As recurrences are often attributed to poor compliance, cultures and sensitivity testing are not used routinely to address the possibility of resistant organisms. A case of recurrent bacterial vaginosis that contained a strain of *G. vaginalis* that was resistant to metronidazole is presented. Oral clindamycin was an effective alternative treatment.

## Case Report

During a 5-year period, a 23-year-old patient was prescribed multiple courses of oral metronidazole 500 mg twice daily for 7 or 10 days for bacterial vaginosis. Initial treatment failures had been attributed to poor compliance, which was unsubstantiated. These infections were diagnosed by the characteristic vaginal discharge, presence of clue cells and absence of other pathogens on microscopic examination of the normal saline preparation on wet mounts, pH>4.5, and an amine odor after the addition of 10 percent potassium hydroxide to the specimen. The patient continued to return to the clinic because of the incomplete resolution of the vaginal discharge with the characteristic foul-smelling odor.

After the patient experienced repeated treatment failures with metronidazole in spite of total monogamy and the strict use of condoms during the treatment period, a vaginal swab was cultured on agar containing 5 percent defibrinated horse blood at 37°C with incubation in an anaerobic environment.[3] Moderate normal genital tract flora were identified. Of note, however, *G. vaginalis* was also identified, with sensitivities as follows: penicillin G, 90 percent minimum inhibitory concentration ($MIC_{90}$) <0.06 μg/mL; clindamycin, <0.12 μg/mL; chloramphenicol, <2 μg/mL; metronidazole, >32 μg/mL; and tetracycline, >16 μg/mL; the presence of a strain of *G. vaginalis* was resistant to both metronidazole and tetracycline but sensitive to clindamycin. No other anaerobic bacteria were identified. The patient was treated with oral clindamycin, 300 mg twice daily for 10 days. After 5 months, she remained asymptomatic and was culture negative for *G. vaginalis* at that point. She remained asymptomatic for 1 year, a longer recurrence-free period than any of the previous treatment courses with metronidazole.

## Discussion

The standard $MIC_{90}$ of metronidazole for *G. vaginalis* is 32 μg/mL,[3] but serum metronidazole concentrations of only 11.5 μg/mL have been found after administration of a 500-mg oral dose.[4] Ralph, et al.[5] demonstrated that 30 percent of *Gardnerella* strains were resistant under anaerobic conditions at a metronidazole $MIC_{90}$ of 16 μg/mL.[5] Jones, et al.[2] found that 54.5 percent of strains had $MIC_s$ ≥32 μg/mL, but no correlation with treatment failures in relation to these strains has been made. Further studies examining the current sensitivity of *G. vaginalis* and other microbial organisms associated with bacterial vaginosis to metronidazole, as well as 1(2-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole, its active

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hydroxy metabolite, are necessary to elucidate further the role of resistance in recurrent cases.

The use of clindamycin could be advantageous because of its high bacteriocidal activity against *G. vaginalis* and other associated anaerobic vaginal organisms,[6-10] whereas metronidazole has high activity against *Bacteroides* strains, with only variable activity against *Mobiluncus*.[2,10] Metronidazole is potentially dangerous for women who consume ethanol, because of the disulfiram-like reaction, or who are in their first trimester of pregnancy.[11] The risk of serious adverse reactions with clindamycin (e.g., pseudomembranous colitis) is considered to be low, and metronidazole has also been associated with this reaction.[12,13] Careful monitoring for diarrhea while taking clindamycin could reduce the risk of developing a severe case of pseudomembranous colitis by discontinuing the suspected offending agent earlier.

Although the use of clindamycin in the treatment of bacterial vaginosis is not new, based upon our experience, clinicians should consider that organisms resistant to metronidazole might be the cause when patients have a recurrence of bacterial vaginosis after a confirmed treatment with a standard course of metronidazole. The latest report from the Centers for Disease Control and Prevention provides only a recommendation on the use of clindamycin as a vaginal cream at bedtime for 7 days during pregnancy,[14] and oral clindamycin might be a reasonable alternative for patients who do not prefer to use vaginal products, cannot afford more costly antimicrobial products (e.g., in Chapel Hill, NC, the average cost to the patient for 2 percent clindamycin vaginal cream is $30.05 versus $15.60 for generic oral clindamycin capsules), or have failed a standard treatment course of oral metronidazole.

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