In Vitro Activity of Nifuratel on Vaginal Bacteria: Could It Be a Good Candidate for the Treatment of Bacterial Vaginosis?*

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Bacterial vaginosis is characterized by a shift of the physiological flora to a diverse spectrum of bacteria, where Gardnerella vaginalis and Atopobium vaginae are the most important markers. In this study, the antimicrobial activity of nifuratel against G. vaginalis, A. vaginae, and lactobacilli was compared with that of the two currently used antibiotics metronidazole and clindamycin. Results suggest that nifuratel has a better spectrum of activity, being highly active against G. vaginalis and A. vaginae without affecting lactobacilli.

The microbial flora of the vagina contains high concentrations of a composite population of bacteria (11, 21). It is dominated mainly by lactobacilli that maintain an acidic pH by H2O2 and lactic acid production (14). Alterations in this ecosystem can lead to bacterial vaginosis (BV) and Candida vaginitis, which account for 90% of vaginal infections (10).

BV is a polymicrobial syndrome characterized by alteration of the vaginal flora, where the normally occurring Lactobacillus species are overgrown by endogenous bacteria (24). In particular, high concentrations of Gardnerella vaginalis and Atopobium vaginae have been shown to be important microbiological markers (1, 18, 27). The association between the presence of A. vaginae and BV has been highlighted only recently (8), thanks to its detection by molecular techniques. Although its exact role is not yet fully understood, the association between A. vaginae and BV is well established (1, 17, 18, 27), as is its involvement, together with G. vaginalis, in the biofilm present on the vaginal epithelium during BV (25).

The therapies of choice for BV are systemic or topical metronidazole and clindamycin. Previous studies reported cure rates of 70 to 96% for both antibiotics, with recurrence rates of 49 to 66%, following 7 days of therapy (2, 13, 16).

Inadequate diagnosis (23), pharmacologic resistance (20), and persistence of an adherent bacterial biofilm after treatment (26) seem to be the main reasons for failures of BV treatment and eradication, as well as the presence of a complex microbial population with putative resistance to antimicrobials.

Nifuratel is a nitrofuran derivative with strong activity against Trichomonas vaginalis (4, 7) and a broad spectrum of antibacterial action (7, 19, 22). The purpose of this study was to investigate the potential of nifuratel in the treatment of BV and compare it with metronidazole and clindamycin against G. vaginalis, A. vaginae, and lactobacilli.

The bacterial strains tested were both clinical isolates and reference strains. Clinical isolates from vaginal swabs (pro-

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did not affect the bacterial growth of all tested strains. Moreover, the MICs of the two control strains, G. vaginalis ATCC 14018 and Bacteroides fragilis ATCC 25285, were in the acceptable ranges for metronidazole and clindamycin (data not shown).

Our results (Table 1) show that clindamycin is highly active against both G. vaginalis (MIC for 90% of the strains tested [MIC90], 0.25 μg/ml) and A. vaginae (MIC90, <0.125 μg/ml), in accordance with previous studies on G. vaginalis (12, 15) and A. vaginae (5). Metronidazole was partially active against G. vaginalis (MICs, <0.125 to 256 μg/ml) and A. vaginae (MICs, 8 to 256 μg/ml). These results are also in accordance with previously published data (5, 12, 15). Nifuratel was more active on G. vaginalis and A. vaginae than metronidazole, with MICs ranging from <0.125 to 4 μg/ml and from <0.125 to 1 μg/ml, respectively.

All tested Lactobacillus strains were highly susceptible to clindamycin (MICs, 0.125 to 1 μg/ml) and resistant to metronidazole (MICs, ≥256 μg/ml). Overall, nifuratel was not effective against lactobacilli (MIC90, ≥256 μg/ml). Only L. iners strains (n = 3) appeared to be more sensitive to nifuratel than the other species, with MICs of 8, 16, and 256 μg/ml. It is interesting that previous studies have shown that L. iners is more common than other lactobacilli in samples that have a Nugent score of >4 (6) and after metronidazole treatment (9). Moreover, it seems to predispose to some extent to the occurrence of abnormal vaginal microflora (28). Although these observations deal only with three L. iners strains, they suggest that nifuratel could not only be useful in the eradication of bacteria associated with BV, like G. vaginalis and A. vaginae, but also encourage the development of species of Lactobacillus other than L. iners. Further analysis should be performed to confirm these partial observations.

In conclusion, our results suggest that nifuratel is a good potential candidate for the first-line treatment of BV. Indeed, it is active in vitro against the pool of bacteria recognized to cause BV and, conversely, does not affect the normal flora of lactobacilli. Based on these encouraging results, two pivotal clinical studies on oral and topical treatments are ongoing in order to confirm if this antibiotic offers a real advantage over standard BV treatments.

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REFERENCES


