Antifungal activity of clotrimazole against *Candida albicans* depends on carbon sources, growth phase, and morphology.

Kasper L, Miramón P, Jablonowski N, Wisgott S, Wilson D, Brunke S, Hube B (2015) Antifungal activity of clotrimazole against *Candida albicans* depends on carbon sources, growth phase, and morphology. *J Med Microbiol* 64, 714-723.

Abstract

Vulvovaginal candidiasis (VVC), a superficial infection predominantly caused by the pathogenic fungus Candida albicans, is frequently treated with clotrimazole. Some drug formulations contain lactate for improved solubility. Lactate may modify C. albicans physiology and drug sensitivity by serving as a carbon source for the fungus and/or affecting local pH. Here we explored the effects of lactate, in combination with pH changes, on C. albicans proliferation, morphology and clotrimazole sensitivity. Moreover, we determined the influence of growth phase and morphology per se on drug sensitivity. We show that utilisation of lactate as a carbon source does not promote fast fungal proliferation or filamentation. Lactate had no influence on clotrimazole-mediated killing of C. albicans in standard fungal cultivation media but had an additive effect on the fungicidal clotrimazole action under in vitro vagina-simulative conditions. Moreover, clotrimazole-mediated killing was growth-phase and morphology-dependent. Post-exponential cells were resistant to the fungicidal action of clotrimazole, while logarithmic cells were sensitive, and hyphae showed

highest susceptibility. Finally, we show that treatment of preformed C. albicans hyphae with sub-lethal concentrations of clotrimazole induced a reversion to yeast phase growth. As C. albicans hyphae are considered the pathogenic morphology during mucosal infections, these data suggest that elevated fungicidal activity of clotrimazole against hyphae plus clotrimazole-induced hyphae-to-yeast reversion may help to dampen acute vaginal infections by reducing the relative proportion of hyphae and thus shifting to a non-invasive commensal-like population. In addition, lactate as an ingredient of clotrimazole formulations may potentiate clotrimazole killing of C. albicans in the vaginal microenvironment.

Involved units

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