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The effects of anti-HIV nucleoside drugs on the virulence of clinically relevant candida species

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ABSTRACT

Candida species are opportunistic yeasts that cause infections in immunocompromised individuals such as HIV and cancer patients. Recent studies show that 5-fluorouracil, a nucleoside analogue used for cancer treatment, increases *Candida* cell virulence. The aim of this study is to determine the effects of commonly used anti-HIV nucleoside analogue drugs on the virulence of *Candida albicans*, the predominant species associated with oral candidiasis.

Oral swabs were collected from antiretroviral-naïve HIV-positive individuals. *C. albicans* was characterised from 39 of these swabs using standard microbiological techniques and polymerase chain reaction. The effect of nucleoside reverse transcriptase inhibitors (NRTIs) zidovudine, stavudine, didanosine and lamivudine, at predicted drug peak concentrations in patients, as well as half and double these concentrations on select virulence factors of *C. albicans* isolates were studied. In addition, antifungal susceptibility to amphotericin B was assessed. Not all 39 isolates were used in the assays because of delays in obtaining reagents from respective manufacturers.

Results show no change in the adherence and biofilm formation of 29 isolates upon exposure to NRTIs. In contrast, a steady increase in the number of viable cells was observed upon exposure to double the peak concentration of lamivudine to 23 of the clinical isolates. All 31 isolates tested were susceptible to amphotericin B (MIC≤1μg/ml).

Although these results suggest that NRTIs may have little effect on the virulence of *C. albicans* it is postulated, that, in a dose-dependent manner, cytidine analogues act similarly to 5-FU by activating a signal-transduction pathway which stimulates proliferation.