Some antiretroviral therapies inhibit the growth of selected cervicovaginal microbes with potential protective role in pre-term birth

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Background: Pre-term birth (PTB, <37 weeks' gestation) is the main cause of infant mortality worldwide and is high in women living with HIV. HIV protease inhibitors have been associated with two-fold increase in PTB rates, whilst nucleoside reverse transcriptase inhibitors (NRTI) have been associated with lower rates of PTB. The mechanism is unclear. Bacterial vaginosis (BV), associated with PTB, is characterised by abundant biofilm microbes. e.g. *Gardnerella vaginalis (G. vaginalis)*, *Lactobacillus iners* (*L. iners*) and reduction in protective *L. crispatus.* Some antiretroviral therapies inhibit gut pathobiont growth. We hypothesized a similar effect against vaginal bacteria.

Methods: The minimum inhibitory concentration (MIC) and half-maximal inhibitory concentration (IC50) values for BV prescribed antibiotics, Metronidazole (MTZ) and Ciprofloxacin (CIP) (controls) against *G.vaginalis* DSM4944, *L. iners* DSM13335, *L. crispatus* DSM20854 were determined using the broth microdilution method. MICs and IC50s of current NRTIs were determined and compared with these controls.

Results: MTZ inhibited the growth of *G. vaginalis* (MIC of 1.8 μg/mL, IC50 6 μg/mL), but not *L. iners*. CIP inhibited *L. iners* (MIC 0.2 μg/mL, IC50 1.3 μg/mL). MIC of ZDV against *G. vaginalis was* 39.9 μg/mL (IC50 142.6 μg/mL) and against *L. iners* 5.4 μg/mL (IC50 19 μg/mL). Abacavir inhibited growht of *G. vaginalis* (4 μg/mL, IC50 13.7 μg/mL), but not *L. iners*. Emtricitabine inhibited the growth of *L. iners (*MIC 78.7 μg/mL, IC50 136.7 μg/mL), but not *G. vaginalis*. Tenofovir disoproxil fumarate and lamivudine did not inhibit *L. iners* and *G. vaginalis*. None of these antiretrovirals inhibited the *L. crispatus* growth.

Conclusion: A direct effect of selected NRTIs on the vaginal microbiota was observed providing insight into their potential effect *in vivo* and possible protective role on HIV PTB.