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The antiretroviral, dapivirine and tenofovir disoproxil fumarate regulate immune function gene expression in cervical cells alone and in combination with medroxyprogesterone acetate

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The concurrent use of hormonal contraception and ARVs is likely to increase with the implementation of programs using ARVs to prevent HIV infection. However, little is known about the combinatorial effects of different ARVs and progestins used in hormonal contraception, both systemically and in the female genital tract. In this study we investigated the effects of the ARVs dapivirine (DPV) and tenofovir disproxil fumarate (TDF) alone and in combination with medroxyprogesterone acetate (MPA) on select immune function gene expression. Cervical TZM-bl cells were exposed to varying concentrations of DPV and TDF on their own, or in combination with 100 nM MPA or the glucocorticoid dexamethasone (DEX). Results show that upregulation of IL-8 mRNA in TZM-bl cells occurs at high concentrations (1, 10 uM) of TDF or DPV in a time-dependent manner. On their own, DEX or MPA also resulted in a pro-inflammatory IL-8 response, which is greatly potentiated upon co-stimulation with 1 μM DPV, while co-stimulation with 1 μM TDF resulted in an additive IL-8 pro-inflammatory response. mRNA levels of the anti-inflammatory gene, GILZ, which is transactivated by DEX or MPA alone, remained unchanged by up to 10 μM of either ARV, while the ARVs alone had no effect on GILZ mRNA levels. Only high concentrations of DPV but not TDF reduced the cell viability. Results from this study suggest that DPV or TDF have differential effects on select immune function genes and may exert cytotoxic effects directly on cervical epithelial cells, which may be potentiated by MPA. These results may aid in the choice of ARV for combination with progestins, to protect against HIV infection and unwanted pregnancies with minimal side effects.

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