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LETTER TO THE EDITOR

Authors' Reply: Pharmacokinetic and Pharmacodynamic Drug Interactions Between Antiretrovirals and Oral Contraceptives

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We thank Atrio [1] for her thoughtful comments.

We wholeheartedly agree that "women should be empowered and educated to access the combination of health care behaviors and medications that optimize their health and well-being". However, the attainment of this ideal is impeded by the fact that the data on which to base recommendations for safe hormonal contraceptive use are extremely limited.

We disagree that the primary mechanism of action of hormonal contraceptives in preventing pregnancy is the development of hostile cervical mucus. Although this is an extremely important secondary mechanism, the primary mechanism of action of combined hormonal methods, as well as depot medroxyprogesterone acetate, the etonogestrel implant and the progestogen-only pill, desogestrel, is the inhibition of ovulation via suppression of the hypothalamo-pituitary-ovarian axis [2, 3].

Inhibition of the metabolism of progestogens caused by certain protease inhibitors, e.g. atazanavir, would be expected to increase progestogen levels; however, protease inhibitors require boosting with ritonavir which, as an inducer of glucuronidation, would result in a reduction in progestogen levels. It is this unpredictability that makes it impossible to be certain that the co-administration of contraceptive steroids and protease inhibitors is safe.

With regard to interactions with ethinyl estradiol, it is true that 10-μg pills have indeed shown similar efficacy to higher dose pills. However, an important factor in their effectiveness is the significant shortening of the overall pill-free interval compared with that of standard combined preparations, which limits the opportunity for follicular development seen in the pill-free interval in some women taking standard-dose pills. A potential strategy to reduce the risk of unwanted pregnancy in women taking combined hormonal contraception and enzyme inducers would be to reduce or eliminate the pill-free interval [3]; however, it is essential that studies are performed to assess whether this is a viable approach in HIV-positive women.

As stated in our paper, there is a paucity of data from randomized clinical trials and cohort studies that enable the correlation of statistical and clinical outcomes, without these, the challenges described above remain.

Finally, we also agree that collaborations between scientists, pharmaceutical companies and clinicians are essential to improve our understanding of the interplay between physiology and pharmacology in women taking antiretroviral therapy and hormonal contraception.

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