HIV Treatment Reduces Incidence, Improves Regression, of Cervical HPV Lesions

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Not only did antiretroviral therapy reduce the incidence of new human papillomavirus (HPV)-associated precancerous cervical lesions in a study of South African women living with HIV, it was also linked to the regression of lesions detected before treatment was started, according to an encouraging paper published online ahead of print by the journal AIDS.

“Our study is among the largest evaluations of the impact of [ARV therapy] on HPV-related cervical disease,” David Adler, MD, of the University of Rochester and his colleagues write. “We found that women on [ARV therapy] were more than twice as likely than non-[ARV] users to demonstrate regression in consecutive cervical smears. In addition, we found that among those women with a baseline normal smear, those on [ARV therapy] were significantly less likely to develop an abnormality on future smears.”

HIV is known to affect HPV-related cervical disease risks in several ways. Compared with HIV-negative women, those living with HIV are more likely to have HPV infection, notably strains of the virus associated with the development of cervical cancer. Women coinfected with both viruses are also more likely to have persistent HPV infection and are less likely to see lesions regress on their own.

“Tremendous progress has been made in the reduction of AIDS-related morbidity and mortality in the last decade and a half due to the use of highly active antiretroviral therapy,” the authors explain. “[ARV therapy] use has not only decreased the incidence of opportunistic infections among AIDS patients, but has also had a positive impact on AIDS-related malignancies such as Kaposi’s sarcoma and non-Hodgkin’s lymphoma. The impact of [ARV therapy] on cervical cancer, however, remains uncertain.”

In turn, Adler and his colleagues conducted a prospective cohort study in South Africa—a country with more people living with HIV than any other nation, with very high rates of cervical cancer. Their study compared the risk of progression, regression and incidence of HPV-related cervical lesions between those on ARV treatment and those not receiving therapy.

Roughly 1,100 Soweto residents living with HIV underwent regular cervical Pap smears. Two

percent of the women were receiving ARV treatment upon entering the cohort, and another 17 percent began treatment while being followed in the study.

The women who started ARV therapy tended to be older (37 versus 33 years old). Other differences, including age, body mass index, smoking history, number of sexual partners and CD4 cell counts, did not differ between the two groups. Most women entered the cohort study with CD4 cell counts between 201 and 500.

The average number of cervical Pap smears collected and analyzed during the study follow-up was three, with the women receiving the Pap smears, on average, every 14 months.

According to the analysis by Adler's team, women who didn't have evidence of cervical lesions upon entering the study were 38 percent less likely to have a follow-up test documenting the presence of HPV-related disease if they were receiving ARV therapy during the follow-up period. Compared with women who didn't receive ARV treatment, this difference was highly statistically significant—too great to have occurred by chance.

Women with lower CD4 cell counts—generally below 200—and those who smoked (a known risk factor for precancerous cervical lesions) were significantly more likely to develop lesions during the follow-up period, regardless of whether or not they were receiving ARV treatment.

The researchers also found that precancerous lesions were more likely to regress in women receiving ARV therapy. The rate of regression was more than 2.5 times higher, compared with women in the study who didn't receive ARV therapy.

Upon looking at progression rates, Adler and his colleagues found that persistent lesions were about 20 percent less likely to worsen among women using ARV therapy. However, compared with women not using ARV treatment, this difference was not statistically significant, meaning the slight reduction could have been due to chance.

The researchers note that other studies exploring the effects of ARV therapy on cervical lesion incidence, regression and progression have been a mixed bag. Whereas the encouraging data reported by Adler and his colleagues confirm those of other reports, other studies have failed to demonstrate a positive effect of ARV therapy on HPV-related cervical disease, notably the regression of lesions.

Additional research is needed, as "the impact of [ARV therapy] on cervical disease has implications for screening practices," the authors conclude. "If it were conclusively found that [ARV therapy] decreased the risk of cervical cancer among HIV-infected women to that of the general population, then screening practices could possibly be relaxed in this population. Although this conclusion is far from being reached and a lack of uniformity remains in the literature on this subject, our large prospective cohort study adds significant weight to the side of the balance supporting the positive impact of [ARV therapy] on the natural history of HPV-related cervical disease in HIV-infected women."

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