

Screening and Early Treatment for Anal Cancer in People With HIV

Topical treatment may be as effective as electrocautery for anal neoplasia but with fewer adverse effects.

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HIV-positive people treated with topical trichloroacetic acid were about equally likely to experience improvement or resolution of precancerous anal cell changes as those who underwent electrocautery, but they were less likely to experience pain and other side effects, according to study results presented at the [European AIDS Conference \(EACS 2023\)](#). Another study, presented at [IDWeek 2023](#), found that many gay men living with HIV are not receiving screening to detect anal cancer at an early, more treatable stage.

[Anal cancer](#), like cervical cancer, is caused by human papillomavirus (HPV), one of the most common sexually transmitted infections. HPV triggers abnormal cell growth, or dysplasia, which can progress to precancerous intraepithelial neoplasia (also known as squamous intraepithelial lesions) and ultimately invasive cancer. HIV-positive people—especially men who have sex with men—are at much greater risk for anal cancer compared with the general population, even if they are on effective antiretroviral treatment with an adequate CD4 T-cell count.

Anal Cancer Screening

Widespread screening and early treatment has dramatically reduced cervical cancer prevalence and mortality, but this is not yet widely done for people at risk for anal cancer.

Many experts and advocates hoped this would change after the ANCHOR study showed that screening and prompt treatment of anal neoplasia [lowered the risk of invasive anal cancer by 57%](#). In that study, participants were screened using anal cytology (Pap tests) and high-resolution anoscopy (examination of the anal canal using a magnifying scope). Those with high-grade squamous intraepithelial lesions were randomly assigned to undergo immediate treatment or active monitoring.

“We believe that screening for anal cancer precursors and treating them should become the standard of care for people with HIV over the age of 35 years,” ANCHOR lead investigator Joel Palefsky, MD, of the University of California at San Francisco, told POZ.

But while some HIV clinics now routinely offer anal cancer screening, rates are still far from

adequate.

As reported at IDWeek, Amit Achhra, MD, MPH, PHD, of Yale School of Medicine, and colleagues evaluated the screening cascade at two academic HIV clinics that have offered annual anal Pap tests for more than a decade. People with abnormal cell changes (atypical squamous cells of undetermined significance, or ASCUS) or anal intraepithelial neoplasia (AIN) are referred for high-resolution anoscopy (HRA) and dysplasia treatment.

The researchers performed a retrospective chart review, spanning 2018 to 2022, of medical records from HIV-positive men who have sex with men ages 35 and older. They identified 432 people who were eligible for anal cancer screening. In this group, the median age was 57, almost all were on antiretroviral treatment and the median CD4 count was 635. More than half (57%) had received an anal Pap test before 2018, and 24% had a prior history of anal dysplasia.

Over five years, 51% received at least one anal Pap or HRA test, while 26% had at least two tests and just 13% had three or more. People with a prior history of anal dysplasia were substantially more likely to undergo screening, but older individuals and those who smoked—both risk factors for anal cancer—were less likely to do so. Screening rates did not differ, however, by race/ethnicity or type of insurance.

Of those screened, about one third had an abnormal Pap test during follow-up, and nearly half of those underwent HRA. Of the 365 anal Pap tests performed, 56% were negative (no abnormality), 18% showed ASCUS and 9% showed grade 1 AIN, but none showed grade 2 or 3 neoplasia. However, of the 112 HRA tests performed, just 29% were negative, 19% showed grade 1 AIN and 54% showed grade 2 or 3 neoplasia. These findings suggest that follow-up anoscopy is needed to accurately diagnose precancerous lesions.

The researchers noted that anal Pap tests are “challenging to administer as a screening test in [the] real world.” Cytologists deemed about half the tests “unsatisfactory” (unable to be analyzed), and Pap tests had “low rates of detection of high-grade lesions” despite a high prevalence of grade 2 or 3 AIN according to anoscopy. “Better [anal cancer] screening tests and implementation models are urgently needed,” they concluded.

Anal Cancer Treatment

Turning to treatment, Stefan Esser, MD, of University Hospital Essen, presented results from a randomized trial comparing 85% trichloroacetic acid (TCA) versus electrocautery for the treatment of anal intraepithelial neoplasia in people with HIV. TCA is a topical medication used to treat genital and anal warts and dysplasia caused by HPV. Electrocautery uses electricity to burn off abnormal lesions. Most people in the treatment arm of the ANCHOR study were treated with electrocautery.

The TECAIN trial enrolled 233 people at seven outpatient clinics in Germany who were diagnosed with AIN by HRA and targeted biopsies between November 2015 and March 2020. Most were white

gay or bisexual men, and the median age was about 49 years. More than 90% had an undetectable HIV viral load, and the median CD4 count was approximately 640. While current CD4 counts were generally high, Esser noted that people with a low nadir (lowest-ever) CD4 count had more HPV-associated lesions and more high-grade lesions. People diagnosed with anal cancer within the past five years were excluded.

Pap test results showed that 21% of participants had ASCUS, 29% had low-grade squamous intraepithelial lesions and 32% had high-grade squamous intraepithelial lesions. Most (77%) had high-risk, or cancer-causing, HPV types, 10% had low-risk types and 7% had no detectable HPV. The highest AIN grade was grade 1 for 37%, grade 2 for 30% and grade 3 for 33%. As a limitation of the study, Esser noted that most participants had a low number of HPV-associated lesions and small lesion size.

About half of the participants were randomly assigned to each type of treatment. They received up to four administrations of TCA or electrocautery spaced four weeks apart. The primary efficacy endpoint was “therapeutic success,” defined as clinically and histologically confirmed resolution or regression of AIN four weeks after the last treatment.

In an intent-to-treat analysis four weeks after the last treatment, 53% people in the TCA group reached this endpoint after an average of 2.8 applications, as did 62% of people in the electrocautery group after a mean 2.3 administrations, which did not meet the prespecified criteria for noninferiority. However, 67% in both groups experienced “histological healing” or a downgrade of their AIN stage. Esser reported that 24% of TCA recipients and 37% of electrocautery recipients experienced “complete clinical healing” four weeks after their first treatment, rising to 70% and 83%, respectively, four weeks after their last treatment.

At 24 weeks after the last treatment, 51% of participants in the TCA arm and 49% in the electrocautery arm experienced clinical and histological healing or an AIN downgrade, which did meet the noninferiority criteria. At this point, 75% and 70%, respectively, showed complete clinical healing. Eight TCA recipients and seven electrocautery recipients received additional interventions between four and 24 weeks, mostly imiquimod cream.

TCA required significantly more treatment administrations for clinical success, but it was associated with fewer side effects. Adverse events were observed in 27% of TCA recipients and 36% of electrocautery recipients. Overall, the most common side effect was pain or a burning sensation during or after treatment administration. People who underwent electrocautery were almost twice as likely to report pain as those who received TCA (25% versus 14%). Electrocautery recipients were more likely than TCA recipients to require local or general anesthesia or sedation during the procedure (39% versus 7%) and more likely to need interventions to control bleeding (4% versus 3%). Nonetheless, Esser said, both types of treatment were generally well tolerated, side effects were mostly mild and temporary, and there were no serious adverse events related to either treatment.

“This is the first prospective, randomized study demonstrating comparable outcomes of TCA and

electrocautery for the treatment of AIN in people with HIV,” the researchers concluded. “TCA is a well-tolerated, cost-effective and simple treatment option for AIN in people with HIV.”

Esser noted that unlike electrocautery, TCA does not require complex equipment and can be applied without anesthesia in a regular doctor’s office by physicians without special training.

He added that longer follow-up is needed to determine the durability of treatment, as recurrence of anal dysplasia is common. However, in this study, 7% of people successfully treated with TCA experienced recurrence during follow-up, compared with 22% of those successfully treated with electrocautery, suggesting that TCA appears to have a “more sustainable effect.”

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