New treatment could be advance against cervical precancers

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Women who undergo regular Pap smears are no doubt familiar with the possibility of "precancerous" cells being detected.

These cells—called cervical intraepithelial neoplasias (CINs)—can progress to full-blown cervical cancers, but a new trial suggests that a vaginal suppository containing the drug imiquimod can halt that process.

The treatment might also help women diagnosed with advanced CIN avoid the most common therapeutic option, surgery.

"The imiquimod treatment was patient-friendly and easy to use, since it could be applied by the patient without requiring an office visit," added study lead author Dr. Sangini Sheth. She's associate professor of obstetrics at the Yale School of Medicine in New Haven, Conn.

Her team presented the findings this week at the annual meeting of the American Association for Cancer Research in San Diego. Their study was published simultaneously in the journal *Clinical Cancer Research*.

As Sheth's team explained, CIN can present in three grades—CIN1, CIN2 and CIN3—all involving the emergence of abnormal cells at the entrance to the cervix. As is the case with cervical cancers, CIN is very often caused by infection with the human papilloma virus (HPV).

Imiquimod is already approved as a topical skin cream to treat genital warts and works by stimulating an immune response. Sheth's team wanted to see if it might also help eliminate CIN when used as a vaginal suppository.

They focused on a group of 133 women who'd been diagnosed with CIN at grades 2 or 3. They did not include women with less severe CIN1, since these cases often regress on their own over time and do not require surgery.

"With CIN1, we don't do surgery, we advise the patients to come back and see us in 6 to 12 months, so we can repeat the pap smear," senior

study author Dr. Alessandro Santin explained in a Yale news release.

"For CIN2, it is different," he said. Santin is professor of obstetrics, gynecology and reproductive sciences at Yale.

Patients in the study were divided into three groups: One received the imiquimod suppository alone; another got the suppository plus the HPV vaccine; and a third group was simply monitored by doctors without receiving either treatment.

The results were impressive: While 79% of women with CIN2 who received monitoring (no treatment) saw their condition regress to the safer CIN1 level, over 95% of those taking imiquimod were able to achieve that result, the researchers reported.

Interestingly, the number was somewhat lower (84%) among women who got both the suppository and the HPV vaccine. That suggests "that the medication and HPV vaccine may impact the success of each other," according to the researchers.

Use of the suppository "was also well-tolerated by the study participants, who experienced minimal side effects," Sheth noted.

The researchers are optimistic that this nonsurgical approach to CIN2 might someday replace surgery.

That could also be true for patients with CIN3, although more study is needed. Only about a quarter of the patients in the latest trial had CIN3, Santin noted, and he hopes that a future trial—one that includes more patients with CIN3—could settle that issue.

More information: Sangini S. Sheth et al, Randomized Phase II Trial of Imiquimod with or without 9-Valent HPV Vaccine versus Observation in Patients with High-grade Pre-neoplastic Cervical Lesions (NCT02864147), *Clinical Cancer Research* (2024). DOI: 10.1158/1078-0432.CCR-23-3639

Find out more about cervical intraepithelial neoplasia at the Cleveland Clinic.