Low Prevalence of High-risk HPV in Older Women Not Attending Organized Cytological Screening: A Pilot Study

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Accepted May 14, 2007.

Sir,

The subjects of most scientific studies of the prevention of cervical cancer comprise women attending organized cytological screening (1–3). However, women who choose not to participate in screening represent a category with the most pronounced risk of cancer. It has not been examined systematically how often these women disclose cell alterations or are infected with high-risk human papilloma virus (HPV) (4–6).

Women not covered by organized screening have been the subject of recent attention, since self-sampling devices have been introduced and offered to non-attending women in an attempt to increase the participation rate (7–9). One such study showed that non-attending women (aged 35–50 years) presented with a considerably higher prevalence of high-risk HPV infections (10). This observation is in accordance with the finding of an increased risk for cervical cancer among non-attending women, and that a persistent infection with high-risk HPV is the most important co-factor for tumour development (4–6, 11, 12).

Organized screening covers women up to 60 years of age. The reason for this limit is that cervical cancer is most prevalent in middle-aged women and that cytological screening has a relatively low sensitivity, especially in older women (13).

The aim of the present pilot study was to investigate the prevalence of high-risk HPV infection among non-attendees aged 55–60 years. The women were offered the opportunity to self-sample vaginal smears at home and have the collected material analysed with an HPV DNA assay. The potential to increase screening coverage for cervical cancer was also considered.

MATERIALS AND METHODS

The study was conducted in the County of Uppsala between May 2006 and August 2006 and enrolled 301 women aged 55–60 years (mean age 57.6 years) selected from the database of the Screening Programme for Cervical Cancer (Department of Clinical Cytology, University Hospital of Uppsala). The women were selected because they had not attended organized cervical cancer screening since October 2001 despite receiving invitations to Pap smear-sampling during the period October 2004 to October 2005. They were sent a letter informing them about the study and offering them the possibility of using a novel self-sampling device (SSD, Qvintip®, Aprovix AB, Uppsala, Sweden) for self-collection of vaginal samples at home. The collected material was to be sent to the laboratory for detection of high-risk HPV DNA. The women were also informed about the study and that they were selected for the study because of not participating in the organized screening for several years and that their participation in the study was voluntary.

The following week they were sent the SSD. After self-sampling, the collected material was sent to the laboratory, where hc2 (Hybrid Capture 2) was performed according to the manufacturer's instructions to detect HPV DNA (hc2, Digene Corp, Silver Spring MD, USA). The hc2 assay is based on a chemiluminescent reaction in which HPV DNA binds to an RNA probe cocktail, which identifies 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) and HPV DNA concentrations over 1 pg/ml, which is proportional to the light emission of the positive control and corresponds to 5000 HPV genomes per specimen in the microtitre well (14, 15).

The use of the SSD was approved by the ethics committee of Uppsala (Dnr. 2004:M-202) and the study was approved by the Board of Cervical Cancer Screening in the County of Uppsala.

RESULTS

Of the 301 women who were sent SSD, 116 (response rate 38.5%) returned vaginal samples for HPV DNA analysis. HPV DNA of high-risk HPV type was detected in 6/116 (5%) of the self-collected samples (Table I). Within 4 weeks, 87% of the samples were received and 100% within 10 weeks. All participants were informed about their HPV results. Those who tested positive for high-risk HPV were invited to a midwife appointment or a visit to the Gynaecological Clinic of University Hospital of Uppsala for Pap-testing. Five responded to the invitation for further examination and Pap-smears were obtained and investigated cytologically. Four women showed normal cytology and one a negative HPV test and normal cervical biopsy. One woman displayed a persistent positive HPV reaction and a cytological CIN II lesion. Cervical biopsy disclosed a CIN III alteration, and a cone resection was performed.

DISCUSSION

This pilot study indicates that the prevalence of high-risk HPV decreases with age. In a previous investigation comprising middle-aged women participating in

Table I. *Response rate and human papilloma virus (HPV) prevalence in women offered a self-sampling device (SSD) for performing vaginal smears at home (n=301)*

Number of women using SSD	116 (39%)
Non-responders	185 (61%)
HPV-positive women	6/116 (5%)
HPV-negative women	110/116 (95%)

 ISSN 0001-5555
doi: 10.2340/00015555-0326

organized screening, the prevalence of high-risk HPV was approximately 7% (9). In that study the HPV prevalence was low in comparison with the prevalence in non-attending middle-aged women (10). The conclusion is that the prevalence of HPV infections decreases with age, and that it is generally higher in women who choose not to participate regularly in the screening.

The major problem with the present cytological screening is that approximately 20% of women invited for Pap-smear collection chose not to participate (15) and, in this category, the prevalence of cervical cancer is high, which is in agreement with a higher HPV prevalence among this group (1–6). The higher incidence of high-risk HPV infections among not screened or only sporadically screened women aged 55–60 years is also indicated by an increase in the incidence of CIN III and cervical cancer, which has been observed in the age group 55 years and above (15–16). This observation can also be explained by a decrease in the sensitivity of the cytological screening among older women (13).

Identification of chronic high-risk HPV infections among older non-attendees is of great importance, as these women are about to leave the organized screening programme as they reach 60 years of age, and HPV testing can guide the need for continued screening.

In conclusion, screening coverage for cervical cancer can be improved by offering non-attending women the opportunity to self-sample vaginal samples at home (7–8). A positive HPV test result is no guarantee that women with a previous history of non-attendance when invited for Pap smear sampling will respond to invitations for further investigation and treatment. Improved cervical cancer screening in women with a history of non-attendance is important, as non-attending women account for approximately 50% of all cases of cervical cancer, and non-attendance is the major limitation on effective screening for cervical cancer (4–6).

ACKNOWLEDGEMENTS

The study was supported by the Medical Faculty of Uppsala and by the Lion Cancer Foundation of Uppsala. The technical assistance of Ingrid Backlund is appreciated.

Conflict of interest: E. Wilander is a shareholder in Aprovix AB.

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