HPV prevalence among partners of women with cervical intraepithelial neoplasia


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Received 4 April 2003; received in revised form 21 August 2003; accepted 27 August 2003

Abstract

Objectives: The objective of this study was to find HPV DNA incidence in women with CIN and normal women and in their respective partners, as well as the relation between the virus groups found in women with CIN or normal women and in their respective partners. Methods: Partners of 30 women with CIN at several grades and of 60 normal women were prospectively assessed. In men, HPV search was performed by collecting samples through penile scraping for Hybrid Capture, followed by peniscopic evaluation and biopsy of acetowhite lesions. Results: The presence of HPV DNA in male partners does not necessarily implicate the presence of HPV or even CIN in their female partners. Conclusions: If these results are confirmed by other authors, obtaining a peniscopy, a penile biopsy, and a HPV DNA search in partners that present with no clinical lesions, but in couples with women having CIN, would not be warranted.

Keywords: Human papillomavirus; Hybrid capture II; Penile; Genital warts; CIN

1. Introduction

Genital infection with human papillomavirus (HPV) is a sexually transmitted disease that affects between 7 and 68% of a population, according to the population studied and the diagnostic methodology used [1]. The significantly increased incidence of genital tract HPV infections in many countries has been attributed to an early start of sexual activity, poor intimate hygiene, great numbers of sexual partners, and inadequate preventive measures [2].

In 1976, HPV-induced lesions in the female genital tract were shown to be associated with cervical intraepithelial neoplasm (CIN), carcinoma in situ, and invasive cervical intraepithelial carcinoma in 50–80% [3]. A cervical neoplasm is often found in women who started sexual activity early [4] and had multiple partners, being nearly absent in women with no sexual activity (nuns, virgins) [5]. In addition, the risk of developing cervical cancer is higher in men’s second wives when their first wives died from cervical cancer [6]. Partners of men having penile cancer showed cervical cancer incidence eight times higher, whereas part-
ners of women having cervical cancer show higher risk of developing penile cancer [7]. All these data suggest sexual activity should play an important role in the genesis of uterus and penile cancer [8]. Although the precise mechanism through which the virus is transmitted is still unknown, some authors believe the wet environment in female genitalia is associated with injury during sexual intercourse and provide virus inoculation [9].

In men, HPV can cause Bowenoid papulosis, which is a penile in situ carcinoma, [10] and several reports show a 30–50% association between HPV, particularly type 16, and penile carcinoma. [11] However, vertical HPV transmission is strongly suggested when one considers laryngeal papilloma occurrence in children below the age of 2 and from some case reports in which a neonate had genital condyloma at birth. These data prove HPV can affect individuals with no sexual activity [12].

All reports about HPV in men used only partners of women in pre-cancer stage or having cervical cancer. The present study included men with partners of women having cervical intraepithelial neoplasia (CIN) and women without CIN (normal women). The study addressed HPV DNA incidence among women with CIN and normal women and their respective partners, as well the relation between virus groups found in women with CIN and normal women and their respective partners.

2. Materials and methods

Thirty consecutive women with cervical intraepithelial neoplasm (CIN) at several grades as follows: 15 CIN 1, seven CIN 2, and eight CIN 3 and 60 consecutive women without CIN (normal women) that came to our hospital for cervical cancer screening (Pap smear), as well as their respective partners, were prospectively assessed. The study was performed between July 1999 and November 2001. A sexual behavior questionnaire was conducted and all couples included in this study were monogamous and had been having sexual relations for at least 2 years.

All 90 women underwent Pap smear and ectocervix and endocervix scraping to brush a HPV virus sample for hybrid capture (Digene’s Hybrid Capture® System—Digene Corporation, Gaithersburg, MD), followed by a colposcopy conducted by an experienced gynecologist (EAGP). The women were separated into two groups: women with normal colposcopy and normal transformation zone (NTZ), considered normal women in the present study, and those with colposcopic changes suggesting abnormal transformation zone (ATZ); the latter underwent cervical biopsy. The women with normal Pap smear and colposcopic changes related to an abnormal transformation zone (ATZ) having negative biopsy for cervical intraepithelial neoplasm were considered normal women, i.e. without CIN, although a non-specific chronic cervicitis was often found among them. The women with positive biopsy were stratified according to histologic grounds into three groups: CIN I, squamous cervical intraepithelial neoplasm grade I; CIN II, squamous cervical intraepithelial neoplasm grade II; and CIN III, squamous cervical intraepithelial neoplasm grade III [13].

HPV survey in men was performed through clinical history, physical examination and laboratory tests. The presence of verrucous lesions on physical examination on external genitalia, penile, pubic area, scrotal skin, and perianal area was searched with the naked eye. Specific tests included samples collected for HPV virus hybrid capture through brushing the penile shaft, the dorsal and ventral prebalanic area, the foreskin, and the urethral meatus to navicular fossa. Afterward, a penniscopy with external genitalia embrocation using gauze soaked in 5% acetic acid was performed, with search for acetowhite lesions though colposcopic observation using 10× magnification. Acetowhite lesions were biopsied and referred for hybrid capture. Women and men found with HPV virus through hybrid capture were divided into two groups: those bearing low oncogenic risk virus (types 6, 11, 42, 43, and 44) and those with high oncogenic risk virus (types 16, 18, 31, 33, 35, 39, 45, 52, 56, 58, 59 and 68) [14].

2.1. Statistical methods

The χ² and the Fisher tests were used to compare the two independent samples (women with
Table 1
HPV DNA incidence in women with CIN and in normal women and their respective partners

<table>
<thead>
<tr>
<th></th>
<th>Women with CIN</th>
<th>Normal women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HPV DNA n (%)</strong></td>
<td><strong>Partners’ HPV DNA n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Low risk</td>
<td></td>
</tr>
<tr>
<td>Women with CIN</td>
<td>23/30 (76%)</td>
<td>7/30 (23%)</td>
<td></td>
</tr>
<tr>
<td>Normal women</td>
<td>9/60 (15%)</td>
<td>7/60 (11%)</td>
<td></td>
</tr>
<tr>
<td><em>P</em></td>
<td>&lt;0.001</td>
<td>0.2580</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>32/90 (35%)</td>
<td>14/90 (15%)</td>
<td></td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasm.

In all cases, the rejection level for null hypothesis was always \( p \leq 0.05 \) [15].

3. Results

None of the male partners studied had evident clinical lesions.

HPV DNA incidence in women with CIN (low and high grade) and in normal women was 76% and 15%, respectively, a significant statistical difference (\( p < 0.001 \)). HPV DNA incidence in partners of women having CIN and in normal women’s partners was 23% and 11%, respectively, a non-significant difference (\( p = 0.2580 \)). In all women, HPV DNA incidence was 35%, and in all partners, it was 15% (Table 1).

The incidence of low-risk, high-risk, and both low- and high-risk HPV DNA was 20%, 73%, and 16%, respectively, for women with CIN and 1.6%, 13%, and 0%, respectively, for normal women, a significant statistical difference for the three risk groups (low-risk, \( p = 0.00504 \); high-risk, \( p < 0.00001 \); low- and high-risk, \( p < 0.01 \)). The incidence of low-risk and high-risk HPV DNA was 13% and 10%, respectively, in partners of women having CIN, a non-significant difference (\( p = 0.164 \)), and it was 5% and 8%, respectively, for normal women’s partners, a non-significant difference (\( p = 0.59 \)) (Table 2).

In that group with women having CIN, 23 couples had HPV DNA in both partners. However, only three couples (13%) had the same virus group HPV DNA. In the group with normal women, 16 couples had HPV DNA in both partners. However, only one couple (6%) had the same virus group HPV DNA. There was no significant statistical difference between these two groups (\( p = 0.1061 \)).

HPV DNA incidence for penile scraping with negative peniscopy was 12% in partners when women had CIN and 10% for normal women’s partners. This difference was not found statistically significant (\( p = 0.53 \)).

Positive peniscopy incidence for partners of women having CIN and for normal women’s partners was 17% and 15%, respectively, a non-significant difference (\( p = 0.918 \)). HPV DNA incidence for partners of women having CIN and for normal women’s partners with positive peniscopy was 60% for biopsy and 20% for scraping. These data were 22% for biopsy and 11% for scraping in normal women’s partners. These data did not show significant statistical difference (biopsy: \( p = 0.20 \)/scraping: \( p = 0.60 \)). HPV DNA incidence in penile biopsy and scraping was 80% for partners when women had CIN, and it was 22% for normal

Table 2
Virus group (low and high oncogenic risk) found in women with CIN, in normal women, and in their respective partners

<table>
<thead>
<tr>
<th></th>
<th>Women with CIN</th>
<th>Normal women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td>Low risk</td>
<td>High risk</td>
</tr>
<tr>
<td>( n ) (%)</td>
<td>6/30 (20%)</td>
<td>22/30 (73%)</td>
</tr>
<tr>
<td>( P )</td>
<td>0.00504</td>
<td><em>&lt;0.00001</em></td>
</tr>
<tr>
<td><strong>Partners</strong></td>
<td>Low risk</td>
<td>High risk</td>
</tr>
<tr>
<td>( n ) (%)</td>
<td>4/30 (13%)</td>
<td>3/30 (10%)</td>
</tr>
<tr>
<td>( P )</td>
<td>0.164</td>
<td>0.59</td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasm.
Table 3
Positive peniscopy and HPV DNA incidence in partners’ penile biopsy and scraping

<table>
<thead>
<tr>
<th>Partners</th>
<th>Peniscopy n (%)</th>
<th>Biopsy n (%)</th>
<th>Scraping n (%)</th>
<th>Biopsy and scraping n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women with CIN</td>
<td>5/30 (17%)</td>
<td>3/5 (60%)</td>
<td>1/5 (20%)</td>
<td>4/5 (80%)</td>
</tr>
<tr>
<td>Normal women</td>
<td>9/60 (15%)</td>
<td>2/9 (22%)</td>
<td>1/9 (11%)</td>
<td>2/9 (22%)</td>
</tr>
<tr>
<td>Total</td>
<td>14/90 (16%)</td>
<td>5/14 (36%)</td>
<td>2/14 (14%)</td>
<td>6/14 (43%)</td>
</tr>
</tbody>
</table>

*P* = 0.918

**CIN**, cervical intraepithelial neoplasm.

women’s partners. Although this difference has not been statistically significant (*P* = 0.06), it came close to the significance level of 0.05. HPV DNA was found in 43% of positive peniscopy cases (Table 3).

### 4. Discussion

Information obtained from cross-sectional studies about HPV prevalence in women using age groups allow the inference that HPV transmission occurs early in sexual life, in teenagers or around the age of 20. [16] Most times the infection is transient, and there will be no clinical evidence of disease, which can be suppressed or healed. [16] Other individuals will have less important lesions with spontaneous recovery; small numbers of individuals develop a persistent infection, seemingly occurring more often from agents considered high-risk HPV, which are associated with a high virus load. These would be the major determinant factors for developing preinvasive neoplastic lesions [16,17].

These HPV are mainly diagnosed when the patient is between 25 and 29 years old, whereas cervical cancer diagnosis is often made between the ages of 50 and 55 [18].

The contribution of male sexual behavior for the risk of women developing the disease has been poorly studied. In our present study, peniscopy was extensively performed in all partners when women had CIN at different grades as in normal women’s partners as well. We did not find any other similar study in literature. A colposcope was used for the peniscopy as it is a more sensitive device although it is well known for the accuracy of the method in penile lesions [19].

The partners role, which used to be greatly valorized a few years ago, has accounted for frequent recurring and persistent infection, now has reduced importance. In our study, we found 10% of normal women’s partners having HPV DNA. This fact shows the mere presence of HPV DNA in the partner does not implicate CIN in women. Treating subclinical lesions in the male partner does not reduce anal and vulvar condyloma recurrence rates, as well as cervical intraepithelial lesions [16]. Some observations suggest that a recurrence after effective treatment in a monogamous relationship is caused rather by latent infection reactivation present in a female partner than by a possible reinfection from the partner [17]. That decreases greatly the diagnosis and treatment importance in subclinical lesions present in the sexual partner, as well as condom use having the sole purpose of preventing any possible recontamination [17,18]. This study shows 76% of women with CIN have HPV DNA, most of it high-risk oncogenic type (73%), only 23% of partners bear the virus, most of it low-risk oncogenic type (13%). In the normal women group, 15% of women have HPV DNA vs. 11% for their partners. Surprisingly, the same virus group is found in only 13% couples whose women have CIN and in 6% couples whose women do not have CIN. These data allow to call in question the importance of transmission among couples and the routine indication for peniscopy, the purpose of which is identifying and treating subclinical lesions, thus preventing reinfection [20].
Reid et al. [21] concluded that tracking the lesions related to HPV to the partner is advantageous for the partner, not for the couple.

An acetic acid reaction is no specific indicator of HPV infection, consequently many false-positive tests can be found in low-risk populations [19–22]. Actually, in our study, in 57% of the cases of positive peniscopy, HPV DNA was not found.

When you find that only part of sexual partners has any acetowhite lesion detectable by peniscopy, 17% of partners in couples where women had CIN, but also in 15% of normal women, we call into question the real need of investigating them CIN, but also in 15% of normal women, we call into question the real need of investigating them HPV DNA was not found.

Male partner clinical evaluation is essential for treating clinical lesions and for making them aware of the sexually transmitted character of that infection, obviating the need of peniscopy [25,26].

5. Conclusions

The presence of HPV DNA in male partners does not implicate necessarily the presence of HPV or even CIN in their female partners. When both partners have HPV DNA, the incidence of the same virus group is small, but it is larger in the group of women having CIN. If these results are confirmed by other authors, obtaining a peniscopy, a penile biopsy, and a HPV DNA search in partners that present with no clinical lesions, but in couples with women having CIN, would not be warranted.

References