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Importance of Different Hpv Genotypes in the Development of Cervical Cancer

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Abstract

Fifteen human papillomavirus genotypes are implicated in the appearance of precancerous and cancerous lesions in uterine cervix. The two vaccines against cervical cancer currently available on the market contain only the two high-risk HPV genotypes (16 and 18) identified as the most prevalent. Other high-risk genotypes like papilloma virus 31, 51, 53 and 58 were isolated more frequently than HPV 18 in our study and in a review of the literature, in women with precancerous and cancerous lesions in uterine cervix. These results could explain the loss effectiveness of the vaccine in certain circumstances and support the need of continuing cervical cancer screening per current guidelines.

Keywords: Papillomavirus; Cervical cancer; Genotypes; Vaccine

Cervical cancer affects nearly 500,000 women worldwide each year and causes more than 270,000 deaths annually. In Spain, where incidence of and mortality from cervical cancer is low in the general population [1], the current data indicates that every year more than 2,000 women are diagnosed with cervical cancer and nearly 800 die from the disease [2].

There are more than 100 known HPV genotypes, and more than 40 of these types can infect the genital area of men and women. Some human papillomavirus (HPV) genotypes are implicated in the appearance of precancerous and cancerous lesions in various locations in the lower genital tract (vulva, vagina, and cervix) [3,4]. To date, 15 HPV genotypes (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82) have been implicated in the etiology of cervical cancer, and it is probable that 4 others (26, 53, 66 and 70) are also involved [5]. The two vaccines against cervical cancer currently available on the market, Cervarix® and Gardasil®, contain only the two high-risk HPV genotypes (16 and 18) identified as the most prevalent. Differences in the prevalence of HPV infection by other high-risk genotypes, however, have been found in different populations studied [6].

The main aim of this review is to analyze the prevalence of HPV genotypes 16 and 18 focusing on the efficacy of the actual vaccines.

In a recent large study of worldwide prevalence of different genotypes of HPV in invasive cervical cancer the most common HPV genotypes isolated were 16, 18, 31, 33, 35, 45, 52 and 58 [7]. These eight HPV genotypes were detected in 91% of cervical cancers. Although HPV 16 and 18 were the more frequent genotypes in all the regions, some discrepancies were noted in the ranking of the rest of genotypes. For example in Europe HPV 33 ranked third instead of HPV 45 or HPV 58 ranked fourth only in Asia. The conclusion of the study is that HPV 16, 18, 31, 33, 45, 52 and 58 should be given priority when the cross-protective effects of current vaccines are assessed, and for formulation of recommendations for the use of second-generation polyvalent HPV vaccines, given special attention to HPV genotypes 16,18 and 45 [7].

Since March 2003 in our department of the early diagnosis of cervical cancer at the Sant Joan de Déu Hospital in Esplugues, Barcelona, a HPV test is done to every patient who came with an abnormal cytological result. We use two very sensible techniques to identify HPV genotypes, "Line Probe" assay (LIPA; Innogenetics Laboratories®) and microarray-based molecular technique (Genomica®) both can detect 25 and 35 most prevalent HPV genotypes, respectively (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 68, 70, 71, 72, 73, 81, 82, 83, 84, 85, 89).

Now we have collected more than one thousand cases, all of them were followed for a minimum of 1 year, and with a colposcopy and cervical punch biopsy in case of abnormal colposcopy. We confirm in our published results [8,9] that HPV 16 is the most prevalent high-risk genotype isolated in our patients, but HPV 18 was very far from the second place observed in the study presented previously. One explanation of such a difference is that determination of HPV was done in the worldwide study in patients with cervical cancer and detected in biopsy specimens. In our study HPV determination was done through a sample taken by swab applied to the surface of the cervix in patients with abnormal cytology. If we analyse, in our study, only the group of patients with confirmed biopsy of intraepithelial neoplasia grade II or III (CIN II-III) we still observed that other high-risk genotypes were more frequent than HPV 18 (table 1) [9]. Our findings could explain why the two vaccines currently available loss effectiveness when we

HPV Genotype	CIN 2/3
16	43.9%
31	10.7%
51	9.4%
53	9.2%
58	8.5%
18	7.3%
33	6.7%
66	5.6%
52	4.4%

Table 1: Frequency of HPV genotypes isolated in women with grade 2 or 3 cervical intraepithelial neoplasia (CIN 2/3).

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analyse genotypes different from 16 and 18, despite the cross-protection observed against genotypes 31, 45 and 52.

In our current studies, we observed that in cervical cancer (although the number of cases is limited) HPV 16 and 18 were isolated in 48.6% and 8.1% respectively, but we found again other high risk genotypes 31, 52 and 45 with a high frequency of 10.8%, 8.1% and 8.1% respectively [10].

These findings are consistent with other studies in Spain and Italy [11-16], and the geographical variations.

We agree with the conclusion of Karen K Smith-McCune editorial [17], that vaccinated women must continue to undergo cervical cancer screening per current guidelines until we can analyze the long term results of actual vaccines.

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