Effect of HPV-vaccination on HPV-prevalence in Belgium

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Introduction:
Persistent infections with high-risk papillomaviruses (HR HPV) are the major risk for occurrence of cervical neoplasms. HPV plays an important role in two of the most common histologic types of cervical cancer: squamous cell (HPV 16: 50% of cases, 18%, 16%, 5%; 31, 45, 41%) and adenocarcinoma (HPV 16: 30% of cases, 18, 17%, 45, 5%, 31, 2%; 10% [1]. Since type 16 and 18 are responsible for 45% and 14% respectively, of the cervical cancer cases in Europe, more and more countries including Belgium set up HPV-vaccine programs, in order to eliminate type 16, 18 and a selected group of other HR HPV types, to reduce the occurrence of cervix cancer. Currently two vaccines are used for HPV, Cervarix® (GlaxoSmithKline Biologicals, Rensselaer, Belgium) and Gardasil® (Merck and co, White House Station, NJ, USA). Though, not all HR types are included in the vaccine and some of these non-vaccine types are quite common amongst sexual active women. Furthermore little is known about long-term effect and protection. Both, Gardasil® and Cervarix® cover HPV 16 and 18. Gardasil® also targets 6 and 11 (2).

Because of the impact on public health of HPV infection, the Flemish government provides since September 2010 vaccination against HPV, prototocols for girls in the first year secondary school (2). It is expected that application of the vaccine will cause a reduction of each HPV type comprised in the vaccine. A reduction of the HPV types comprised in the vaccine can be seen as a potential effect of vaccination. Therefore, this study aimed to assess the effect of vaccination 2 years after the onset of the program by profiling the HPV 16 and 18 states in Belgian women in 2012 (2). (Vaccination is recommended for women that never had sexual contact and thus are not infected with HPV)

Results:
Of the study population 10.8% and 10.5%, belonged to the age-groups >25 and 25-30 year, respectively, while 10.8% are member of the group 31-40 year old. 56% is older than 60 years and for 2% of the patients the age was not known. Although it is expected that prevalence of HPV 16 and HPV 18 would be reduced after starting the vaccination program, no significant reduce of the 3 groups could be established.

The prevalence of HPV 16 in the tested women was 4% with the highest prevalence in the group aged 25-35 years old, while HPV 18 was detected only in 1% of the cervical samples. Other HR HPV types counted for 13% and showed the highest prevalence.

An overview of the prevalence compared with figures from 2009, before introduction of the vaccination program, and distribution of HPV types according to age is shown in the table below.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>≤24*</th>
<th>25-30*</th>
<th>25-35*</th>
<th>31-40*</th>
<th>&gt;40*</th>
<th>Total (2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other HR HPV</td>
<td>28 (100%)</td>
<td>38 (22,4%)</td>
<td>80 (24,6%)</td>
<td>82 (25,5%)</td>
<td>42 (4,0%)</td>
<td>212 (10%)</td>
</tr>
<tr>
<td>HPV 16 pos</td>
<td>1 (0,5%)</td>
<td>3 (1,8%)</td>
<td>5 (1,5%)</td>
<td>3 (0,9%)</td>
<td>6 (1,2%)</td>
<td>19 (1,5%)</td>
</tr>
<tr>
<td>HPV 16 pos</td>
<td>3 (1,7%)</td>
<td>13 (7,6%)</td>
<td>24 (7,3%)</td>
<td>14 (4,4%)</td>
<td>15 (1,6%)</td>
<td>58 (3,7%)</td>
</tr>
<tr>
<td>All 14 HR types</td>
<td>32 (18,2%)</td>
<td>54 (31,7%)</td>
<td>109 (33,3%)</td>
<td>99 (30,7%)</td>
<td>63 (6,8%)</td>
<td>302 (15,2%)</td>
</tr>
</tbody>
</table>

*Prevalence of infection with HPV types by age group

Overall, the percentage of HPV 16 and HPV 18 infections slightly reduced since the onset of the vaccination program. On the contrary, the amount of women infected with other HR HPV increased compared with figures represented in Arbyn et al [3].

Methods:
Study population and study design: Cervical smears of 1625 women between 17 and 64 years and resident of Flanders (North Belgium) were screened during a 12-month period. All samples were tested by qPCR, using the Cobas® 4800 HPV test (Roche Diagnostics, Woerden, Belgium). The test targets a sequence of 200 nucleotides with the polymorphic L1 region of the HPV genome 14 high-risk HPV types identifying 3 subgroups, namely HPV 18, HPV 16 and others [1, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68] at clinically relevant detection levels.

Genomic organization of human papillomavirus type 16: L: Late genes, R: Early genes

Distribution of HPV types in Belgium in before introduction of the vaccination program (2)

The prevalence of HPV infection is shown for age groups 25 to 35 years, and for women aged 25 to 35 years old tested HR HPV positive compared with 18,2% in women younger than 25.

Discussion:
Although it is expected that vaccination will be associated with a reduction in prevalence of HPV infections, overall no significant decrease in HPV prevalence in the total study population is observed. While previous studies showed a decrease of HPV prevalence progressively with age, we found a peak of the HPV prevalence in the age-group 25-35 years. An explanation for this observation is that the vaccination program was only started 2 years ago and could only effect the prevalence in the youngest group.

It is plausible that vaccination, which resulted in a decrease in HPV infection in the patients aged younger than 24, is recommended for girls under 16 years old.

An additional explanation for the age shift from the group >25 years to 25-35 years may be that those women which were part of the 20-25 age group are now member of the age group 25-35 and vaccination is only supported for women are not infected with HPV.

Conclusion:
We noticed a short-term effect of HPV vaccination through a reduction in HPV prevalence in the age group >25 years. However, if a reduction in HPV infection will also occur in women older than 25 ye, as a result of vaccination, has to be evaluated on a longer term.

**Notes**