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Letter to Editor

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Feasibility of quadrivalent HPV vaccination as immunologic booster to prevent relapses in an Italian cohort of women treated for cervical intraepithelial Neoplasia (CIN)

Abstract

It is clear in Literature the effectiveness of HPV (Human Papilloma Virus) vaccine in women when administered before first sexual intercourse whit reduced benefit in those who are already HPV positive. What remains to be clarified is whether the HPV vaccines have any impact on HPV infections and any benefit in women who have been previously treated for pre-invasive cervical disease. HPV vaccine is currently indicated as preventive tool for cervical cancer, cervical and vulvar dysplasia and also genital warts. So it is possible to assume that it could play a preventive role against clinical relapses of these diseases. The aim of our study is evaluate the feasibility of HPV quadrivalent vaccine in an Italian cohort of women under 45 years of age whit previous history of CIN and evaluate the effectiveness of HPV vaccine as a tool also to prevent recurrent disease.

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Letter to editor

To date it's clear that the HPV (Human Papilloma Virus) vaccine is most effective in women when administered before first sexual intercourse with reduced benefit in those who are already HPV positive; for this reason World HPV vaccination programs are provided before the mean age of sexual debut.[1,2] HPV vaccines have been approved for safe administration from 9years of age up to 45. In particular, studies have focused on children and adolescents aged 9-15years for the increased activity of immune system at this age and for the higher probability that subjects result still naïve to the virus.[3] In Italy, the free offer of vaccination is directed to all teenagers from 12years of age and the right to free vaccination is up to the limit of 18years for the start of vaccination series. Vaccination before the start of sexual intercourse is particularly advantageous, because it induces effective protection before a possible virus infection, which is usually acquired soon after the onset of sexual activity, and because the immune response is greater in this age group than that observed in older women.[3] The unclear matter is whether the vaccine has any impact on existing HPV infections and any benefit in women who have been previously treated for pre-invasive cervical diseases.[1,2] Most of available clinical data have demonstrated an absence of benefit in women who are HPV positive for the types contained in the vaccine and that HPV vaccines have not a therapeutic efficacy.[1] However, preliminary studies applied in different realities from countries except Italy have shown that HPV vaccine can also induce protection in older women, and especially the administration of vaccine in patients previously treated for HPV-related disease can reduce the recurrence rate of disease.[4–6]

Recent studies have shown that the vaccine could be able to stimulate the immune response in women of older age and to protect against HPV although the probability of having already been infected is high.[4–6] Vaccination is now possible up to 45years as a personal preventive tool, at the expense of the patient, as indicated in the data-sheet of the quadrivalent vaccine currently available on the market. In fact, the vaccine is also safe at this age, is well tolerated and is able to determine an antibody response, as demonstrated in many studies.[7,8] From available data in literature and in our experience, it is estimated that recurrence rate of HPV-related disease is about 30-35% for genital warts and about 10-15% for pre-invasive disease three years after the initial surgery.[5] As mentioned above, Australia tried to expand vaccination coverage by administering HPV vaccine even in women who had already contracted the virus. Collected data regarding the efficacy of HPV vaccination in reducing the recurrence rate of HPV-related disease were very satisfactory. Results have shown that the vaccine is able to reduce the risk of recurrence of pre-neoplastic pathologies and genital warts in women already treated for HPV-related diseases.[4,5]

A retrospective analysis of two randomized trials (FUTURE I and II) showed an important reduction in recurrence of high grade cervical disease in vaccinated women who underwent an excisional treatment. However, it's important to recognize that this study could not directly evaluate vaccine's impact on women who had undergone treatment before vaccination, because all enrolled women had been vaccinated before the treatment.[1,4,5] Kang et al.,[5] tried to answer this specific question in their non-randomized trial of 737 women from 20 to 45 years of age who were treated for CIN 2/3 (cervical intraepithelial neoplasia) with LEEP (loop electrosurgical excision procedure). The risk of cervical disease recurrence resulted lower in women who received the vaccine after the excisional treatment, showing an efficacy of the HPV vaccine in preventing recurrent disease.[1,2,5] These studies suggest that the high antibody levels that typically follow vaccination could prevent new areas of HPV infection, caused by dissemination from existing sites of infection or from new virus exposure.[2] In conclusion, HPV vaccine is currently indicated as a preventive tool

not only for cervical cancer and cervical and vulvar dysplasia but also for genital warts. It's possible to assume that it could play a preventive role against clinical relapses of these diseases through two mechanisms: prevention of new infections and boosting of antibody type-specific immunity induced by previous infection.[4–6] The aim of our study was to evaluate the feasibility of the HPV quadrivalent vaccine in an Italian cohort of women under 45years of age with previous history of CIN. The exclusion criteria, evaluated at a follow-up visit 3months after treatment, were: positive HPV test for ≥2 HPV types included in the vaccine (6, 11, 16 or 18); positive cervical cytology or HPV-related disease evident at enrollment colposcopy; pregnancy state at enrollement. Women who did not meet the exclusion criteria at 3month follow-up visit after treatment were considered eligible for vaccination. From December 2014 to November 2015 we enrolled a total of 85 women (mean age 29, 3years; range 21-42) who had been treated for cervical disease at Colposcopy and Laser-surgery Center of Careggi University Hospital, in Florence. Among them, 40(47%) were treated with laser vaporization for CIN 1 and 45(53%) received a treatment of laser conization for a diagnosis of CIN 2/3 (42cases) or carcinoma in situ (3cases).

Laser procedures were performed by a Smart Xide2 (DEKA M.E.L.A. S.r.l., Italy) CO_2 laser, used in super-pulsed mode at 22Watt and connected to a Zeiss OPMI colposcope (Carl Zeiss, Oberkochen, Germany). The beam spot diameter ranged from 0.5 to 1mm, guided by a micromanipulator. Laser procedures were performed in day-surgery regimen under local anesthesia, in an outpatient setting. HPV DNA was found in 88%(75/85) of total cases. 39%(33/85) of patients were positive to HPV types 16 or 18; one patient resulted positive for HPV 6. At first follow-up visit 3months after treatment, 23(27%) patients were excluded from the study protocol because of the presence of one of the exclusion criteria: one of these women (4.3%) was positive for two HPV types (16 and 18), one (4,3%) was diagnosed as pregnant and 21(91.4%) of them had a positive pap smear after the treatment. Of positive Pap tests after treatment, 2(9.5%) were ASCH (atypical squamous cells - cannot exclude HSIL)-HSIL (high-grade squamous intraepithelial lesion), 9(42.9%) were LSIL (low-grade squamous intraepithelial lesion) and 10(47.6%) were ASCUS (atypical squamous cells of undetermined significance). 38% (8/21, 2 ASCUS and 6 LSIL) of positive Pap tests were related to low-risk (LR) HPV, 24%(5/21, 3 LSIL and 2 ASCH-HSIL) to high-risk (HR) HPV and 38% (8/21, ASCUS) to a negative HPV test.

Therefore, respecting initial hypothesis, 8 positive Pap tests (ASCUS) constituted the exclusion criterion although resulting HPV negative. These might be considered for a potential catch-up vaccination constituting false positive pap smears. Respecting the initial exclusion criteria, patients who resulted eligible for HPV vaccination were 62(73%) with an exclusion rate of 27%. Considering the potential catch-up vaccination of patients with positive Pap test and negative HPV test, 70patients (82.4%) would become eligible for vaccination with an exclusion rate of 17.6%. The overall recurrence rate was 8.2%(7cases). Of total cases of recurrence, 6(85.7%) were related to HR HPV and one (14.3%) to LR HPV. Among high grade CIN (CIN 2/3- carcinoma in situ), histologic relapse of disease was found only in one case (2.2%) and this can be considered a persistence of disease due to a failing treatment since it occurred in a positive margin conization. Among low grade CIN (CIN 1), 6(15%) histologic relapsing lesions were found. Among these, 5(83.3%) were related to HR HPV, while only one (16.7%) was related to LR HPV. Our data suggest that HPV quadrivalent vaccine is feasible in the majority (more than 80%) of Italian women under 45years of age previously treated for HPV-related diseases and may be used as a tool to prevent recurrent disease.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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None.

Conflict of interest

The author declares no conflict of interest.

References

1. Huh WK. HPV vaccination in women treated for CIN2/3: it's still all about prevention. *Gynecol Oncol*. 2013;130(2):255–256.
2. Brotherton JM, Wrede CD. Offering HPV vaccination to women treated for high-grade cervical intra-epithelial neoplasia: what do you need to know? *Aust N Z J Obstet Gynaecol*. 2014;54(4):393–394.
3. Joura EA, Kjaer SK, Wheeler CM, et al. HPV antibody levels and clinical efficacy following administration of prophylactic quadrivalent HPV vaccine. *Vaccine*. 2008;26(52):6844–6851.
4. Joura EA, Garland SM, Paavonen J, et al. Effect of the human papillomavirus (HPV) quadrivalent vaccine in a subgroup of women with cervical and vulvar disease: retrospective pooled analysis of trial data. *BMJ*. 2012;344:e1401.
5. Kang WD, Choi HS, Kim SM. Is vaccination with quadrivalent HPV vaccine after loop electrosurgical excision procedure effective in preventing recurrence in patients with high-grade cervical intraepithelial neoplasia (CIN2-3)? *Gynecol Oncol*. 2013;130(2):264–268.
6. Olsson SE, Kjaer SK, Sigurdsson K, et al. Evaluation of quadrivalent HPV 6/11/16/18 vaccine efficacy against cervical and anogenital disease in subjects with serological evidence of prior vaccine type HPV infection. *Hum Vaccin*. 2009;5(10):696–704.
7. Ault KA. Effect of prophylactic human papillomavirus L1 virus-like-particle vaccine on risk of cervical intraepithelial neoplasia grade 2, grade 3, and adenocarcinoma in situ: a combined analysis of four randomised clinical trials. *Lancet*. 2007;369(9576):1861–1868.
8. Sangar VC, Ghongane B, Mathur G. Develpoment of Human Papillomavirus (HPV) Vaccines: a Review of Literature and Clinical Update. *Rev Recent Clin Trials*. 2016;11(4):284–289.