Editorial

Prophylactic vaccines for patients with human papillomavirus diseases (HPV)

Vacinação profilática para pacientes com doenças causadas pelo papilomavírus humano (HPV)

The presence of types 16 and 18 in 70-76% of carcinomas of the uterine cervix, and in 63-95% of anogenital tumours, underscores the need for prevention for this disease. Among the tools available for this task, prophylactic HPV vaccines appear to be the most promising. Added to this, a meta-analysis suggested that 80% of anal carcinomas could be prevented by vaccination against these serotypes.

Currently, two vaccines are available: bivalent (bHPV) and quadrivalent (qHPV), whose prospective studies showed efficacy against specific types of HPV and sufficient evidence for their use. bHPV immunizes against HPV types 16 and 18, and qHPV, besides these, immunizes against HPV types 6 and 11, that are responsible for 90% of warty lesions in this area. Both vaccines use virus-like particles (VLP) to generate neutralizing antibodies against L1, the major protein of the viral capsid.

The primary goal of these vaccines is to prevent anogenital carcinoma. The assessment of their effectiveness is based on the possibility of preventing persistent infection and intraepithelial neoplasia, the precursor lesion of carcinoma. Phase I and II clinical trials have shown the safety of these vaccines and their ability to produce very high levels of antibodies, which are low or nonexistent after natural infection. Phase II and III trials confirm these features, showing almost 100% efficacy to prevent infection and intraepithelial neoplasia associated with oncogenic types immunized by the vaccines. Other studies have observed cross-protection against infection by other oncogenic HPV types, such as 31 and 45. Regarding the time of immunization conferred by these types, it is possible to state that the clinical trial with longer follow-up of qHPV amounts currently to 10 years, and serologic tests demonstrate that the antibody level remains high.

The Agência Nacional de Vigilância Sanitária (ANVISA) (National Health Surveillance Agency) has released vaccine application both for women and men aged 9 to 26 years old, provided they have not yet started their sexual life or had contact with the HPV types involved in immunization. qHPV vaccine is given intramuscularly in three doses, with the second and third doses applied two and six months after the first. In the case of bHPV the scheme is the same, but with the second and third doses applied one and six months after the initial dose.

At moment, we still do not know if there will be a need for a booster or a new vaccination. It is important to note that HPV vaccination is no substitute for routine screening for cervical cancer, as is currently recommended. Although condoms prevent contamination in the vast majority of cases, there is no effective way to prevention, except by complete sexual abstinence. The treatment of warts and cytological abnormalities consists of the removal of affected cells and in a follow-up for detection of recurrences.

Although the government agencies indicate that the vaccination should be applied between the ages of 9 and 26, qHPV was effective in women between 24 and 45 years who were not already infected with HPV types. Other clinical trials have shown qHPV usefulness in women under 55 years old. The rate of new infections declines with age and typically does not progress to high-grade cervical intraepithelial neoplasia (CIN) in older women. Because of this, the potential benefit of prophylactic vaccination at older ages is low.

Definitely, the vaccines do not treat pre-existing infections or HPV-induced lesions. Aiming that, therapeutic vaccines are being developed, in order to stimulate cellular immunity against infected cells. Prophylactic vaccines can only prevent infections by HPV types against which immunized people were not contaminated, even if they have previous or current history of HPV-induced lesion.

However, it was observed among those who participated in clinical trials for qHPV and who progressed with anogenital HPV infection that the best results in the follow-up were noted among those who received all three doses of the vaccine, compared with those in placebo group. In a group of 17,622 women aged 15 to 26 years, 587 of the vaccinated group and

---

*Study conducted by the Proctology Technical Team, Instituto de Infectologia Emilio Ribas, São Paulo.*
763 who had received placebo had their clinical and subclinical HPV cervical lesions resected. Recurrences occurred in 6.6% and 12.2%, respectively.

These data have statistical difference, and the authors concluded that the vaccine caused a reduction of relapses and of high-grade CIN.\textsuperscript{15}

In another study of 18,174 women, of whom 15% had evidence of infection by immunized types, it was found that the vaccine appeared to prevent reinfection and reactivation of the disease for these viral types.\textsuperscript{16} A report involving 602 men aged 16 to 26 who received qHPV revealed that the rates of appearance of infection by HPV types were 17.5% and 13%, whereas the reduction of high-grade intraepithelial anal neoplasia (IAN) occurred in 54.2% and 74.9%, and the reduction of relapses was 59.4% and 94.9%, respectively, among those who received placebo and those who were vaccinated.\textsuperscript{17}

Yet in another study, 36 men aged 16 to 26 who received qHPV and 89 in the placebo group developed genital warts. After treatment, persistent infection was better controlled in those of the vaccinated group, 47.8% and 27.1%, respectively.\textsuperscript{18} However, in a study of bHPV that included 419 women in the vaccine group and 440 in the placebo group and who had evidence of prior infection with types 16 and 18, the evaluation of the results of this subgroup suggested that bHPV neither improved nor reduced the progression of high-grade CINs, and that the cytological screening should be recommended.\textsuperscript{19}

These data suggest that qHPV may have influenced the best evolution of carriers of HPV types. And some researchers suggest the use of qHPV as adjunctive therapy in patients with recurring lesions\textsuperscript{20} and high-grade CIN.\textsuperscript{21} It is known that the HPV present in warts and in subclinical lesions continuously infects those with this infection. When penetrating the epithelium, the viral particles reach and invade the basal layer cells of the host, which may perpetuate the infection. Among those vaccinated, the presence of viral antibodies would prevent this action, interrupting self-contamination.

However, the established disease should be treated, because as long as there is cell contamination the infection will persist and new lesions may appear.

These results bring great encouragement to people with diseases caused by HPV and to those responsible for their treatment. However, further studies with larger numbers of cases and longer evolution times are needed to confirm this observation, before the vaccination against this virus can be definitely authorized by the competent agencies.

REFERENCES


Sidney Roberto Nadal¹*, Luis Roberto Manzione Nadal¹*²

¹ Instituto de Infectologia Emilio Ribas, São Paulo, SP, Brazil
² Serviço de Cirurgia Geral, Hospital do Servidor Público Estadual do Estado de São Paulo, São Paulo, SP, Brazil

*Corresponding author.
E-mail: srnaladoterra.com.br (S. R. Nadal).

© 2014 Sociedade Brasileira de Coloproctologia. Published by Elsevier Editora Ltda.
Este é um artigo Open Access sob a licença de CC BY-NC-ND
http://dx.doi.org/10.1016/j.jcol.2014.02.001