



VACCINE OF THE HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER: A REFLECTION

A VACINA DO PAPILOMAVÍRUS HUMANO E O CÂNCER DO COLO DO ÚTERO: UMA REFLEXÃO LA VACUNA DEL PAPILOMAVIRUS HUMANO Y EL CÁNCER DEL CUELLO UTERINO: UNA REFLEXIÓN

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ABSTRACT

Objective: to promote reflection on the vaccine against human papillomavirus related to poor adherence. **Method:** a descriptive study, reflective analysis type, from official documents of the Ministry of Health of Brazil, international reference nursing book (with adaptation to the Brazilian reality), national and international articles, both found in the VHL and MEDLINE. **Results:** treated HPV vaccine types available in Brazil, recommended age for administration, current immunization schedule. The reality of poor adherence was discussed from reflections related to gender issues and post-vaccination adverse effects. **Conclusion:** it is thought that the low uptake of the HPV vaccine is related to the population's right to choose and that these choices are mediated by multiple factors. **Descriptors:** Nursing; Uterine Cervical Neoplasms; Papillomaviridae; Woman's Health; Public Health.

RESUMO

Objetivo: promover reflexões sobre a vacina contra o papilomavírus humano relacionadas à baixa adesão. **Método:** estudo descritivo, tipo análise reflexiva, a partir de documentos oficiais do Ministério da Saúde do Brasil, livro de enfermagem de referência internacional (com adaptação à realidade brasileira), artigos nacionais e internacionais, ambos encontrados na BVS e MEDLINE. **Resultados:** tratou-se da vacina contra o HPV, tipos disponíveis no Brasil, idade preconizada para administração, calendário vacinal atual. A realidade da baixa adesão foi discutida a partir de reflexões relacionadas às questões de gênero e dos efeitos adversos pós-vacinais. **Conclusão:** cabe pensar que a baixa adesão à vacina contra o HPV está relacionada ao direito de escolha da população e que estas escolhas são mediadas por múltiplos fatores. **Descritores:** Enfermagem; Neoplasias do Colo do Útero; Papillomaviridae; Saúde da Mulher; Saúde Pública.

RESUMEN

Objetivo: promover la reflexión sobre la vacuna del virus del papiloma humano relacionados con baja adhesión. **Método:** estudio descriptivo, de tipo análisis reflexivo, a partir de documentos oficiales del Ministerio de salud de Brasil, libro de enfermería de referencia internacional de (con adaptación a la realidad brasileña), artículos nacionales e internacionales, ambos encontrados en la BVS y MEDLINE. **Resultados:** se trató de la vacuna contra el VPH, tipos disponibles en Brasil, edad recomendada para la administración, calendario de la vacuna actual. Se discutió la realidad de la baja adhesión de reflexiones relacionadas con las cuestiones de género y los efectos adversos posteriores a la vacuna. **Conclusión:** es importante pensar que la baja adhesión a la vacuna contra el VPH se relaciona con el derecho de escoja de la población y que estas opciones están mediadas por múltiples factores. **Descriptores:** Enfermería; Neoplasias del Cuello Uterino; Papillomaviridae; Salud de la Mujer; Salud Pública.

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INTRODUCTION

Cervical cancer is characterized as a public health problem, particularly in the poorest regions in the world, although there are programs for early detection. Human papillomavirus (HPV), the human papillomavirus or HPV virus del human papillomavirus is associated with cervical cancer and is considered a sexually transmitted infection (STI) with the highest prevalence in the world, being one of the main responsible for the deaths of Women in Brazil. In the world, it is the second most common type, leading to death of 230,000 women per year and is most prevalent in developing countries, compared to developed ones.¹⁻²

In Brazil, it is also listed as the second most common, second only to breast cancer, with an estimated 18,430 cases in 2011. The risk is estimated at 18 cases per 100,000 women. In cervical cancer, genital warts and precancerous lesions of the male and female anogenital tract, they are also associated with HPV. About 32 million new cases of genital warts are described in the world annually and Brazil reaches 1.9 million cases.²⁻³

Brazil, despite being a developing country, understood the need to carry out actions of screening and prevention that can reduce the incidence of cervical cancer, receiving support from the Ministry of Health (MOH), in line with the World Health Organization (WHO). The health care of direction allows to qualify the screening process, helping to identify errors that could compromise the investigation process of the disease, as cervical cancer requires scientific knowledge about the characteristics of the scenario presented, enabling the identification faults that can interfere with the efficacy of actions.⁴

Among the strategies developed by MH, we can mention the Care Policy of Integral Health of Women (CPIHW) established in 2004 (and reaffirmed in 2009, 2011), establishing some goals, such as promoting to improve the health of women and legally constituted.⁵ Guaranteeing rights are principles and guidelines that guide Action Plans for strategies focused on the problems.

Another effort of MH directed to the control of cervical cancer was the creation of Ordinance No. 310 of February 10, 2010, which resolved to establish a working group in order to evaluate the National Program of Cervical Cancer Control, delegating to the National Cancer Institute (INCA) the technical

and administrative coordination necessary for the development of group activities.⁶

INCA, given the provisions of the ordinance, formulates an executive summary entitled 'Action Plan for reducing the incidence and mortality from cancer of the cervix', with the aim of analyzing the National Program for Control of Cervical Cancer and formulate proposals to improve its actions.⁶

The proposals made by the group were systematized in five areas: 1 - strengthening of organized screening in primary care and the decentralized management of the screening program; 2 - quality assurance of cervical cancer screening; 3 - Appropriate treatment guarantee of precursor lesions; 4 - intensified control actions of cervical cancer in the North and the axis 5 - evaluation of alternative actions to control cervical cancer. In the Plan of Action the HPV vaccine is mentioned as a new technology for prevention and control of cervical cancer and what is the cancer reduction proposal in 30-40 years.⁶

Cervical cancer is characterized by the uncontrolled replication of the organ lining epithelium, compromising the underlying tissue (stroma) and can invade adjacent structures and organs or distance. There are two main categories of invasive carcinomas of the cervix, depending on the origin of the affected epithelium: squamous cell carcinoma, the most common type, affecting the squamous epithelium (represents about 80% of cases), and adenocarcinoma, rarest type and that affects the glandular epithelium.⁷

It is known that among the main risk factors for the development of cervical cancer are: smoking; physical agents; low intake of vitamins; multiple partners; early onset of sexual activity; prolonged hormone therapy; multiparity; genital infections of repetition and low socioeconomic conditions. Moreover, one of the most important discoveries in etiologic cancer research for the past 30 years was to demonstrate the relationship between HPV and cervical cancer. At least 13 types of HPV are considered oncogenic. Among the high-risk oncogenic HPV types 16:18 are present in 70% of cases of cervical cancer.^{1,8}

HPV is a DNA virus of the small family Papillomaviridae. Infectious particles with HPV genome may be found in the nucleus of cells infected women with normal uterine cervix. The precursor lesions and cervical cancer occur at the time that the genome of HPV joins the chromosome of the host cell, which is observed in some women with low grade lesions, the majority of women with high-grade lesions or cervical carcinoma.⁹

The relationship between HPV and cervical cancer spurred the development of molecular biology techniques, culminating in innovative strategies in primary and secondary prevention of cervical cancer, based on the introduction of the first prophylactic vaccines against the virus and testing HPV detection, respectively.¹⁰

Approximately 100 types of HPV have been found and had their genome mapped. Of these, it is known that the most significant subtypes are: low-risk genotypes - HPV-6 and HPV-11 (cause of genital warts and low-grade benign); high risk - HPV-16, HPV-18, HPV-31, HPV-33 and HPV-45. HPV-16 and HPV-18 are most commonly associated with cervical cancer, with 75% incidence of cases of this type of cancer.^{1,7,11}

Studies confirm the presence of HPV in almost 100% of the cases of these cancers. Most of these infections are asymptomatic and transient, becoming completely undetectable within one to two years, but persistent infection favors the development of precancerous lesions and subsequently the neoplasia.¹²

Another important point is that treatment for HPV infection will not necessarily eradicate the virus, however, the quadrivalent vaccine, which is discussed below, is also able to protect against warts (HPV-6 and HPV-11). It is able to prevent genital warts in boys / men and cervical cancer in girls.¹³ This is a delicate point, because when it comes to prevention of HPV, one must reflect on the prevention of other STDs, especially HIV / AIDS and hepatitis, with condom use.

Therefore, by presenting this relevant framework for public health, in addition to actions already put in place, the MH makes use of another strategy: prevention through immunization, since the primary prevention of cervical cancer is related to decreased risk of contagion by HPV.⁷

In Brazil two prophylactic HPV vaccines were approved, the bivalent GlaxoSmithKline® (2009) and the quadrivalent Merck Sharp® and Dohme® (2006). The latter has been provided by the MH in vaccination posts since 2014, initially for girls from 11 to 13 years. In 2015 extending the girls from 9 to 13 years and 14-26 years if they are carriers of the human immunodeficiency virus (HIV).^{2,14}

On January 10, 2016 the General Coordination of Immunization Program (CGPNI) established changes in vaccination schedule through the Briefing Note No. 149/2015 in order to adopt a single vaccination schedule, standardizing actions. With respect to HPV vaccine scheme to be

adopted is composed of two doses with a 0 and 6 month schedule, the administration of the third dose is not necessary.¹⁵

Some factors were listed to justify the rejection of the population in relation to the vaccine against HPV, including the fact that a routine vaccine will not be considered, or is not inserted in the calendar since the first consultations in the health unit. The low frequency of adolescents to health services emerges as a first barrier to joining the vaccine.¹⁶

Considering the context above, it is presented as objective of this article: to promote reflections on the vaccine against human papillomavirus (HPV) related to poor adherence.

It is expected, with the presentation of this reflection, a broadening and strengthening of the discussion related to the vaccine against HPV, also offering a compilation of information on the subject, available in specialized literature, national and international. A theoretical, reflective and informative inclination about the difficulties related to the ministerial campaign, with respect to adherence to the strategy. That Article screen can contribute also as a teaching tool for undergraduate education and graduate as informative, bibliographical study and the development of new research initiatives on the subject in question.

METHOD

Descriptive study, type of reflective analysis, from official documents of the Ministry of Health of Brazil, international reference nursing book (with adaptation to the Brazilian reality), national and international articles, both found in the VHL and MEDLINE. The tessitura of reflection happened, at first, from addressing the prophylactic HPV vaccine reflecting its low membership based on gender and adverse effects expected. Finally, to find articles that have dealt with serious adverse effects, fulfilled the authors show these findings for reflection and complete it for the purposes of this paper, but certain that there is still a lot to think about the HPV vaccine. Thus, the articles were analyzed allowing the grouping of similar themes and presented in analytical categories.

RESULTSAND DISCUSSION

◆About prophylactic HPV vaccine

Vaccines represent the intervention strategy with the best cost-effective to date applied in public health. The history of

vaccines and their application in the prevention of infectious diseases accumulate over 200 years of dedication and work.¹¹

Since the eighteenth century immunization is one of the most important public health interventions, for its wide acceptance and positive assessment by much of the population, including the impact on the reduction or elimination of many diseases, which for many years have claimed lives and left side effects. Vaccines and surveillance were responsible for the elimination of smallpox, the interruption of transmission of poliomyelitis and measles.¹⁷

More studies have emerged to prove the relationship of HPV as the primary causative agent of cervical cancer. It is associated with virtually all cases observed and, therefore, are highly relevant epidemiologically.^{11,18}

Annually, about 5-15% of women without previously HPV virus are infected with any type of high-risk HPV and about 25% of the incidence of infection is concentrated in the age group of 15-19 years.¹⁹ For this reason, recommendation is that the vaccine be performed before starting sexual life.

Studies with young people before and after starting sexual life, to determine the onset of infection, have shown that infection occurs most often in the first sexual intercourse. In one study it was found that the incidence of infection was 20% in the first 12 months, declining to 14% and 9% in consecutive years, showing that infection occurs most often in early sexual life.¹⁹

The quadrivalent vaccine is recommended for men and women 9-26 years of age, while the bivalent should be used in women of 10 to 25 years, noting that the main indication focuses on girls who have not started sexual life, have greater efficacy in non exposed.²⁰

After the onset of sexual life, the chances of contact with HPV increases and there is no scientific evidence of significant benefit in vaccinating women already exposed to HPV. The mechanism of action of the vaccine is based on generating antibodies which block the HPV cell entry, ie, studies show that women infected with one or more types present in the vaccine before immunization may benefit only partially gaining immunity only against those viruses which they have had no contact. The women with absent infection to the four viruses in the vaccine before immunization benefit from it.¹¹

Considering the efficacy of the vaccine in reducing cervical cancer as well as the indication for it to be performed before starting sexual life, MH include vaccination for

boys in 2017, becoming the seventh country in the world to insert the vaccine in the national program and the first of Latin America.^{2,21}

It advocated by a period of 10 years to assess the immunization against HPV in terms of efficacy, safety and shelf life of immunization. However, partial results suggest there is no need for booster shot for now, although the duration of immunization is still unknown.²

♦The reality of poor adherence to the vaccine

After a year of introduction of the vaccine against HPV in the national immunization schedule were observed some difficulties, among them the great resistance of the population due to fear of side effects from the adolescents and their parents, as well as unreliable information disseminated through social networks.¹⁶

In consultation with the National Program of Immunization Information System (SI-PNI-2015) the data presented for the periods of introduction of HPV vaccine bring this reality very significantly: in 2014, the first phase of the campaign, the country hit a coverage of 101.33%; comparing the second phase, only 60.15% returned to vaccine stations/schools to give continuity to the vaccine scheme.²²

This result is even more remarkable when we evaluated the first half of 2015, during which there was an expansion of the age range for immunobiological administration, as only 58.85% of the target population were vaccinated with a reduction of 23.71% who returned to continue the scheme.²²

Some factors were listed to justify the rejection of the population in relation to HPV vaccine, including the fact that a routine vaccine will not be considered, or is not inserted in the calendar since the first consultation in child care at the facility. The low frequency of adolescents to health services emerges as a first barrier to joining the vaccine.¹⁶

We should also point out that the broad access to communication networks and mass dissemination of information, often erroneous, increase resistance related to the vaccine. Disclosure of post-vaccination adverse events (AEFI) assumes a prominent role in the media, making the perception of the population about the benefits of vaccination more difficult.¹⁶ At the same time, one must recognize that knowledge of adverse effects of vaccines by population it is a positive aspect when viewed from the angle that people are able to get information and

make decisions, even without judgment is agreed or not.

Among the HPV vaccine resistance factors, we cannot fail to include in this understanding, a peculiarity in the vaccination procedure. It should be administered with the child/teenager sitting and after administration it should remain under observation for a few minutes before being released from the unit. This event does not occur with the application of other biopharmaceuticals and the waiting time for observing reactions generates fear, and not always, the health team gets time to perform the appropriate host to this population.¹⁶⁻⁷

Although the vaccine has already been studied, as well as any other drug, can present unexpected events, being necessary to have professional training for the correct handling of situations, notification and investigation of all events that may occur.¹⁶⁻⁷ However, with respect to the HPV vaccine cannot ignore other points of reflection, showing that it is far from exhausting its possibilities of discussion.

♦ Starting points and reflection on cultural issues and studies on the adverse effects

The HPV vaccines are designed to provide a useful and objective approach in the fight against cervical cancer, as well as other vaccines that have already been used and which have a satisfactory outcome, where the positive effects outweigh the effects related to adverse reactions that may occur.^{17,23}

Discuss the weaknesses of previously pointed scenario allows us to reflect on some aspects that need to be addressed when the subject is the HPV vaccine. As a vaccine that protects against a sexually transmitted virus, some parents associate the vaccine as a stimulus for sexuality, what they see as precocity. Address issues of sexuality, sexual initiation, especially in girls, and prevention of STIs is bumping into taboos of Brazilian society, especially when linked to sensitive religious issues, who oppose the administration of vaccines.¹⁶

In more recent studies, performed on the sexuality of women received either no vaccine against HPV, it was observed that the vaccine is not associated with increased sexual activity. The results show that the average age of first sexual intercourse has not changed substantially between different groups.^{15,24}

We must consider, in effect, that any strategy related to the prevention of STIs, whatever it may be (in this case against HPV), will find gender barriers in relation to female

sexuality. Obstacles that need to be thought of and addressed from a responsible sex education, which considers that women's sexuality is not subject to repression and male controls, is the family, society or the state. The liability related to the prevention of STIs means discussing the strategies available, and consequently of free choice, in order to avoid STIs and diseases that can generate, regardless of the concepts, taboos, myths, dogmas, and other aspects that are intertwined in delicate (and expensive) theme which is the beginning of the sex of women, ie, the aforesaid 'loss of female virginity.

About AEFV, the MHexpects between them, local reactions (pain at the injection site, edema and moderate erythema) and systemic reactions (headache, fever 38 ° C or more, syncope and hypersensitivity reactions). Because it is a new vaccine, with a large target audience, active surveillance of AEFI composed of identification, registration and proper management is essential to assess the safety of products.¹⁵ It is clear, however, that because it is a voluntary act, it is not always possible to estimate the frequency of reactions, to establish a causal relationship to vaccines.²³

In this scenario it is necessary that the professionals involved in this strategy are prepared to act in various situations that may arise and especially to carry out the reporting of AEFI not serious and serious, for further investigation, confirmation or disposal of cases.¹⁷ Only analyzing the real data existing is that it becomes possible to evaluate the cost-effectiveness of a particular treatment,² however, this is an issue that needs further attention, since there have been studies showing serious adverse events related to the administration of the vaccine. A non screen article object discusses or refutes the ministerial strategies, but it fulfills shed light on these studies. They are starting points. After all, for a newly inserted vaccine in the immunization schedule, adverse events that may arise in the long term must have particular observation.

A survey portrayed a syndrome called inflammatory syndrome induced by adjuvants (ISIA). It is a syndrome that occurs after stimulation of the immune system by agents with adjuvant characteristics and signals that post-vaccination autoimmune phenomena have been cited as possible causes, including the quadrivalent HPV vaccine. This same study correlates the primary ovarian insufficiency (POI stands for primary ovarian insufficiency) as a result of ISIA, bringing to discuss three cases where three young women received

three doses of quadrivalent HPV vaccine and developed reactions commonly expected, but also the POI. They also described the POI as a complex etiology clinical condition in which about 20 to 30% of cases are associated with autoimmune mechanisms.²³

A more recent study describes the POI as a multifactorial condition and is currently being associated with the quadrivalent HPV vaccine due to the increase of reported cases after vaccination. In this research, the authors refer to aluminum a metal present in the composition of quadrivalent considered an adjuvant (a substance that acts to accelerate, prolong or enhance an antigen-specific immune response), and can cause toxic effects on various organs and systems. Also cite the inflammatory syndrome induced by adjuvants as a post-vaccination effect and POI inducer. It concludes, however, that the reported cases of POI cannot be considered solely as an adverse effect of HPV vaccination and that future studies should bring greater elucidations about the effects of adjuvants.²⁵

A review of case-control adverse effects reported in an American database of quadrivalent vaccines, studied 48,852 events in a time frame of 2006 to 2014. The authors conclude that their study provides epidemiological evidence supporting the significant relationship between the administration of the vaccine quadrivalent HPV4 and the onset of autoimmune serious adverse events. Among the specific outcomes examined include: gastroenteritis; rheumatoid arthritis; thrombocytopenia; systemic lupus erythematosus; vasculitis; alopecia; demyelinating conditions of the nervous system (multiple sclerosis, optic neuritis, transverse myelitis); irritable bowel syndrome. With respect to ovarian damage, these include: atrophy; cysts; abscesses; bankruptcy; necrosis; among others.²⁶

The development of a vaccine to control the cancer associated with HPV brings interesting perspectives in relation to the real benefit in terms of disease control. Its availability generates an expectation of a future reduction of new cases of the disease. But in fact, the greatest impact of the vaccine formulations were economical, produced by pharmaceutical companies. The high cost of the vaccine has provided significant profits to manufacturers, arousing the interest of many laboratories. And the main goal - reducing the incidence of cervical cancer - remains a doubt for the people served are the least likely to feel the base symptoms of the disease.¹¹

CONCLUSION

The considerations that enclose this article more direct to starting points, than to conclusions. Cervical cancer is a major public health problem, the intensification of strategies for early detection is necessary, and the preventive measures to control HPV infection. Regardless of the discussion related the vaccine against HPV remains urgent encouraging the use of condoms during sexual intercourse, as well as cervical cancer screening by Pap smear uterus with appropriate samples.

Think of low adherence to ministerial campaign related to the vaccine against HPV as a strategy against cervical cancer, demands that professionals and managers understanding that may be related to the free choice to vaccinate or not the girls / adolescents. Choices that may be mediated by a mistaken understanding of female sexuality, as surrounded by taboos, but also by expectations related to adverse vaccine events. Whether by unenlightened fears regarding waiting on the drive after administration, with the aim to observe possible effects (and seen by the population). Be responsible for these girls / teens who have access to research that has dealt with the serious adverse events related to the administration of the vaccine in the long term, and who choose not to vaccinate. Complies warn that these serious developments need to be the subject of research and academic debates more often.

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Submission: 2016/09/16

Accepted: 2016/10/11

Publishing: 2017/01/01

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