Libyan International Medical University

Faculty of Basic Medical Science

Human Papillomavirus (HPV) Vaccines

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Abstract:
The aim of this report is to discuss the Pathogenicity of human papilloma virus and the use of vaccines against it.

Introduction:

human papillomavirus which are a group of more than 200 related viruses. More than 40 types can be easily spread through direct sexual contact, other types of virus are responsible for non-genital warts, which are not sexually transmitted. HPV is the most common viral infection of the reproductive tract and is the cause of a range of conditions in both men and women, including precancerous lesions that may progress to cancer. Although the majority of HPV infections do not cause symptoms and resolve spontaneously, persistent infection with HPV may result in disease. In women, persistent infection with specific HPV types (most frequently HPV-16 and HPV-18) may lead to precancerous lesions which, if untreated, may progress to cervical cancer.(1) HPV infection is also associated with oropharyngeal and anogenital cancers and other conditions in men and women. HPV. HPV vaccination can reduce the risk of infection by the HPV types targeted by the vaccine. The Food and Drug Administration (FDA) has approved three vaccines to prevent HPV infection: Gardasil®, Gardasil® 9, and Cervarix®. These vaccines provide strong protection against new HPV infections, but they are not effective at treating established HPV infections or disease caused by HPV.(2)

Discussion:

Human papillomavirus:

Pathogen Human papillomaviruses belong to the family Papillomaviridae. The virions are non-enveloped and contain a double-stranded DNA genome. The genetic material is enclosed by an icosahedral capsid composed of major and minor structural proteins, L1 and L2 respectively. These viruses are highly tissue-specific and infect both cutaneous and mucosal epithelium. Based on the genomic sequence of L1, the gene encoding the principal capsid protein, over 200 HPV types have been identified and characterized.22, 23 Papillomavirus isolates are traditionally described as ‘types’. HPV types may be classified in many ways, including the locations on the body that each virus tends to infect (cutaneous or mucosal types) and by their potential to induce cancer, i.e. high-risk vs low-risk types. The International Agency for Research on Cancer currently defines 12 high-risk HPV types which are associated with cancers in humans (types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59) and additional types for which there is limited evidence of carcinogenicity (types 68 and 73).(1)

The link between HPV and cancer:

Cancer often takes years, even decades, to develop after a person gets HPV. The types of HPV that can cause genital warts are not the same as the types of HPV that can cause cancers.There is no way to know which people who have HPV will develop cancer or other health problems. People with weak immune systems (including individuals with HIV/AIDS) may be less able to fight off HPV and more likely to develop health problems from it. HPV cancers include cancer of the cervix, vulva, vagina, penis, or anus. HPV infection can also cause cancer in the back of the throat, including the base of the tongue and tonsils (called oropharyngeal cancer).HPV cancer usually does not have symptoms until it is quite advanced, very serious and hard to treat. For this reason, it is important for women to get regular screening for cervical cancer. Cervical cancer screening can find early signs of disease so that problems can be treated early, before they ever turn into cancer.Because there is not screening for the other cancers caused by HPV, it is very important to prevent infection with HPV vaccination. (1)

Vaccines:

The U.S. Food and Drug Administration approved Gardasil (HPV4), a Merck vaccine for four types of HPV, in 2006. The FDA approved another vaccine, Cervarix (HPV2) from GlaxoSmithKline, which protects against two high-risk types of HPV, in 2009. A nine-valent vaccine (HPV9, Gardasil 9) was approved in 2014. All HPV vaccines use just a protein from the shell of certain HPV types: they contain no viral RNA or DNA and so cannot cause disease. The HPV vaccines have been shown to be effective in preventing precancerous cervical changes and precancerous anal changes in women and men caused by high-risk cancer-causing HPV strains. HPV4 and HPV9 additionally offer protection from several low-risk, wart-causing HPV types.[2]

Mechanism of action:

The HPV vaccines are based on hollow virus-like particles (VLPs) assembled from recombinant HPV coat proteins. The virus possesses circular double stranded DNA and a viral shell that is composed of 72 capsomeres. Every subunit of the virus is composed of two proteins molecules, L1 and L2. The reason why this virus has the capability to affect the skin and the mucous layers is due to its structure. The primary structures expressed in these areas are E1 and E2, these proteins are responsible for the replication of the virus.[2] E1 is a highly conserved protein in the virus, E1 is in charge of the production of viral copies is also involved in every step of replication process.[2)] The second component of this process is E2 ensures that non-specific interaction occurs while interacting with E1[3]. As a result of these proteins working together it assures that numerous copies are made within the host cell. The structure of the virus is critical because this influences the infection affinity of the virus. Knowing the structure of the virus allowed for the development of an efficient vaccine, such as Gardasil and Cervarix. The vaccines target the two high-risk HPVs, types 16 and 18 that cause the most cervical cancers. Gardasil's proteins are synthesized by the yeast Saccharomyces cerevisiae. Its protein makeup allows it to target four types of HPV. Gardasil contains inactive L1 proteins from four different HPV strains: 6, 11, 16, and 18. Each vaccine dose contains 225 µg of aluminum, 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 µg of polysorbate 80, 35 µg of sodium borate, and water. The combination of ingredients totals 0.5 mL.(Together, these two HPV types currently cause about 70 percent of all cervical cancer[4]Gardasil also targets HPV types 6 and 11, which together currently cause about 90 percent of all cases of genital warts[4]Gardasil and Cervarix are designed to elicit virus-neutralizing antibody responses that prevent initial infection with the HPV types represented in the vaccine. The vaccines have been shown to offer 100 percent protection against the development of cervical pre-cancers and genital warts caused by the HPV types in the vaccine, with few or no side effects. The protective effects of the vaccine are expected to last a minimum of 4.5 years after the initial vaccination. The vaccines have been shown to offer 100 percent protection against the development of cervical pre-cancers and genital warts caused by the HPV types in the vaccine, with few or no side effects. The protective effects of the vaccine are expected to last a minimum of 4.5 years after the initial vaccination[5]

Timing of Vaccination:

The Advisory Committee on Immunization Practices and the College recommend routine HPV vaccination for girls and boys at the target age of 11–12 years (but it may be given from the age of 9 years) as part of the adolescent immunization platform in order to help reduce the incidence of anogenital cancer and genital warts associated with HPV infection. Bivalent, quadrivalent, and 9-valent vaccines are approved for females aged 9–26 years and quadrivalent and 9-valent vaccines are approved for males aged 9–26 years. Recently, the bivalent vaccine has been withdrawn from the U.S. market. The 9-valent vaccine[6], which covers five additional cancer-related HPV serotypes will soon replace the quadrivalent vaccine. Studies show that two doses of HPV vaccine given 6 months apart in individuals aged 9–14 years resulted in antibody titers equal

to those in individuals aged 15–26 years who were given three doses. Hence, only two doses, 6–12 months apart, are needed if HPV vaccination is initiated before 15 years of age in boys and girls[7]. The 6-month interval between these two doses is critical for ensuring adequate immune titers and durability of protection. If the interval between the two doses is less than 5 months, a third dose is recommended. In addition to the ability to use two doses instead of three doses, earlier vaccination also is preferred because HPV vaccines are most effective when given before prior exposure and infection with HPV, which coincide with the onset of sexual activity. Statistics show that one in three ninth graders and two in three 12th graders have engaged in sexual intercourse [8]. In Sweden, vaccine effectiveness in preventing genital warts was 93% among girls vaccinated between 10 years and 13 years of age compared with 48% and 21% if vaccinated at ages 20–22 years and 23–26 years, respectively [9].All of these findings underscore the importance of vaccination at the target age (11–12 years), which is before the onset of potential exposure in the vast majority.

Disadvantages:

Probably the most important "con" for the HPV vaccine is potential side effects. That said, side effects aren't common.Most people receive the HPV vaccine without having any serious side effects. Mild to moderate side effects occur more often but are still uncommon. Mild to moderate side effects can include: pain or swelling at the injection site, slight fever, headache, fatigue, muscle pain, joint pain, fainting, nausea, vomiting, pain in the abdomen, diarrhea. One other con of the HPV vaccines is that they're limited in what they do:The vaccines don't prevent all HPV-related cancers, only some. Therefore, it's vital that women still get a routine Pap test to check for any signs of cervical cancer.The vaccines don't protect against other sexually transmitted infections (STIs) or treat existing HPV-related illnesses or infections .[10]

Studies:

WHO position paper, May 2017 on vaccines against diseases caused by human papillomaviruses (HPV). It focuses primarily on the prevention of cervical cancer, but also considers the broader spectrum of cancers and other diseases preventable by HPV vaccination. It incorporates recent developments concerning HPV vaccines, and provides guidance on the choice of vaccine.[11] A study has been done by NATIONAL CENTER INSTITUTE(NCI)2012 found that these vaccines provide nearly 100% protection against persistent cervical infections with HPV types 16 and 18 and the cervical cell changes that these persistent infections can cause. Gardasil 9 is as effective as Gardasil for the prevention of diseases caused by the four shared HPV types (6, 11, 16, and 18). The trials that led to approval of Gardasil 9 found it to be 97% effective in preventing cervical, vulvar, and vaginal disease caused by the five additional HPV types (31, 33, 45, 52, and 58) that it targets.[12] Another study by The American College of Obstetricians and Gynecologists (committee opinion) June 2017.

Conclusion:

Human papillomavirus (HPV) is associated with anogenital cancer (including cervical, vaginal, vulvar, penile, and anal), oropharyngeal cancer, and genital warts. The HPV vaccination significantly reduces the incidence of anogenital cancer and genital warts.

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