The Libyan International Medical University

Faculty of Basic Medical Science

The Use of Vaccine Against Human Papilloma Virus

Fatima Wanis El-Kerghali

2206

Supervised by: Khadija Mansur

Assisted by: Sara El-Mgherhi

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Abstract

Our immune system usually controls HPV infection but sometimes HPV infection are not successfully controlled by our immune system especially people with weak immune system may be less able to fight HPV and more likely to develop health problems. When high risk HPV persist for many years it can lead to cell changes that if untreated may get worse over time and become cancer. Early detection of precancerous lesions can prevent progression to cancer. Three different vaccines, which vary in the number of HPV types they contain and target. The all prophylactic vaccines, designed to prevent initial HPV infection and subsequent HPV-associated lesions.

Introduction

Pathogen human papillomavirus belongs to the family papovaviridae. The viron are non-enveloped, 55 nm in diameter and contain a double strand DNA genome. The genetic material is enclosed by an icosahedral capsid composed of 72 capsomers, which contain at least two capsid proteins. HPV is a group of more than 200 related virus. More than 30 types can be easily spread through sexual contact. Other types of virus are responsible for non genital warts which are not sexually transmitted. HPV is the most common cause of range of conditions in both men and women including precancerous lesion that may progress to cancer. The majority of HPV infection do not cause symptoms and resolve spontaneously but long lasting infection with specific HPV type (most frequently HPV-16 and HPV-18) may lead to precancerous lesion which if untreated may progress to cervical cancer. It is also associated with oropharyngeal , anogenital cancers and other conditions in both men and women.(1)

Cervical cancer is the most common cancer in women worldwide and may contribute up to 25% of all female cancer which is a cancer that is starts in the cervix the lower narrow part of the uterus. It happens when the body's cervical cells multiply very fast and grow out of control . The incidence of cervical cancer mortality rate have declined in recent years, largely due to the widespread implementation of screening programs.cervical cancer . screening can find early signs of disease so that problem can be treated early before they ever turn into cancer including papanicolaou stained smear (PAP TEST) which is the primary method for detection of HPV , this method was named for pathologist George papanicolaou. The pap smear is screening tool that looks for changes in cells of the transformation zone of the cervix and for definitive diagnosis for HPV can not be made without HPV DNA Test which is a lab test in which cells are scraped from the cervix to look for DNA of HPV.HPV vaccination can reduce the risk of infection by the HPV targeted by the vaccine.(2)

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 HPV infection . but they are not effective at treatingestablished HPV infections or disease caused by HPV .

Aim

The aim of this report is to discuss the the relationship between HPV and cervical cancer and the use of vaccine against it.

Methods And Material

In the first study HPV DNA prevalence was analyzed in cervicovaginal specimens from females aged 14 to 34 years in NHANES in the prevaccine era (2003–2006) and 4 years of the vaccine era (2009–2012) according to age group. Prevalence of quadrivalent HPV vaccine (4vHPV) types (HPV-6, -11, -16, and -18) and other HPV type categories were compared between eras.(6)

In the second study Two large, randomized trials to compare quadrivalent HPV vaccine with placebo among more than 17,000 females aged 15 to 26 .(7)

Results

Resulting from the first study between the prevacccine and vaccine eras, 4vHPV type prevalence declined from 11.5% to 4.3% among females aged 14 to 19 years and from 18.5% to 12.1% among females aged 20 to 24 years.(6)

Resulting from the second study After three years, the efficacy of quadrivalent HPV vaccine for preventing CIN2 or more severe disease due to HPV vaccine types was 97 to 100 % among HPV-naïve populations and 44 % among the overall population.(7)

Disscusion

THE LINK BETWEEN HPV AND CERVICAL CANCER

The link between genital HPV infections and cervical cancer was first demonstrated by Harold zur Hausen, a German virologist in the early 1980s . Since then, the link between HPV and cervical squamous cell carcinoma has become well established. The magnitude of the association between HPV and cervical squamous cell carcinoma is higher than that for the association between smoking and lung cancer .

Studies suggest that whether a woman will develop cervical cancer depends on a differernt of additional factors including, conditions that impair cell-mediated immunity such as human immunodeficiency virus disease increase the risk of progression of HPV. Long-term use of oral contraceptives is a significant risk factor for high-grade cervical disease(2) .High-risk strains of HPV are now well established as the causative agents responsible for cervical dysplasia and cervical cancer The American Cancer Society estimated 11,150 new cases of invasive cervical cancer in the United States in 2007 and about 3670 cervical cancer deaths that same year. Although cervical cancer as a cause of death in the United States has drastically declined over the last 50 years due to Papanicolaou testing, it is still the second leading cause of cancer-related death in women worldwide.HPV has also been implicated as etiology for other less common genital cancers, including vulvar, vaginal, and anal carcinomas. Low-risk strains of HPV are responsible for genital warts. Although not a life-threatening condition, genital warts are a major cause of morbidity as well as psychosocial distress and embarrassment for many patient. Most HPV infections are acquired within the first years of sexual activity, as demonstrated by a study of 603 college students, in which it was found that approximately 40% of HPV infections are acquired within 2 years of the first sexual experience.The risk of infection is proportionately related to number of sexual partner .It is very important to prevent infection with HPV vaccination.(3)

Prevention by HPV vaccine

The U.S. Food and Drug Administration approved Gardasil (HPV4), a Merck vaccine for four types of HPV (6, 11, 16, 18), in 2006. The FDA approved another vaccine, Cervarix (HPV2) from GlaxoSmithKline, which protects against two high-risk types of HPV(16 , 18), in 2009.

A nine-valent vaccine (HPV9, Gardasil 9) protect against infection with HPV types (6, 11, 16, 18, 31, 33, 45, 52, 58) was approved in 2014. the vaccines exhibited excellent safety and immunogenicity profiles(3).

Both Cervarix® and Gardasil® are non-infectious subunit vaccines composed primarily of virus-like particles (VLPs). The VLPs spontaneously self-assemble from 360 copies of L1, the major structural protein of the virion . Although referred to as "virus-like", the VLPs are completely non-infectious and non-oncogenic, since they do not contain the viral DNA genome or specific viral genes required for these activities.

VLP vaccines are based on the concept of forming a structure that sufficiently resembles the outer shell of an authentic HPV virion such that antibodies that are induced to it react with and inactivate the authentic virus. Cervarix® and Gardasil® differ in several aspects, including valency, dose, production system, and adjuvant .Cervarix® is a bivalent vaccine, containing the VLPs of HPV16 and 18, the two types that cause 70% of cervical cancer worldwide, and even greater proportions of HPV-associated vulvar, vaginal, penile, anal, and oropharyngeal cancers .Gardasil® targets the same two cancer-causing types, but in addition contains VLPs of HPV6 and 11, which cause approximately 90% of external genital warts in both men and women .

The VLPs for Cervarix® are produced in insect cells infected with L1 recombinant insect virus vectors. Gardasil®'s VLPs are produced in baker's yeast (*Saccharomyces cerevisiae*) expressing L1. Each VLP type is produced and purified separately and the different types are mixed during final formulation . Delivery of both vaccines is via three intramuscular injections in the deltoid area over a 6-month period. Like other protein subunit vaccines, the two HPV VLP vaccines are formulated with adjuvants to increase their immunogenicity. Gardasil® contains a simple aluminum salts adjuvant (aluminum hydroxyphosphate sulfate), whereas Cervarix® contains a more complex adjuvant system, designated AS04, consisting of monophosphoryl lipid A (MPL) and an aluminum salt (aluminum phosphate).

MPL is a detoxified form of bacterial lipopolysaccharide and is a toll-like receptor (TLR)-4 agonist. TLRs are an evolutionarily conserved class of host sensors of microbial constituents that activate innate and adaptive immune responses to invading microbe.(4)

HPV Vaccine Schedule and Dosing

A 2-dose schedule is recommended for people who get the first dose before their 15th birthday (9-14 years old). In a 2-dose series, the second dose should be given 6–12 months after the first dose (0, 6–12 month schedule). The minimum interval is 5 months between the first and second dose. If the vaccination schedule is interrupted, vaccine doses do not need to be repeated. Immunogenicity studies have shown that 2 doses of HPV vaccine given to 9–14 year-olds at least 6 months apart provided as good protection as 3 doses given to older adolescents or young adults.

A 3-dose schedule is recommended for people who get the first dose on or after their 15th birthday, and for people with certain immunocompromising conditions .In a 3-dose series, the second dose should be given 1–2 months after the first dose, and the third dose should be given 6 months after the first dose (0, 1–2, 6 month schedule).The minimum intervals are 4 weeks between the first and second dose, 12 weeks between the second and third doses, and 5 months between the first and third doses.A history of genital warts, a positive HPV test result, or abnormal cervical, vaginal, vulvar, or anal cytology all indicate a prior HPV infection but not necessarily with the HPV types included in the vaccines. Vaccination is still recommended in individuals within the recommended age range who have evidence of prior HPV infection, as it can still provide protection against infection with HPV vaccine types not already acquired.(5)

Efficacy of vaccines

The efficacy of HPV vaccination is greatest when given to HPV-naive women.

Given the high correlation between HPV infection and onset of sexual contact, the ideal time to give the vaccine is prior to initiation of sexual activity**.** In clinical trials, the most common side effects were injection site pain, swelling, and erythema. The only absolute contraindication to Gardasil is hypersensitivity to the active substances or to any of the inactive ingredients in the vaccine, and individuals who develop symptoms suggestive of hypersensitivity after receiving a dose of the vaccine should not receive further doses. The vaccine is not recommended for use in pregnant women, and caution should be used in women who are breastfeeding. Effectiveness does not appear to be altered by use of oral contraceptives but The immunologic response may be decreased in patients receiving immunosuppressive therapies.(3)

In a phase 3 efficacy trials 4HPV vaccine had high efficacy for preventing of genital warts among 4055 males aged 16 to 26 years. Efficacy for preventing of HPV6, 11 ,16 and 18 related genital wart was 89.3% . no efficacy was observed among males who were infected with HPV type .(8)

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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