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HPV Vaccines

HPV Aşıları

Mehmet Yasin Yüksel[1]* Funda Ekimci Deniz[1]

1.Ağrı İbrahim Çeçen University, Faculty of Medicine, Department of Family Medicine

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*Corresponding Author:
Mehmet Yasin Yüksel
Ağrı İbrahim Çeçen University Faculty of Medicine 04100 Ağrı/Türkiye
E-mail: myyuksel@agri.edu.tr
ORCID: 0000-0001-6067-1138

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HPV

Human papillomavirus (HPV) is a non-enveloped, double-stranded DNA virus belonging to the papillomavirus family (1). HPV is a highly prevalent virus that can be transmitted through fissures in the skin and mucous membranes, during sexual intercourse, from contaminated surfaces, and from mother to newborn during childbirth. The virus primarily targets basal epithelial layer cells, initiating infection in these cells, and various genotypes of HPV influence their differentiation and proliferation (2,3). There are over 200 known genotypes of HPV worldwide, approximately 40 of which infect mucosal surfaces in the anogenital region. Among these, certain genotypes, particularly HPV-16 and HPV-18, are recognized as high-risk types with the potential to cause cervical cancer. In contrast, low-risk genotypes typically result in the formation of genital warts (1,4).

Epidemiology

HPV infection is the most common sexually transmitted infection among individuals with an active sexual life, both women and men (1). It is estimated that at least 20 million people in the United States are infected, with approximately 6 million new cases reported each year. More than 90% of cervical cancer cases are attributed to HPV (5). It is estimated that about 80% of sexually active women and men will be infected with HPV at least once during their lifetime (6). Most HPV infections are asymptomatic and are typically cleared spontaneously by the immune system; however, high-risk HPV types (particularly HPV-16 and HPV-18) can lead to abnormal cellular changes that may progress to cancer as a result of persistent infections. Ninety-nine percent of cervical cancer cases have been associated with these high-risk HPV types (7). According to the World Health Organization (WHO), approximately 660,000 new cervical cancer cases were diagnosed globally in 2022, with about 350,000 deaths from the disease (8).

Risk Factors for HPV Infection

Sexual intercourse is the main route of transmission of HPV infection (9). Several factors significantly contribute to the risk of HPV infection, including having multiple sexual partners, initiating sexual activity at an early age, and having an uncircumcised male partner. The presence of multiple sexual partners increases the likelihood of risky encounters and facilitates the spread of HPV. The increased risk associated with uncircumcised male partners is attributed to the larger mucosal surface area on the uncircumcised penis, which raised the likelihood of infection (10). Low socioeconomic status, inadequate nutrition, and poor hygiene conditions can weaken individuals' immune systems, making them more susceptible to HPV infection. In particular, in low-income areas, a lack of access to medical resources leads to more frequent and severe occurrences of these infections. Other infections, such as HIV, genital herpes, and chlamydia, increase the likelihood of HPV developing into a persistent infection that can lead to cancer (8,10). Immunosuppressive medications weaken the body's immune response to infections, thereby increasing the risk of all types of infections. HIV infection suppresses the immune system, making HIV-positive women six times more likely to develop cervical cancer than people without HIV(11). Additionally, the use of tobacco products is a significant factor that increases the risk of progression of HPV infection. Smoking can cause DNA damage in cervical mucosal cells, thereby accelerating cancer development. Furthermore, the use of tobacco products may suppress the immune response, contributing to the persistence of HPV in the body (1,10).

Conditions Associated with HPV Infection

More than 90% of individuals exposed to HPV infection will have the virus cleared by the immune system within two years; however, approximately 10% may experience a persistent infection (9). If untreated, a persistent infection, particularly with high-risk HPV types (HPV-16, HPV-18), can lead to cervical cancer within 15 to 20 years. In individuals with compromised immune systems (such as those with HIV infection or those undergoing immunosuppressive therapy), this progression may occur more rapidly, potentially resulting in cancer within 5 to 10 years. Besides cervical cancer, these high-risk HPV types can also cause cancers of the anus, vulva, vagina, penis, and oropharynx (10,12). The mechanism by which HPV induces cancer in these areas is associated with the integration of viral DNA into the host

cell genome and the activation of cellular oncogenes, leading to genetic mutations (13). Low-risk HPV types (HPV-6, HPV-11) cause genital warts but do not increase the risk of cancer (5,7).

Types and Features of HPV Vaccines

There are three approved and available vaccines against HPV: 2v HPV (bivalent), 4v HPV (quadrivalent), and 9v HPV (nonavalent) (5). All vaccines protect against HPV types 16 and 18. The quadrivalent vaccine is effective against HPV types 6 and 11, which cause anogenital warts, while the nonavalent vaccine protects against HPV types 6, 11, 31, 33, 45, 52, and 58 (9). The quadrivalent vaccine was first licensed in 2006, followed by the bivalent vaccine in 2007 and the nonavalent vaccine in 2014 (5). All vaccines are licensed for use in males and females aged 9 and older, with an upper age limit of 26 for the bivalent and quadrivalent vaccines, and 45 for the nonavalent vaccine (7).

The bivalent HPV vaccine primarily protects against HPV types 16 and 18, which are high-risk types responsible for more than 70% of cervical cancer cases. The bivalent vaccine is recommended for use in women aged 9 to 26, but the most effective period for significantly lowering the risk of cervical cancer is before the onset of sexual activity, ideally around ages 11-12. Although the bivalent vaccine is more commonly administered to females, it can also be used in males to prevent HPV carriage, thereby reducing the incidence of cervical cancer and promoting herd immunity (5). For individuals aged 9-14, a two-dose schedule is recommended, with the second dose given 6-12 months after the first. For those aged 15 and older, a three-dose schedule is implemented: the second dose is administered 1-2 months after the first, and the third dose is given 6 months after the first (14). The efficacy rate has been reported at 98% in clinical trials. The bivalent vaccine is highly effective in preventing cervical precancerous lesions associated with the targeted HPV types. Protection is maximized when vaccinated individuals complete their vaccination program before initiating sexual activity (7).

The quadrivalent HPV vaccine provides protection against HPV types 6, 11, 16, and 18. This vaccine offers protection against high-risk HPV types (HPV-16 and HPV-18), thus preventing cancers of the cervix, vagina, vulva, penis, and anus, as well as protecting against low-risk HPV types (HPV-6 and HPV-11) to prevent the development of anogenital warts. It is approved for both males and females, with particular recommendations for individuals aged 9-26. Vaccination for females is aimed at protecting against cervical cancer, while for males, it is recommended to reduce the risk of anogenital warts and HPV-related cancers (7). In individuals aged 9-14, a two-dose schedule is recommended with the second dose given 6-12 months after the first. For individuals aged 15 and older, a three-dose schedule is advised: the second dose is administered 1-2 months after the first, and the third dose is given 6 months after the first (14). The quadrivalent vaccine has a very high efficacy rate, providing nearly 100% protection against HPV-16 and HPV-18. It is also highly effective in preventing genital warts (7).

The nonavalent HPV vaccine protects against a broader range of HPV types. In addition to HPV-6, HPV-11, HPV-16, and HPV-18, it is effective against HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58. This extensive coverage is particularly important for the prevention of both cervical and other anogenital cancers and genital warts. The nonavalent vaccine is available for both males and females, with the primary target population being individuals aged 9-45. Vaccination for women is recommended to prevent cervical, vulvar, vaginal, and anal cancers, while for men, it protects against genital warts as well as anal and oropharyngeal cancers (7). For individuals aged 9-14, a two-dose schedule is recommended with the second dose given 6-12 months after the first. For those aged 15 and older, a three-dose schedule is recommended: the second dose is administered 1-2 months after the first, and the third dose is given 6 months after the first (14). The nonavalent vaccine provides high protection against HPV-related diseases. According to clinical studies, its efficacy against HPV-16 and HPV-18 exceeds 99% and it also offers high protection against additional HPV types (7). This extensive coverage helps protect against cervical cancer as well as cancers of the vulva, vagina, penis, anus, oropharynx, and genital warts.

All three vaccines are generally well tolerated, with the most common side effects including pain at the injection site, headache, and muscle pain. Serious side effects are rare, and extensive research has shown that the vaccines are safe (7).

Overview of HPV and HPV Vaccination in Türkiye

Cervical cancer screenings are conducted in Türkiye through Family Health Centers (FHC) and Cancer Early Detection, Screening and Education Centers (KETEM) (9). According to the 2022 WHO (World Health Organization) report, HPV vaccines are included in the national vaccination schedule in 125 countries worldwide (15). However, HPV vaccines are not currently included in Türkiye's national vaccination schedule.

Conclusion

It is important to protect against HPV infection, which is prevalent in the community and causes numerous diseases, including cervical cancer. Vaccination against HPV is recommended before the onset of an active sexual life. Including the HPV vaccine in the national vaccination schedule will be beneficial for public health in the long term.

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