Human papillomavirus vaccine

Introduction

Human papillomavirus (HPV) can cause a variety of infections in humans. Infections that give rise to the most concern are the sexually transmitted types, which can lead to genital cancers and anogenital warts. In this article, we discuss HPV and HPV vaccines.

Human papillomavirus types

More than 100 HPV types have been identified. Of these, approximately 60 infect the cutaneous epithelium, causing common skin warts. The remaining 40 types infect the mucosal and genital epithelium. These 40 types can then be classified as low risk (non-cancer causing) or high risk (carcinogenic). Infection with low-risk types can cause benign cervical cell abnormalities, genital warts and respiratory papillomas (growths in the airways). The low-risk types 6 and 11 are responsible for 90% of anogenital warts and almost all cases of respiratory papillomatosis.

High-risk types, including 16, 18 and others, act as carcinogens in the development of cervical cancer and other anogenital cancers, such as cancer of the vulva, vagina, penis and anus. Infection with a high-risk HPV type is necessary for the development of cervical cancer. Types 16 and 18 cause approximately 70% of all cases of invasive cervical cancer worldwide. Cervical cancer is the most common cancer in women in South Africa and the second most common cancer in women worldwide.

HPV is the most common sexually transmitted disease worldwide. Infection is most likely to occur within the first 10 years of a person becoming sexually active. Usually, individuals who are infected with HPV have no signs or symptoms.

HPV is transmitted by direct, skin-to-skin contact with an infected person. HPV infection of the respiratory tract mucosa is thought to occur during passage of the baby through an infected birth canal. Generally, transmission of mucosal HPV infection occurs during sexual intercourse, but also during oral sex, anal sex or any other contact involving the genital area, e.g. hand to genital contact. The risk of contracting HPV increases with the number of sexual partners.

Although the incidence of infection is high, infections resolve spontaneously in the majority of individuals and are cleared from the body within two years. HPV infection does not induce an effective immune response. Only approximately half of all infected women with HPV develop detectable antibodies, but these antibodies do not necessarily protect against subsequent infection with the same HPV type.

Individuals who do not clear the HPV become persistently infected. Persistent infection may lead to the development of cervical cancer precursor lesions. These lesions are often detected during routine Papanicolaou (Pap) smears. If left untreated, these cervical cancer precursor lesions can progress to cervical cancer. Usually, it takes approximately 20 years from initial infection with HPV for cervical cancer to develop. Therefore, it is very difficult to determine the source of the infection.

Prevention of HPV infection

Abstaining from sexual activity (any genital contact) is the best way to prevent genital HPV infection. A monogamous relationship with an uninfected partner is likely to prevent genital HPV infections. Correctly and persistently used condoms can reduce HPV transmission. Vaccines are now available to protect against certain HPV types.

HPV vaccines

Two HPV vaccines are available, Gardasil® and Cervarix®. Both are for prophylactic use only and do not clear existing HPV infection or treat HPV-related disease. The intention should be to administer both vaccines before the onset of sexual activity and the first exposure to HPV infection as this is when the individual would derive the most benefit from the vaccine. Vaccination of an individual who is already sexually active should still be considered. A history of an abnormal Pap smear, genital warts or HPV infection
is not a contraindication to the HPV vaccine. The HPV vaccine does not have a therapeutic effect on an existing infection. If an individual has already been infected with one or more of the HPV types that are present in the vaccine, the HPV vaccine will not protect against these infections. However, it will still protect against HPV infections that are caused by other types that are present in the vaccine.

Both vaccines are highly immunogenic. Nearly all individuals develop an antibody response one month after completing the three-dose series. It is not yet known how long the protective efficacy of these vaccines lasts. However, to date, it has been maintained for the duration of the observation periods: 9.4 years for Cervarix® and five years for Gardasil®.

It should be noted that individuals who are immuno-suppressed, such as HIV infected patients, may not exhibit as good an immune response to the HPV vaccine as expected.

It is recommended that the same vaccine is used for the entire series. If it is not known which vaccine was used to start the series, or if the initial vaccine is not available when the next dose is required, either vaccine should be used to complete the series in order to provide protection against HPV 16 and 18. A series of less than three doses of the vaccine, to provide protection against HPV 6 and 11, may not provide the required defense against genital warts.

**Gardasil®**

Gardasil® is a quadrivalent vaccine that contains virus-like particles for HPV types 6, 11, 16 and 18. It is indicated for the prevention of cervical, vaginal and vulval pre-cancers and cancers, as well anogenital warts that are caused by HPV types 6, 11, 16 and 18 in females aged 9-26 years. In South Africa, Gardasil® is also registered for use in boys aged 9-17 years for the prevention of anogenital warts.

Internationally, Gardasil® is used up to the age of 26 years in men and 45 years in women. Gardasil® is given as a series of three intramuscular injections at 0, 2 and 6 months. It is delivered into the deltoid muscle or in the higher anterolateral area of the thigh.

**Cervarix®**

Cervarix® is the bivalent vaccine that contains virus-like particles for HPV types 16 and 18. It is indicated for the prevention of cervical pre-cancers and cancer caused by HPV types 16 and 18 in females from nine years of age. Cervarix® is not indicated for use in males. Cervarix® is given as a series of three intramuscular injections at 0, 1 and 6 months, delivered into the deltoid muscle.

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### Contraindication and precautions to HPV

The HPV vaccine is contraindicated in individuals who have had a severe allergic reaction to a previous dose of the vaccine or components thereof. The vaccine should be deferred in individuals with a moderate to severe acute illness until they have recovered. The HPV vaccines are given by intramuscular administration. Therefore, they should be used with caution in individuals with thrombocytopaenia or any coagulation disorders. This is because bleeding may occur.

### Pregnancy and lactation

The HPV vaccine should not be administered to pregnant women, owing to lack of safety data. The HPV vaccine has not been associated with adverse pregnancy outcomes or with adverse effects in the developing foetus. Inadvertent administration of the HPV vaccine during pregnancy is not expected to be problematic.

If a pregnant woman would like to be vaccinated against HPV, the vaccine series should be postponed until after pregnancy. If she has already started the vaccine series and then falls pregnant, the remaining doses should be delayed until after the pregnancy. The HPV vaccine can be used during lactation as inactivated vaccines pose no risk to breastfeeding mothers or their babies.

### Side-effects

The most common noted side-effects are local reactions at the injection site, i.e. pain, redness and swelling. Local reactions may increase in severity with increasing doses. Systemic side-effects, such as fever, have been reported, as well as nausea, dizziness, muscle pain and malaise. Nausea, dizziness, muscle pain and malaise were reported in equal frequency in both the vaccine and placebo recipients.

Fainting has occurred following administration of the HPV vaccine to adolescent vaccinees. Therefore, it is recommended that the vaccine recipient should be seated during its administration and observed for 15 minutes thereafter.

### Conclusion

HPV infection is extremely common and may have dire consequences, because of the development of cervical cancer. Vaccines are now available that protect against HPV types 16 and 18 (these potentially cause cancer), as well as the non-cancer-causing types, 6 and 11. Mothers of pre-adolescents and adolescents should be informed of the benefits of vaccination as the best time to vaccinate is before the adolescent becomes sexually active. Young people who are already sexually active should be counselled on the benefits of vaccination. It must be remembered that the HPV vaccine does not
eliminate the need for continued Pap smears as 30% of cervical cancers are caused by HPV types that are not included in the vaccine.

Bibliography