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Review of HPV Vaccine in regards to Cervical Cancer

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Cervical cancer is the fourth most common cancer type, affecting more than 12,000 women per year, and the second most prevalent cancer in women in underdeveloped countries (Wang et al.). Research over the years has observed an association between cervical cancer and Human Papillomavirus (HPV). Eighty-four percent of HPV-related cancers are diagnosed to be cervical cancer (Wang et al.) and researchers are striving to find a solution that would aid in reducing HPV and in turn, diminish the number of cervical cancer cases per year. Currently, there are three types of prophylactic vaccines that are commercially available that help prevent HPV (Wang et al.). These vaccines have been successful in preventing against 70-90% of HPV infections, but scientists are currently trying to develop new therapeutic vaccines (Wang et al.). Currently, there are more than 200 million doses of the prophylactic HPV vaccine provided worldwide, with 118 million receiving only the first dose (Wang et al.).

Introduction

Human Papillomavirus (HPV) is a common STD causing 14 million people annually to be infected with over 100 different strains. Out of these 100+ strains, at least 14 are carcinogenic due to unchecked cell proliferations and mutations (Wang et al.). In cervical cancer, HPV16 and HPV18 are the most prevailing types consisting of 70% of cervical cancer and precancerous lesions (Wang et al.).

Cervical Cancer control is made up of three areas: primary prevention, such as vaccination; secondary prevention, such as screening and lesion treatment; and tertiary prevention, such as diagnosis and treatment. There are three prophylactic vaccines that are commercially available currently. The quadrivalent and nonvalent HPV vaccines protect against HPV6 and HPV11 which cause anogenital warts and the bivalent HPV vaccine protects against HPV16 and HPV18 (Wang et al.). Gardasil is a quadrivalent 4vHPV vaccine that targets HPV6, HPV11, HPV16, and HPV18. Ceravix is a bivalent 2vHPV vaccine that targets HPV16 and HPV18. Gardasil 9 is a 9vHPV vaccine targeting HPV6, HPV11, HPV16, HPV18, HPV31, HPV33, HPV45, HPV52, and HPV58. The 4vHPV vaccines, with the main use being for the prevention of precancerous lesions, genital warts, and cervical cancer in females and males ages 9-26 (Wang et al.). The 9vHPV vaccine protects against 5 additional HPV genotypes as well as the prevention of lesions, genital warts, along with cervical, vaginal, vulvar, and anal cancers in females and males ages 9-45 (Wang et al.). The 9vHPV vaccine has maintained efficiency for up to 6 years and has shown prevention and coverage for about 90% of cervical cancers and HPV-related illnesses (Wang et al.).

The prevailing prophylactic vaccines have restricted benefits for anyone who is infected by HPV before to trying the vaccine. HPV vaccines are based on virus-like particles (VLPs), which are made from the recombination of HPV capsid proteins and are not infectious due to the absence of a viral DNA (Wang et al.). The vaccination with VLPs can produce multiple types of specific type nAbs, which can bind to the original virus particles and will neutralize the virus by not allowing uptake by the target cell (Wang et al.).

The “perfect” HPV vaccine should help improve the immune system and protect against all high-rising

HPV types and various carcinogenic types. The idea of a therapeutic vaccine has been made aware to scientists with the aim to stimulate cell-mediated immunity and kill infected cells rather than neutralize antibodies, so it will have an effect if someone is currently diagnosed with HPV. The idea is that the therapeutic vaccine should target the E6 and E7 proteins to prompt a tumor-specific T cell and a cytotoxic lymphocytic response where CD4 and T cells would secrete multiple cytokines (specifically IFN-ɤ and IL2), labelling malignant and infected cells and cytotoxic CD8 T Cells, and destroy infected cells by secreting granzyme B and perforin to cause cell death (Wang et al.).

The E6 and E7 proteins are constantly expressed in HPV infections along with most cervical cancers and precancerous lesions, but it is not constantly expressed in normal tissues (Wang et al.). The expression of these proteins is crucial for the maintenance and the induction of malignant and cancerous cells, making them the perfect target proteins for the developing antigen-specific immunotherapy of HPV infections and related diseases (Wang et al.).

Recent Progress

Dr. Jiayoa Lei and their team conducted a recent study to test the success of an HPV vaccine regarding the prevention of cervical cancer. This study vaccinated 1,672,983 females from ages 10-30 years old, and all participants received at least one dose of the vaccine, with 438,932 of the participants initiating the vaccine before age 17. During the study, 19 women who received the vaccine and 538 women who did not were diagnosed with cervical cancer. This vaccination process is essential to helping with the prevention of cervical cancer, as the collective instances of cervical cancer rapidly increase at age 23 in both unvaccinated and vaccinated women (Lei et al.). In unvaccinated women, the cases rose fast with 94/100,000 women getting diagnosed with cervical cancer, while on the other side of the spectrum, 47/100,000 vaccinated women were diagnosed with cervical cancer by age 30 (Lei et al.). When observing the age of the first vaccination, women between the ages of 17-30 years old had a collective incidence with 54/100,000 being diagnosed with cervical cancer at age 30 while the incidence with those who began the vaccine under the age of 17, 4/100,000 were diagnosed with cervical cancer by age 28 (Lei et al.). With the introduction of a buffer period between vaccine rounds, the risk of cervical cancer among vaccinated women consistently stayed lower than unvaccinated women, with 8 cases of cervical cancer diagnosed in vaccinated women per year in comparison to the 549 cases per year in unvaccinated women (Lei et al.).

Discussion

HPV corresponds with the diagnosis of cervical cancer, which is the fourth most common cancer affecting women. The introduction of HPV vaccines has led to a significant decrease in cervical cancer through the prevention of HPV. While the current vaccination option of prophylactic vaccines has been shown to help reduce HPV infection, it does not appear to help the patient if they receive the vaccine during or after infection. This problem has led to scientists researching a therapeutic vaccine that targets any and all forms of HPV, killing the virus before the individual contracts it and fighting the virus if the individual currently has the virus upon vaccination. The development of these HPV vaccines has been proven to help reduce the cases of cervical cancer, as seen in a study done by Dr. Jiayao Lei and Dr. Lei's team. The HPV vaccine has undergone many studies with the side effects including redness at the site of injection, swelling, and soreness (*HPV vaccine: Get the facts*). Occasionally, fainting and dizziness will occur after injection along with vomiting, nausea, headaches, weakness, or fatigue (*HPV vaccine: Get the facts*).

The problem the public has with this vaccine is the lack of information. Many parents feel as if the vaccine is not safe because they do not have the correct or enough information to make an informed decision (Jaber). Some other parents feel as if there is no need for their child to have the vaccine because they are not sexually active or they believe it is not needed (Jaber)

There is still research that needs to be done on this topic, but with the results seen by the prophylactic vaccines, it is hopeful that the therapeutic vaccines will also be successful.

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