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Short Communication

Human Papillomavirus Infection: Prevention, Barriers to Vaccination, and the Need for Education

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Abstract

While there is no known cure for HPV, prophylactic vaccination provides effective method of primary prevention against HPV related diseases. However, many females and males never receive the HPV vaccine as recommended. There are multiple barriers to vaccination, and these barriers can be identified as parental, provider, or system-level. Understanding these barriers and developing strategies that provide accurate information about HPV, its risks, and the need for vaccination are essential in the form of sustained educational campaigns for parents, young adults, and providers.

ABBREVIATIONS

HPV: Human Papillomavirus; STI: Sexually Transmitted Infection; US: United States; CDC: Center for Disease Control; ACS: American Cancer Society; ACIP: Advisory Committee for Immunization Practices; VLPs: Virus Like Particles; FDA: Food and Drug Administration

INTRODUCTION

Human papillomavirus, or HPV, is the most common sexually transmitted infection (STI) affecting both females and males in the United States (US) [1]. HPV can infect the genital areas of females and males including the skin of the vulva, penis, and anus; the linings of the vagina, cervix, and rectum; and the linings of the mouth and throat [2]. It is the cause of nearly all cases of cervical cancer [3]. Unlike other STIs, most signs and symptoms of HPV are nonexistent; therefore, most individuals are unaware of the infection. Currently, approximately 79 million Americans are infected with HPV and about 14 million people will become newly infected each year [2]. Approximately 360,000 people develop genital warts each year and more than 11,000 women develop cervical cancer in the US as a result of HPV disease [2]. Even though the rate of HPV infections is high, effective prevention is available. HPV vaccines are safe, effective, and could prevent the majority of HPV-attributable cancers, if vaccination coverage is high [4]. Understanding the barriers to HPV vaccination and providing education to overcome these barriers is essential.

HPV INFECTIONS

There are over 40 types of HPV that infect mucosal surfaces and are sexually transmitted [5]. Despite the fact the immune system typically clears the virus from the body within two years; some individuals will have a persistent HPV infection that can cause various types of cancers and genital warts [6]. In fact, most all cervical cancers are caused by HPV [7]. "Low-risk" HPV types can cause warts on or around the genitals and anus of both females and males [3,8] and can cause recurrent respiratory papillomatosis, which is a rare growth of warts in the throat and airway [8]. Females may also have warts on the cervix and in the vagina. Because these genital HPV types rarely cause cancer, they are called "low-risk" viruses [3,8]. "High-risk" HPV types cause cancer [3]; 13 HPV types can cause cervical cancer [2]. Types 16 and 18 are the most oncogenic strains of the virus and are responsible for causing over 75% of cases of cervical cancer and the majority of other types of genital cancers [3,6]. When high-risk HPV lingers and infects the cells of the vulva, vagina, penis, anus, or the oropharynx, it can cause cell changes or precancers [1]. These precancers may eventually develop into cancer if they're not found and removed in time. These cancers are much less common than cervical cancer. Much less is known about how many people with HPV will develop cancer in these areas [1].

VACCINES

While there is no known cure for HPV, prophylactic vaccination provides effective method of primary prevention against HPV related diseases. The Advisory Committee for Immunization Practices (ACIP), the CDC, and the ACS make recommendations regarding vaccines. All three groups recommend routine HPV vaccination for females and males ages 11 or 12 years and catch-up vaccines for females through age 26 and for males through age 21 [2,3,9]. The vaccine is also recommended for gay and

bisexual males through age 26 and for females and males who have compromised immune systems through age 26, if they did not get fully vaccinated when they were younger [2].

Ideally, vaccination should occur before the first sexual contact and prior to exposure to HPV; however, vaccination after the first sexual contact is also recommended [7]. Young adult females are of particular concern. The prevalence of HPV peaked in females aged 20-24 years when nearly 45% of these females were found to be infected [10]. Unfortunately, the statistics for prevalence may not tell the true rate of occurrence. Since HPV infections can clear quickly and go away on its own, the incidence of HPV may be even higher than reported [2]. HPV is not curable, but it is preventable [2]. Significant reductions in new infections are possible and urgently needed. Routine HPV vaccination has the potential to decrease the burden of HPV related diseases.

Three vaccines are available for HPV prevention and are highly effective in preventing infection when given before initial exposure to the virus. HPV vaccines work by stimulating the body to produce antibodies that, in future encounters with HPV, bind to the virus and prevent it from infecting cells [11]. Current HPV vaccines use virus-like particles (VLPs) formed by HPV surface components. VLPs lack the HPV virus DNA and are strongly immunogenic, meaning the VLPs induce high levels of antibody production making the vaccines highly effective [11].

In 2006, Gardasil® was approved by the US Food and Drug Administration (FDA) as a quadrivalent vaccine (4vHPV) which prevents HPV types 6, 11, 16, and 18 [12]. Another vaccine, Cervarix®, was released in 2009 and is a bivalent vaccine (2vHPV) that prevents HPV types 16 and 18, which can cause cervical cancer and precancerous lesions [13]. In December 2014, the FDA approved Gardasil 9® [9-valent human papillomavirus vaccine (9vHPV)] for the prevention of diseases caused by nine types of HPV: 6, 11, 16, 18, 31, 33, 45, 52, and 58 [12]. Gardasil 9® added protection against five additional types of HPV beyond the quadrivalent vaccine; these additional types are responsible for approximately 20% of cervical cancers that are not covered by previously approved HPV vaccines [12]. Gardasil 9® is approved for use in females ages 9-26 and in males ages 9-15. Vaccination of females is recommended with 2vHPV, 4vHPV, or 9vHPV, and vaccination of males is recommended with 4vHPVor 9Vhpv [14]. The added benefit from 9vHPV will mostly benefit females because it protects against the higher proportion of HPV associated cancers for females; however, it is approved for males as well as females [14]. Gardasil and Cervarix® provide nearly 100 percent protection against HPV types 16 and 18 and the cervical cell changes that these persistent infections can cause [11]. In studies, both Gardasil and Gardasil 9® were effective in prevention of disease from the four shared HPV types (6,11,16, and 18); Gardasil 9® was 97% effective in preventing cervical, vulvar, and vaginal cancers caused the additional types added to the vaccine [12].

FACTORS INFLUENCING VACCINATION

While most studies [15] have found positive attitudes towards HPV vaccination, the percentage of females and males receiving the vaccine in the US has been low. In 2012, 17 year old females were the most highly vaccinated age group and only 44.5% received all three doses [16]. In 2013, only 36.9% of females aged 19–26 years reported receipt of ≥ 1 dose of HPV vaccine [17]. In 2014, coverage for all three doses was only 39.7% for females 13-17 years and 21.6% for males [18]. Most female adolescents in commercial and Medicaid health plans are currently not receiving the recommended doses of HPV vaccine by age 13 years [19]. Even those already exposed to HPV should still be vaccinated. There are numerous types of HPV, and vaccination after exposure will still protect against other strains during future encounters, as cervical cancer is a result of persistent infections with high-risk strains [10]. In addition to low uptake of the HPV vaccine, it is equally concerning that young adults have reported low intentions of receiving the vaccine [20,21]. Since the first HPV vaccine was introduced in 2006, vaccine-type HPV prevalence among young females decreased by 56% [6] but has still not reached levels of other recommended vaccines [17].

Unfortunately, there are multiple barriers to vaccination among females and males. These barriers can be identified as parental, provider, or system-level. While parental consent is not needed to vaccinate adolescents under 18 years of age, adolescents typically seek approval [22]. Parents have reported (a) lack of knowledge or needing more information before vaccinating their children [4,22,23], (b) a concern about the vaccine's effect on sexual behavior [23], and (c) a concern about the safety of the vaccine [15]. Parents also view their children at low perceived risk of HPV infection and view vaccine costs/financial concerns as barriers [23]. Parents have also voiced concern about the safety of the HPV vaccine [15,24,25] but not vaccination in general [24,25]. For parents of sons, lack of vaccination was related to a perceived lack of direct benefit [23]. Unfortunately there are social disparities for vaccine series completion as well. Disproportionately more African American females and males and females living below at or below the poverty level have lower rates of series completion [16].

When vaccination does not occur before the age of 18, barriers perceived by young adult females and males, aged 19-26, becomes important. Lack of knowledge is a barrier to HPV vaccine uptake [5,26,30]. Other barriers for young adults include cost [5,23,31] safety of the vaccine [26,31,32], perceived low susceptibility to HPV [5,28], low perceived benefits [33], and low intention to receive the vaccine [21,31]. In particular, males are less likely than females to receive the vaccine when they have to pay for it, and females have more concerns about safety of the vaccine than males [31].

A lack of provider recommendation was consistently found to be a key barrier to increasing vaccination rates [4]. Health care professionals may lack information on HPV vaccination [4]. Clinicians reported a lack of knowledge about the relationship between HPV and urogenital or oral cancers [23]. Additionally, providers reported recommending the vaccine only to select populations rather than all 11 and 12 year olds [23]. Some providers offered vaccination only to those they perceived as high risk (often low income and/or patients of color) while others reported only vaccinating older teens or females, but not males [23]. Other providers recommend the vaccine more for females than males [4]. Time was also a barrier; physicians reported that discussing the HPV vaccine took more time than discussing the other recommended vaccines for 11-12 year olds [4].

System-level barriers include limited opportunities during a provider visit to offer HPV vaccine and a lack of flexible tracking and reminder capabilities for completion of the vaccine series [4]. Another significant barrier is cost to patients and providers. Providers consistently mentioned poor insurance coverage or reimbursement and the costs to purchase and store the vaccine as barriers [23].

METHODS TO PROMOTE VACCINATION

To overcome barriers to vaccination, health care providers must recommend vaccination to parents of all 11 and 12 year olds and before children become sexually active as part of regular primary prevention interventions. Parents and providers believe that preventing cancer is the most important reason to vaccinate against HPV [34]. Parents consistently cited health care provider recommendations as a key influencing factor in their decision to vaccinate their children [23,25,32,34]. Parents and young adults must also learn about the risk of HPV-related infections and equate the vaccine as part of the social norm of health care [32,34,35]. Providers should give clear and accessible information and strongly recommend the vaccine as safe, prevents cancer, and co-administer it with tetanus, diphtheria, and acellular pertussis vaccine and quadrivalent meningococcal conjugate vaccine [4,8,34]. Providers must help parents overcome perceived distrust of the vaccine [8,15].

Additionally, system barriers must be addressed. Not only is vaccine uptake important, providers must stress the need to complete all three vaccinations. Innovative communication reminders such as text messaging may lead to increased series completion [23]. Providers must address disparities with vaccination messages and focus on all 11 and 12 year olds. Providers must take advantage of missed opportunities to vaccinate when adolescents are seeking care within health care systems [22,23] such as times when seeking physical exams for athletics [23]. Systems must be developed to help providers manage the additional costs associated with purchasing and storing the vaccines.

Education about HPV and vaccination should vary slightly for females and males. For females, genital HPV infections occur mostly at a younger age and less commonly in females over 30 [2]. Certain types of sexual behavior increase a female's risk of getting an HPV infection; therefore, females must learn about the risks of having sex at an early age, having multiple sex partners, having a partner who has had many partners, and having sex with uncircumcised males [3]. Since females have reported more concerns about the safety or effectiveness of HPV vaccines, interventions should focus more on reducing these barriers [3]. Educational campaigns should address the safety of the vaccine and the need to return for all three doses [31].

For males, the main risk for an HPV infection is having multiple sex partners. In addition, males who are not circumcised are more likely to be infected and pass it on to their partners [3]. The reasons for this association are unclear. Circumcision does not completely protect against HPV infection – circumcised males can still get HPV and pass it on to their partners [3]. Education content must emphasize the use of condoms for those who are sexually active and the use of latex condoms the correct way every time they have sex. A condom can lower the risk of getting HPV; but areas that are not covered by a condom can still become infected [2]. Since cost is a greater barrier for males, cost as a behavioral barrier should receive greater attention when advocating HPV vaccination among males [31]. Messages could be aimed at finding convenient times to receive the vaccine or directing a patient to a clinic that offers the vaccine at a reduced rate [26].

EDUCATIONAL CAMPAIGNS

Overall educational campaigns must address not only the need to receive the initial vaccine but to return for the remaining two dosages. Health care providers should institute reminder/recall strategies for parents to bring their children back for all dosages of the vaccine [8]. Providers must develop educational programs that meet cultural and literacy needs unique to patient populations [36]. For parents, educational campaigns must address lack of knowledge in order to change parent's distrust of the HPV vaccine. Education campaigns should be planned before school begins in the fall [24]. Even use of simple educational pamphlets about HPV and HPV vaccination can influence acceptance rates and are cost effective [25]. These pamphlets must be made available in health care provider offices and distributed at encounters within the health care system. Acquiring tailored educational materials to meet the needs of specific populations is important also, such as educational materials in Spanish-language for Hispanic mothers who do not speak English [25].

Vigorous marketing should target young adult females and males. For females, a key message is to decrease cervical cancer, and for males, a key message is to decrease anogential cancer incidence for both genders [30]. For young adults, emphasizing a disadvantage of not performing vaccination as a health behavior (loss-framed message) has been shown to have a greater persuasive advantage for females and males who want to avoid the negative effects of HPV, such as cancer [31]. Thus, educational messages must focus on the importance of receiving the vaccine in order to prevent cancer and STIs. While listening to professional lectures or receiving fact sheets for young adults has shown mixed results in the literature [37,38], these strategies should be continued as part of health education on college campuses. These programs may lead to increased awareness and uptake of the vaccine for those not vaccinated previously. Additionally, emphasizing the severity of HPV related disease is central to increasing regret if one does not get vaccinated and has increased intention to seek vaccination [39]. Since college males have been shown to be less knowledgeable about the existence of the HPV vaccine, educational campaigns on college campuses should increase awareness about the vaccine [15,28] and target males in particular.

Safety of the HPV vaccine should be part of all educational campaigns. Parents and young adults have voiced concerns about the safety of the vaccine [15,16,31,32]. Research has demonstrated that the 9vHPV is well tolerated with most adverse events are localized with site-related pain, swelling, redness and headaches [12,14], reactions not different from other vaccines. Therefore, all educational campaigns must emphasize the safety of HPV vaccination.

CONCLUSION

HPV is so common that nearly all sexually active females and males will develop an infection at some point in their lives [2]. Since there is no one way to prevent infection from all the different HPV types, there are effective strategies that can lower the chances of becoming infected. Primary prevention strategies about HPV, its risks, and the need for vaccination are essential in the form of sustained educational campaigns for parents, young adults, and providers. The burden of following these educational campaigns falls on health care providers and those who interact with larger populations of young adults, such as student health services on college campuses. Special attention should be provided to the social determinants of seeking vaccinations and the system-level barriers that exist within the healthcare system.

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