Ethics and Current Climates Surrounding HPV Vaccination

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Abstract

Human papillomavirus (HPV) is the most prevalent sexually transmitted infection (STI) worldwide, affecting both males and females. Roughly 150 HPV types have been identified, 35 to 40 of which can infect the anogenital tract. Infection with certain oncogenic strains is associated with cancers of the cervix, anus, vulva, vagina, and oropharynx. Although vaccination against HPV has been shown to be safe and effective at preventing HPV infection, controversies surrounding the widespread uptake of the available HPV vaccines persist. We examine the notable ethical debates surrounding HPV vaccination programs, including issues of cost efficacy, adolescent autonomy and consent, parental involvement in vaccine decision-making, male inclusion in vaccination programs, and perceived barriers to vaccination. A common theme that emerged within many of the topics we present involved the dynamics of adolescent-parent relationships, which we consider at length to inform future interventional strategies. Despite the safety and efficacy of the HPV vaccine, the potential of becoming infected by HPV remains high, likely due to overall low vaccination uptake. In this review, shortcomings in previous vaccination programs are addressed, while interventions that may enable the success of future strategies are highlighted.

Introduction

Human papillomavirus (HPV) is the most prevalent sexually transmitted infection (STI) worldwide (1, 2). When it was discovered in the 1980s that HPV had a causal relationship to cervical cancer (1), vaccination research and investigation into the strategic implementation of HPV vaccination programs came to the forefront of international public health. While the HPV vaccination has been shown to be largely effective in combating cervical cancer and other HPV-associated cancers, the advent of national HPV vaccination programs has not been without ethical controversy.

In this review we introduce and examine notable ethical debates surrounding the adoption of HPV vaccination programs. We explore issues including cost efficacy, adolescent decision-making capacity, consent, the role of sexual behavior, male inclusion in vaccination programs, educational strategies, and potential conflicts of interest. As these topics are presented, we will discuss how they relate to ethical considerations in the context of patient autonomy, beneficence, and social justice. The synthesis of these considerations is pertinent to the development and application of HPV-related public health policy.

Methods

The electronic database PubMed was the primary source for article identification. The database was searched for articles from the years 2000 to 2021. Appropriate free text and MeSH terms were used to identify all studies. Articles identified using search term "vaccine," "epidemiology," "etiology," "prevention," "gender," "consent," "parents," "program," "ethics," and "education" were paired with "HPV" or "human papillomavirus." Articles were independently appraised and assessed for quality, and reference lists were scanned for additional studies of potential relevance.

Discussion

Background

HPV is the most common sexually transmitted disease in the United States (2). To date, more than 100 HPV serotypes have been identified. Although the mechanisms by which these serotypes manifest are highly variable, ranging from innocuous lesions to various forms of cancer, transmission occurs primarily through direct skin-to-skin contact (3).

In 1996, the World Health Organization, along with the International Agency for Research on Cancer, recognized the link between HPV and cervical cancer (1). Since then, the association between oncogenic strains of HPV and cervical cancer has been well established, with HPV types 16 and 18 associated with 70% of cervical cancers and cervical intraepithelial neoplasia (CIN) (4). Furthermore, oncogenic strains of HPV have been linked to cancers of the anus, vulva, vagina, and oropharynx (2). Indeed, while HPV has been implicated as a common cause of cervical cancer among women, it is notable that, among males, the incidence of HPV associated penile, anal, and oropharyngeal cancers are on the rise (5).

Worldwide, cervical cancer is attributable to more than 250,000 deaths per year, having a disproportionately higher incidence rate in developing countries where resources for preventive methods and secondary treatment are scarce (2). Epidemiological studies have shown that, following the introduction of the Papanicolaou (Pap) cytology test, and the implementation of well-organized screening programs, rates of cervical cancer mortality have significantly declined (6–9). Despite these efforts, cervical cancer remains the second most common cancer among women worldwide (2).

Discussion

HPV prevention

Engaging in sexual activity at an early age, or having multiple partners, increases the risk of HPV infection. Likewise, "safe-sex" practices and condom usage as a method of contraception cannot guarantee protection from HPV infection, as transmission can occur via skin-to-skin contact (2). Thus, the primary means by which HPV infection is prevented is via vaccination.

HPV vaccine

In 2006, the World Health Organization recognized the high efficacy of the tetravalent HPV vaccine in preventing genital warts and CIN associated with HPV 16 and 18 (2). Currently, the vaccine is recommended for adolescents 9 to 14 years of age and is most effective when administered prior to the onset of sexual relations. The HPV vaccine is safe and effective at preventing HPV infection, and reported side effects are rare, generally mild, and no vaccine-related deaths have been reported (2). There is also a bivalent HPV vaccine that is recognized to prevent CIN associated with HPV 16 and 18, but it does not protect individuals against HPV serotypes associated with genital warts (10). The most recent FDA-approved HPV vaccine is a nonavalent serotype that protects against 5 additional strains of HPV that have been linked to 20% of cervical cancers not previously protected by the tetravalent HPV vaccine (11).

Male vaccination, herd immunity, cost efficacy

Advocates for HPV vaccination of males emphasize the legitimate health risks HPV infection and associated sequelae confer upon the male sex. According to CDC data gathered between 2011 and 2015, while 60% of HPV-related cancers occur in women, 40% of occur in men. While cervical cancer is commonly attributed as the largest contributor to HPV-associated morbidity and mortality, HPV has also been linked to a substantial number of non-cervical cancers, including vaginal and vulvar cancer in females, and anal, oropharyngeal, and penile cancers in men (2). In fact, one study published in the *Journal of Clinical Oncology* projected that by 2020 the annual number of HPV-positive oropharyngeal cancers will surpass the annual number of cervical cancers, with the majority occurring in men (5). These considerations raise an issue as to whether female-selective vaccination programs unjustly exclude males.

In addition to the direct health benefits that male vaccination provides against male HPV-related infections and sequelae, proponents of male HPV vaccination programs also argue that male inclusion will contribute to more comprehensive protection for females against HPV infections and cervical cancer. Because males comprise half of the epidemiological chain of HPV transmission, some argue that gender-neutral vaccination may be a more effective strategy to combat HPV transmission. By immunizing both sexes, it is argued that a collective, or herd, immunity effect can be created, which would help further mitigate the risk of HPV exposure to females and unvaccinated individuals of both sexes (2). One dynamic transmission model examined reduction rates in HPV-16 prevalence in unvaccinated females in response to a female-only vaccination program versus a male and female program and found that, assuming 80% vaccine coverage in both programs, the gender-neutral program resulted in a 86–96% reduction in prevalence compared to a 7–31% reduction in the female-only program (12).

While the data remain disputed, if it can be definitively demonstrated that the vaccination of males contributes significantly to herd immunity and thus, by extension, confers a population-wide benefit on the reduction of HPV transmission, then "public-good" or social justice arguments for male HPV vaccination may be valid.

Health economists proposing subsidies for female-only vaccination programs base their arguments on cost-effective means to optimally reduce disease burden. According to a study evaluating vaccination programs via disease transmission modeling, "vaccination against HPV-16 and HPV-18 can be cost-effective, although including male participants in a vaccination program is generally not cost-effective, compared to female-only vaccination" (13).

While the relative benefits of male vaccination programs remain largely debated, it appears that the contribution of said programs to HPV eradication is more significant under certain conditions. The cost efficacy of male vaccination programs appears to depend on a multitude of factors, including vaccine efficacy, female vaccination coverage, and the breadth of HPV-related outcomes considered. According to the CDC, "adding male vaccination to female-only vaccination becomes more cost-effective when all HPV-associated health outcomes are included in the model and vaccine coverage of females is low" (14). This suggests that the relative benefit of implementing male vaccination programs may be more pronounced in countries with less extensive vaccine uptake and could thus be a more effective strategy for combating HPV transmission in underdeveloped and low-income nations.

Conflicting interest: parents and children

Due to the nature of the HPV vaccine as a method of STI prevention — with a target population consisting of adolescent males and females — a controversy arises regarding the conflicting interests of two parties: parent and child.

Currently, minor consent laws in all states allow adolescents to provide informed consent for the confidential treatment of STIs; however, with respect to vaccination, these laws do not reflect issues of decision-making (15). Furthermore, it has been observed that adolescents seeking confidential medical treatment may be among those most likely to benefit from vaccines that prevent STIs, such as the HPV vaccine (15). Because these state consent laws do not specifically address the capacity of an adolescent to consent to vaccination, a consensus among some health care providers has been reached by interpreting these laws to include vaccination as part of routine medical care and STI treatment, circumventing the need to obtain additional parental written or verbal consent (15). Nonetheless, a minor's right to consent to vaccination is not established in United States law (16); herein lies the foundation of the controversy at hand — when the views of the parent conflict with those of the adolescent, at what point, and to what extent, does the adolescent's autonomy become restricted?

Although conflicting interests between parent and child can present a potential barrier to vaccination, studies suggest that adolescents play an important role in the process of vaccine decision-making, especially when the parents' perception of their adolescent's sexual activity is considered (17–19). In this study, more than half of responding parents who perceived their adolescent to be sexually active were likely to report that their adolescent was involved in the decision-making process (17). While these findings suggest increased parent-adolescent communication may increase vaccine uptake, this may not be indicative of increased favorability with respect to parental perceptions on adolescent decision-making capacity. In a study comparing parent and adolescent views on decision-making, it

was reported that more than half of all responding adolescents considered adolescents to be capable of reasonable decision-making at an earlier age; on the other hand, more than half of all responding parents thought otherwise (20). Indeed, there is continued debate surrounding discussions of when an adolescent attains the capacity to make informed decisions. While some argue that adolescents should have the full authority to make their own personal health-related decisions, others question the capacity of adolescents to make informed decisions (15).

Parent and adolescent consent

Patient autonomy is one of the most important components of consent. As the sexual health of adolescents has become a major healthcare topic globally, countries have begun to support the term "adolescent autonomy" in an effort to counter the controversies surrounding adolescent ethical decision-making. The notion of adolescent autonomy is illustrated well in an example from the United Kingdom. In England, more than 30 years ago, contraception was made available for adolescent females under the age of 16, following proper education from a health care provider, but without parental consent (21). It is worth noting that, in this case, adolescent consent was emphasized, rather than parental rights or authority under the law. Although the term "adolescent consent" is not widely used in the United States, a crucial role of health care professionals is informing and educating patients, both adults and adolescents alike (21). However, United States law authorizes parents/guardians with the right to refuse to consent to adolescent vaccinations. Therefore, when considering adolescent consent, the role of parental decision-making cannot be overlooked.

Parental decision-making processes are deeply affected by methods of communication, disease prevalence prior to vaccination, and depth of knowledge regarding vaccine efficacy and safety (20). Indeed, it has been shown that parents who have access to high-quality information, perceive vaccines to be safe, or have a child presenting with a mild illness, will be more likely to consider and consent to the vaccination of their child (20). In a qualitative study conducted in England, parents unopposed to vaccination acknowledged that adolescent decision-making was an indication of maturity, citing that the will of an adolescent to request a vaccination was indicative of their capacity to make well-informed decisions (21). In this same study, the largest group of responding parents agreed that adolescents who were well informed and understood the implications of the HPV vaccine should be allowed to consent to vaccination, without parental involvement. However, this view is in direct contrast with that of the second largest group of responding parents, which reported that parental involvement in adolescent decision-making is necessary, and should be given precedence (21). Despite these conflicting views among parents, it has been shown that providing both parents and adolescents with high-quality education is an important factor in facilitating informed consent and increasing vaccine uptake (22).

Because HPV is a sexually transmitted disease, and patient autonomy is a central component of informed consent, there is a logical argument for making the HPV vaccine readily available to adolescents who opt to be vaccinated, even if their parent/guardian has refused to consent. If the notion of adolescent autonomy becomes more widely discussed in the United States, additional research will be necessary in order to better understand how and why vaccine preferences differ between parent and adolescent. Likewise, future research should aim to provide insight into the nuanced conversations and discussions between parents and adolescents with respect to individual autonomy, ethical consent, adolescent decision-making, and the role of policy in healthcare delivery and access.

Sexual abstinence and HPV vaccination

Adolescents who intend to remain sexually abstinent, whether due to education, religious beliefs, or personal choice, would not technically be considered at risk for contracting or transmitting HPV, and thus would not be a necessary subgroup to vaccinate. However, even if an attitude of sexual abstinence is maintained throughout an individual's entire premarital life, it is not likely that this practice will be continued after marriage, warranting the need for vaccine administration prior to marriage and the onset of sexual relations.

While the HPV vaccine has been approved for use in adults younger than 26 years of age, current recommendations indicate routine vaccination of adolescents age 11 to 12 years old (23). When considering HPV vaccine uptake outside of this recommended age range, as would be the case of abstinent adolescents who opt to delay vaccine uptake prior to marriage, it is necessary to compare vaccine efficacy among both adults and adolescents in order to ensure accurate and informed decisions can be made. In a study comparing data on HPV vaccine immunogenicity between adolescent males and females 10 to 15 years of age and males and females 16 to 23 years of age, the immunogenic response was greater (1.7 – 2.7-fold) in the younger cohort than the older. However, no statistically significant difference was reported, suggesting that current data on vaccine efficacy is comparable between younger and older adolescents (24).

Considering the high likelihood of becoming infected by some form of HPV (25), and the absence of studies assessing rates of HPV vaccine uptake, or rates of HPV infection, among adults who opted to delay vaccination prior to marriage, there is a strong case to be made for abstinent individuals to also opt for HPV vaccination during adolescence. Administration of the vaccine would not undermine their autonomy and choice but would rather serve to safely and effectively decrease the risk of future HPV infection (26).

Sexual promiscuity and HPV vaccination

One perceived barrier to HPV vaccination is the parental concern that vaccination may implicitly promote earlier and riskier sexual behaviors among adolescents. The prevalence of this perception is not well known, and while one regional study reported less than 1 in 5 parents (19%) considered this a possibility, there is no factual basis to support this concern, as vaccination against other infectious agents have not been associated with increases in sexual or otherwise risky behaviors (27). The perception that vaccination against STIs may facilitate or enable riskier sexual behaviors among adolescents is unique when considering the history of vaccine requirements for school attendance. The hepatitis B vaccine, which protects against a virus largely transmissible through sexual contact, is currently required for school attendance in 47 states and the District of Columbia (28).

The role education has on promoting parental acceptance of the HPV vaccine is unclear. After parents of adolescent girls and boys who originally opposed vaccination were provided an educational pamphlet on the prevalence and seriousness of HPV infection, 20% opted to have their child vaccinated; however, following the educational intervention, some parents incorrectly concluded that the vaccine would increase sexual promiscuity (22). While education is only one aspect of a multicomponent approach to promoting public health, high-quality physician recommendations have been positively associated with HPV vaccine uptake (29). An interesting line of question for future research may be to better understand if parental education, coupled with physician recommendations, is able to curb the misperception of adolescent promiscuity and thus increase vaccine uptake.

To our knowledge, there is currently no literature available representative of this perceived barrier on a state or national level. With respect to HPV vaccination, efforts should be made through future research to better understand the implications of this incorrect perception, as parental acceptance of vaccination is an essential component for the immunization of adolescents (30).

Ethical concerns of HPV education programs and strategies to avoid them

When implementing programs that aim to increase public awareness and understanding of the HPV virus and vaccine, ethical issues that emerge tend to be rooted in the strategies used to increase vaccine uptake. The ethical question that each strategy must answer is “Do the ends justify the means?”

A study conducted in Bangladesh demonstrates this very ethical dilemma. The study analyzed a vaccine education program which targeted adolescent females 10 to 12 years of age and was considered successful as far as achieving a vaccine coverage rate of 94% (10). However, the methods employed to achieve the observed rate of vaccine coverage may not have been justified. While this program used educational sessions to increase knowledge and awareness of HPV and cervical cancer risk, it deliberately rebranded the vaccine as a “cancer vaccine.” Details regarding the mechanisms of HPV transmission were also omitted in order to avoid confronting regional taboos regarding adolescent sexual behaviors, which may have otherwise negatively influenced vaccine uptake. It is likely that the combination of these two strategies contributed significantly to the high vaccine coverage achieved (10). Furthermore, informed consent was not technically attained in this case, but rather the absence of a parent at the time of vaccination was interpreted as "implied consent" (10).

Vaccine programs may utilize several strategies in order to avoid ethical issues and mitigate factors that may negatively impact vaccine uptake. A meta-analysis and review of strategies found that behavioral interventions, such as reminder/recall systems, and informational interventions such as factsheets, brochures, and expert or peer-narrated videos, were the most effective in vaccine series initiation (31). However, with respect to vaccine series completion, behavioral interventions were the only strategy shown to produce significantly higher rates. Although informational interventions were shown to successfully improve beliefs and attitudes toward vaccination, they were shown to have no effect on vaccine completion (31). Additionally, the effects of environmental interventions, which include programs implemented in schools, clinics, and postpartum units, were highly variable, affecting different target groups, or only certain aspects of vaccine behavior. For example, studies investigating the effect of a school-based vaccination program found that increased accessibility to vaccines led to increased vaccine uptake (31). Additionally, college females who viewed a combined peer-expert narrative video were significantly more likely to later vaccinate than females who viewed a control informational video that lacked a narrative which contained separate peer and expert narratives (31).

As new vaccine programs and strategies are implemented, effective interventions should adhere to the highest ethical standards, maintain transparency about possible long-term consequences of HPV infection, while also incorporating behavioral and informational components in an effort to create an optimal vaccine program.

Ethics and HPV screening

Another issue that effective vaccine programs aim to resolve is increased awareness of and access to preventive cervical cancer screening technology, but sometimes programs (e.g., the Bangladeshi program) fail to mention the importance of screening, which may have established a false sense of security in vaccinated females who received the divalent serotype, which only prevents 70% of cervical cancer (10).

Screening is used to detect any precancerous lesions and address them before they can cause harm. There are two screening methods currently accepted: the Pap cytology test and the hrHPV test. When compared to cytology alone, hrHPV testing alone, as well as co-testing (cytology plus hrHPV testing), have been shown to be twice as effective at detecting cervical dysplasia (32). However, Zhao et al. (2015) reported that roughly 30% of women participating in their study were diagnosed with cervical cancer 3 to 5 years after having previously received only one of the aforementioned screening methods, which demonstrates flaws in the precision of these screening techniques.

Current CDC-recommended screening intervals for cytology alone are every 3 years for women 21 to 65 years of age; screening intervals for hrHPV testing alone, as well as co-testing, are recommended every 5 years for women 30 to 65 years of age (34). A concern among some physicians when consulting on screening preferences is that, for patients who opt to be screened on an interval of every 5 years, there is an increased likelihood that a patient may be lost to follow-up. In contrast, some physicians may be more comfortable with, and even promote, less frequent screening for patients when considering each patient’s socioeconomic status or potential risk. Regardless of the screening method a physician and patient agree on, it is imperative that vaccination programs promote regular cervical cancer screenings to the same degree that they promote vaccination.

Conclusion

Current ethical dilemmas surrounding HPV vaccination range from vaccine program strategy to conflicts of interest between parents and adolescents, the capacity for adolescents to make informed decisions, and methods of implementing new state

and national legislation. While current vaccination strategies focus on female-only coverage, recent findings suggest there are additional benefits when males are included in vaccination programs, such as robust population-wide protection against HPV transmission and decreased disease burden. Issues regarding the cost efficiency of implementing and funding programs are controversial but warrant further examination and discussion.

Vaccination may be declined in some cases because of personal beliefs or in other cases because of misinformation that parents have perceived to be true. Several strategies involve the facilitation of communication between parents/guardians and adolescents, while others aim to promote public awareness, but regardless of strategy, the focus remains increasing vaccine delivery. Moving forward, it will be imperative to establish a more accepted consensus regarding adolescent decision-making capacity, both with respect to vaccine uptake, and as it relates to health care delivery more broadly. HPV vaccination provides a means to reduce HPV infection and transmission, and extensive vaccine uptake is particularly important for conferring population-wide immunity and reducing HPV prevalence. To that end, there are logical arguments that could be made in support for expansion of HPV vaccination inclusion and coverage. In conclusion, we support the continued use, implementation, and expansion of HPV vaccination programs, in addition to the utilization of supplemental preventive methods, such as routine screening and proper patient education.

Disclosures

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