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IN REVIEW

A Review of the Evidence Comparing the Human Papillomavirus Vaccine Versus Condoms in the Prevention of Human Papillomavirus Infections

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ABSTRACT

Objective: To examine the evidence related to the efficacy of condom use versus the human papillomavirus vaccine in the prevention of human papillomavirus infections.

Data Sources: Cochrane, CINHAL, PubMed, and Clinical Evidence. Various combinations of the keywords HPV, vaccine, and condoms were used for the search.

Study Selection: Randomized, double-blinded placebo-controlled trials were reviewed for evaluation of the human papillomavirus vaccine. Several longitudinal studies and a meta-analysis were used for review of condom efficacy related to human papillomavirus transmission.

Data Extraction and Synthesis: Studies evaluating the use of either condoms or the human papillomavirus vaccine and its impact on human papillomavirus transmission rates, detected through either human papillomavirus DNA testing or clinical disease.

Conclusions: The evidence indicates that the greatest degree of protection from specific types of human papillomavirus infection is provided by the vaccine. However, the use of condoms in addition to the human papillomavirus vaccine provides the greatest protection from the untoward effects of human papillomavirus infection and may also provide protection against human papillomavirus types not in the vaccine and other sexually transmitted infections.

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The human papillomavirus (HPV) is the most common sexually transmitted infection in the United States (Centers for Disease Control and Prevention [CDC] 2004a; Weinstock, Berman, & Cates, 2004) and is associated with the development of cervical cancer and genital warts. An estimated 6.2 million new cases of HPV infections occur in the United States each year, and approximately 20 million Americans are infected with HPV at any one time, with an overall prevalence of 26.8% (CDC, 2004a; Dunne et al., 2007). At least one half of all sexually active men and women are infected with HPV at some point in their lives, and as many as 80% of all women will have acquired HPV by age 50 (CDC, 2004a). Sexually active young adults, particularly 15- to 25-year-olds, are at the greatest risk for acquiring HPV, with a prevalence of 24% to 44% (Dunne et al., 2007; Schiffman, 1992).

Over 100 different types of HPV have been identified by DNA sequencing, and approximately 40 of them can infect the genital tract (deVilliers, Fauquet, Broker, Bernard, & zur Hausen, 2004). The majority of HPV infections are asymptomatic and transient, although clearance rates vary substantially. Approximately 70% of new HPV infections clear within 1 year and 90% clear within 2 years (Ho, Bierman, Beradsley, Chang, & Burk, 1998). Persistent infection with specific high-risk types of HPV is the primary cause of cervical cancer. The etiologic link between HPV infection and cervical cancer is well known and is one of the most firmly established relationships ever identified in cancer epidemiology. Human papillomavirus DNA was detected in 99.7% of cervical cancer samples in a large international cross-sectional study (Walboomers et al., 1999).

In the United States in 2006, 10 women died each day from cervical cancer.

Cervical cancer is the second most common cause of cancer mortality in women worldwide. Approximately 490,000 cases of cervical cancer are reported annually, and nearly half that many women die each year (Ferlay, Bray, & Pisani, 2005). Cervical cancer rates are lower in the United States than in developing countries as a result of widespread Pap smear testing. However, approximately 10,000 women were diagnosed with cervical cancer in the United States in 2006, with close to 4,000 deaths from the disease. Consequently, 10 women died each day from cervical cancer (American Cancer Society, 2006).

Condoms provide protection against most sexually transmitted infections; therefore, one could assume that condoms also protect against HPV. However, the transmission rate of HPV with condom use is less clear, as demonstrated by several longitudinal studies and a meta-analysis (Manhart & Koutsky, 2002; Winer et al., 2003, 2006). In June 2006, the Food and Drug Administration (FDA) approved a quadrivalent HPV vaccine to protect against HPV types 6, 11, 16, and 18. Several randomized controlled trials of the vaccine have demonstrated impressive protection against these four types of HPV (The FUTURE II Study Group, 2007; Garland et al., 2007; Villa et al., 2005; Villa, Ault, et al., 2006; Villa, Costa, et al., 2006). This article will evaluate the research evidence to compare the efficacy of condom use versus the HPV vaccine in the prevention of HPV infection.

Search Methodology

A review of literature was conducted using four main databases: Cochrane, CINHAL, PubMed, and Clinical Evidence. Various combinations of the terms HPV, vaccine, and condoms were used for the search. The search was limited to English, humans, meta-analysis, randomized controlled trials, clinical trials, and reviews. The search was not limited to a given age range. However, most of the studies reviewed focused on 15- to 25-year-olds since this age group has the greatest risk for acquiring HPV (Schiffman, 1992). The majority of studies pertaining to HPV were not conducted until the mid-1980s because HPV DNA testing was not available until that time; therefore, time limitations were not used for the search.

Overview of Condoms

The condom is one of the oldest forms of contraception, and its history and use can be traced back thousands of years. It is believed that a form of modern-day condoms was used by the Egyptians as far back as 1000 BC. The first published description and trials regarding prophylactic condom use were recorded by the Italian Gabrielle Fallopius in the 1500s. He claimed to have invented a sheath made of linen and conducted trials among 1,100 men using the condom, none of whom became infected with syphilis. The crepe rubber condoms that developed in the 1800s were superseded by the liquid latex condoms manufactured in the 1930s. Latex condoms continue to be primarily used today (Durex Web site, n.d.).

Studies have shown that when latex condoms are used correctly and consistently, they are highly effective in providing protection against sexually transmitted infections such as HIV, chlamydia, gonorrhea, syphilis, and trichomoniasis (CDC, n.d.; Holmes, Levine, & Weaver, 2004). HIV studies of discordant couples where one person is infected with HIV and the other is not have shown the strongest and most consistent evidence of infection protection provided by condoms. In a longitudinal study of discordant HIV couples, among 123 couples who reported consistent condom use, none of the uninfected partners became infected with HIV. Among the 122 couples who used condoms inconsistently, 12 of the uninfected partners became infected with HIV (DeVincenzi, 1994). In comparison, a meta-analysis of 25 studies of 504 discordant heterosexual HIV couples concluded that condoms provide an efficacy of 87% protection against the acquisition of HIV (Davis & Weeler, 1999).

Condom Use and HPV Infection

Although well-documented evidence exists regarding the effectiveness of condom use for prevention of many sexually transmitted infections, condom protection against HPV infection is not as clear. Manhart and Koutsky (2002) conducted a meta-analysis of 20 different studies evaluating whether or not condoms prevent genital HPV infection, external genital warts, or cervical neoplasia. Five of the studies assessed more than one outcome, for example, HPV DNA detection, genital warts, low-grade and high-grade dysplasia, and invasive cervical cancer, providing a total of 27 different estimates on the relationship between

HPV-related conditions and condom use. The authors noted two main limitations of the studies evaluated in the meta-analysis. First, the studies were not intended to explicitly evaluate condom use and therefore did not necessarily include a precise measure of proper and consistent condom usage. Second, many studies did not establish the temporal sequence. Temporal sequence can determine whether condoms were used before or after HPV infection. Without determining if individuals began using condoms while they were still free of infection, it is difficult to precisely evaluate the role that condoms play in preventing new infections.

Manhart and Koutsky (2002) found some degree of protection from HPV-associated conditions among 17 of the 27 populations studied; however, protection was small in most of the studies. The authors of the meta-analysis were unable to develop exact estimates of condom protection against HPV due to inconsistencies with the available data. These inconsistencies included the reported number of sexual partners, frequency of sexual intercourse, length of relationships, marital status, age of coitarche, number of lifetime partners, visits with prostitutes, known previous HPV exposure (e.g., warts), smoking, and oral contraceptive use. Despite these inconsistencies, Manhart and Koutsky (2002) concluded that although condoms may not prevent HPV infection, condom use may lower the risk for genital warts, high-grade dysplasia, and invasive cervical cancer. Based on the findings described below, it is doubtful that condoms offer the same level of protection against genital HPV infection as they do for HIV and other sexually transmitted infections.

Six studies included in Manhart and Koutsky's (2002) meta-analysis measured HPV DNA detection as the outcome, with only one of the studies showing a statistically significant protective effect with condom use. Manhart and Koutsky reported that this cross-sectional study showed an 80% decreased likelihood of cervical HPV DNA detection in women whose male partner always used condoms versus those who did not (adjusted odds ratio [OR_{adj}], 0.2; 95% confidence interval [CI], 0.1-0.6). Similarly, a cohort study found that women who reported always using condoms were less likely to become HPV DNA positive compared to women who reported never using condoms, but this difference was not statistically significant (OR_{adj}, 0.8%; 95% CI, 0.4-1.4). In contrast, another study they analyzed demonstrated a statistically significant increased risk for HPV DNA acquisition among women who reported condom use. Women who reported using condoms "always" or "most of the time" were 50% more likely to have HPV DNA detected than those who reported never using condoms (OR_{adj}, 1.5; 95% CI, 1.1-2.0). An additional study showed a small but not significant increased risk of HPV DNA detection in adolescent women who used condoms more than 75% of the time in comparison with those who used them less than 25% of the time (odds ratio [OR], 1.2; 95% CI, 0.7-2.1). Variations in the characteristics of the different samples may contribute to these mixed results.

Studies analyzed by Manhart and Koutsky (2002) measuring the relationship between condom use and the detection of both low-grade and high-grade cervical intraepithelial neoplasia (CIN) lesions showed mixed results. Four studies demonstrated no positive association between condom use and the development of low-grade CIN I. In fact, one showed an 80% increased risk of squamous intraepithelial lesions among women who reported using condoms (OR, 1.8; 95% CI, 1.4-2.4). The reported evidence also varied among the six studies evaluating the protective role of condoms with high-grade CIN II and III. One study analyzed found that women who reported any use of condoms with their husbands were 70% less likely to have CIN II or III than women who reported no use of condoms (OR_{adj}, 0.3; 98% CI, 0.1-0.8). A similar protective effect was found by another study where women were 40% less likely to have CIN II or III if they reported ever having used condoms versus those who had never used condoms (OR_{adj}, 0.6; 95% CI, 0.4-0.9). In women who already had histologically confirmed CIN, those who reported using condoms most or all of the time were 30% less likely to have CIN II (OR_{adj}, 0.7; 95% CI, 0.3-1.8) and 70% less likely to have CIN III (OR_{adj}, 0.3; 95% CI, 0.1-0.8). In contrast, one study analyzed showed no relationship between condom use and CIN II or III (OR_{adj}, 1.0; 95% CI, 0.5-2.7).

Of the five studies included in Manhart and Koutsky's (2002) meta-analysis, which examined the relationship between condom use and invasive cervical cancer, four of the studies showed a protective effect for invasive cervical cancer from 20% to 80%. One of these studies concluded that women whose husbands had ever used condoms were 80% less likely to have cervical cancer than those whose husbands had never used condoms (OR_{adj}, 0.2; 95% CI, 0.1-0.6). A case-controlled

study evaluating monogamous Thai women whose husbands visited with prostitutes found that women whose husband always or frequently used condoms in their visits with prostitutes were 50% less likely to have cervical cancer than women whose husbands rarely or never used condoms with prostitutes (OR_{adj}, 0.5; 95% CI, 0.2-1.0). In contrast, another study analyzed found no difference on the risk of cervical cancer for women who had used condoms for contraceptive for at least 5 years compared with those who had never used them (OR_{adj}, 1.0; 95% CI, 0.6-1.5). As before, differences in sample characteristics may contribute to differences in the findings from these studies.

The final two studies included in the meta-analysis (Manhart & Koutsky, 2002) indicated that condoms provide some protection against genital warts. In a study of 432 male military recruits, those using condoms were 70% less likely to have genital warts compared to those irregularly or never using condoms (OR, 0.3; 95% CI, 0.2-0.5). Similarly, in a study of men and women attending an STD clinic, those who reported always using condoms were 60% less likely to acquire genital warts compared to those who reported never using condoms (OR_{adj}, 0.4). However, for reasons that are not completely understood, women received slightly less protection from the condoms than did men.

To specifically evaluate the temporal relationship between male condom use and HPV infections in newly sexually active women, a longitudinal study was conducted (Winer et al., 2006). The study followed 82 female university students, aged 18 to 22 years, who reported their first intercourse with a male partner either during the study period or within 2 weeks prior to enrollment in the study. Cervical and vulvovaginal samples for HPV DNA testing and Pap smear testing were collected at a gynecologic examination at enrollment and every 4 months for almost 3 years. Every 2 weeks, women used electronic diaries to record information about their daily sexual behavior and condom usage. Women whose partners used condoms for all instances of vaginal intercourse were 70% less likely to acquire a new infection (37.8/100 patient-years) than were women whose partners used condoms less than 5% of the time (89.3/100 patient-years; adjusted hazard ratio [HR_{adj}], 0.3; 95% CI, 0.1-0.6; hazard ratio adjusted for number of new partners and number of previous partners of the male partner). Even women whose partners used condoms more than half of the time had a 50% risk reduction as compared with those whose partners used condoms less than 5% of the time (HR_{adj}, 0.5; 95% CI, 0.3-0.9). In women reporting 100% condom use by their partners, no cervical squamous intraepithelial lesions were detected in 32 patient-years at risk, whereas 14 lesions were detected during 97 patient-years at risk among women whose partners did not use condoms or used them less consistently (HR_{adj}, 0.0; 95% CI, 0.0-1.8). Therefore, the study demonstrates that among newly sexually active women, consistent condom use by their partners appears to significantly reduce the risk of cervical and vulvovaginal HPV infection (Winer et al., 2006).

Overview of HPV Vaccine

In 2002, the hallmark HPV vaccine trial for HPV type 16 demonstrated in a double-blinded placebo-controlled trial of 2,392 women that HPV infection could be prevented (Koutsky et al., 2002). In fact, results from the 48-month follow-up revealed that none of the vaccine recipients had developed HPV type 16–related CIN II and III (95% CI, 65%-100%; Mao et al., 2006). Success of this initial trial led to the development of the bivalent HPV 16/18 vaccine and the quadrivalent HPV 6/11/16/18 vaccine. The quadrivalent vaccine was FDA approved in June 2006 (FDA, 2006). The bivalent vaccine has yet to be FDA approved. Human papillomavirus types 16 and 18 are the most common oncogenic types of high-risk HPV and are associated with approximately 50% and 20% of cervical cancers, respectively. Human papillomavirus types 45 and 31 are the next most common oncogenic types of high-risk HPV, accounting for another 5% each. Low-risk HPV types, primarily 6 and 11, account for 90% of genital wart infections (Bosch et al., 1995; Walboomers et al., 1999). It is estimated that the HPV vaccine could prevent most high-grade precancerous lesions (CIN II or III), invasive cancers, and genital warts (Koutsky et al., 2002).

The HPV vaccine is composed of virus-like particles, which are recombinant proteins manufactured in benign biological systems (such as yeast), and have no known oncogenic or disease-causing potential (Frazer et al., 2006). The quadrivalent vaccine does not contain live virus and has been classified as a category B drug by the FDA. The vaccine is administered intramuscularly as a series of three injections at 0, 2, and

6 months (FDA, 2006). Studies have shown that the HPV vaccine is well tolerated without severe adverse events. The most common side effects include headache and injection site erythema and soreness (Harper et al., 2004, 2006; Villa et al., 2005).

Human Papillomavirus Vaccine and HPV Infection

The efficacy of the bivalent HPV 16/18 L1 virus–like particle vaccine was demonstrated in a double-blinded, randomized placebo-controlled trial in 1,113 women between the ages of 15 and 25 years (Harper et al., 2004). Study participants were randomly assigned to receive three doses of HPV vaccine types 16/18 or placebo at 0, 1, and 6 months, with follow-up through 27 months. Of the initial 1,113 participants, 776 women took part in an extended follow-up phase for up to 4.5 years from initial enrollment (Harper et al., 2006). The outcome showed the vaccine to be safe, effective, and immunogenic.

When the vaccine was administered according to protocol, 97% of women received protection against incident HPV types 16 and 18 infections compared to 89% of all participants (vaccine administered not according to protocol; 95% CI, 81.3-99.9). Protection against persistent HPV 16 and 18 infection occurred in 100% of women who received vaccination according to protocol and in 94% of all participants (95% CI, 33.6-100). No cases of CIN caused by HPV types 16 and 18 were reported in the vaccine group compared to eight cases in the placebo group (95% CI, 42.4-100). More than 98% of the vaccine recipients sustained seroconversion for more than 4.5 years for both types of HPV. The vaccine appeared to provide some cross protection against other types of HPV, as 94% and 55% of participants also demonstrated protection against incident infection with HPV types 45 and 31. The vaccine proved to be well tolerated without serious adverse events. Local injection site reactions were slightly more common in the vaccine group (94%) than in the placebo group (87.7%), but overall adverse events rates were equivalent in both groups (Harper et al., 2004, 2006).

The efficacy of the quadrivalent HPV 6/11/16/18 L1 virus–like particle vaccine has been demonstrated in several randomized, double-blinded placebo-controlled trials (The FUTURE II Study Group, 2007; Garland et al., 2007; Villa et al., 2005; Villa, Ault, et al., 2006; Villa, Costa, et al., 2006). The initial study included 552 women aged 16 to 23 years who were randomly assigned to receive three doses of HPV vaccine types 6/11/16/18 or placebo at 0, 1, and 6 months, with follow-up through 3 years. The trial results revealed a 90% decrease (95% CI, 71-97) in the combined incidence of persistent HPV 6, 11, 16, or 18 infection or associated genital disease in women who received the vaccine versus those who received placebo. There were no reported cases of CIN caused by these four strains for vaccine recipients compared to seven cases in the placebo group. The vaccine also demonstrated 100% protection against external genital warts caused by HPV types 6 and 11 compared to four cases in the placebo group (Villa et al., 2005). At 36 months, seroconversion rates after administration of all three vaccine doses were 94%, 96%, 100%, and 76% for HPV types 6, 11, 16, 18, respectively (Villa, Ault et al., 2006). Overall efficacy for HPV 6, 11, 16, and 18 was 100%, 100%, 86%, and 89%, respectively (Villa et al., 2005).

A subset of 241 of the same cohort of women were followed for another 2 years (for a total of 5 years) and demonstrated that vaccine-induced anti-HPV titers remained at or above those following natural infection. Therefore, the combined incidence of HPV types 6-, 11-, 16-, and 18-related persistent infection or disease was reduced in the vaccine recipients by 96% (95% CI, 83.8-99.5). Similar to the first part of the study, there were no cases of HPV types 6-, 11-, 16-, and 18-related CIN or genital warts in vaccine recipients compared to six cases in the placebo group (95% CI, 12.4-100). One case of persistent HPV type 18 infection occurred in the vaccine group compared to 22 cases of persistent infection or disease in placebo group (95% CI, 69.4-99.9). Therefore, the prophylactic quadrivalent HPV vaccine was effective through 5 years for prevention of persistent infection and disease caused by HPV types 6, 11, 16, and 18 (Villa, Costa, et al., 2006).

Two phase 3 trials were conducted to evaluate the efficacy of the quadrivalent vaccine (The FUTURE II Study Group, 2007; Garland et al., 2007). Both trials were placebo-controlled double-blinded trials that randomized women to receive either placebo or vaccine at 0, 2, and 6 months. The women were followed for an average of 3 years after receiving the first dose of vaccine or placebo. The first trial, involving 5,455 women between the ages of 16 and 24 years, was 100%

effective (95% CI, 94-100) in preventing anogenital disease (i.e., vaginal, vulvar, perineal, and perianal intraepithelial lesions or warts) compared to 60 cases in the placebo group. The vaccine was 100% effective (95% CI, 94-100) in the prevention of CIN compared to 65 cases in the placebo group (Garland et al., 2007). More vaccine recipients (87%) reported adverse events at the injection site, particularly pain, compared to placebo recipients (77%).

The second phase 3 trial involved 12,167 women between the ages of 15 and 26 years. The trial demonstrated a significantly lower occurrence of CIN II or greater in the vaccine group compared to those in the placebo group. Vaccine efficacy for the prevention of the primary endpoint was 98% (95% CI, 86-100). The endpoint was defined as CIN grade II or III, adenocarcinoma in situ, or cervical cancer related to HPV types 16 or 18. One woman in the vaccine group and 42 women in the placebo group received the diagnosis of CIN II or greater associated with HPV 16 or 18 (The FUTURE II Study Group, 2007). Seroconversion rates at 24 months were 96%, 97%, 99%, and 68% for HPV types 6, 11, 16, and 18, respectively. Similar to previous trials, pain at the injection site was reported more commonly among the vaccine group (84.4%) compared to the placebo group (77.9%).

Vaccine Versus Condom Use

The evidence-based efficacy of condom use in the prevention of HPV infection is inconsistent compared to the HPV vaccine. Several longitudinal studies, including a meta-analysis of cross-sectional, case-controlled, and cohort studies, showed substantial variability in condom protection of HPV infection from 0% to 80% (Manhart & Koutsky, 2002; Winer et al., 2006). In comparison, several double-blinded, randomized placebo-controlled HPV vaccine trials demonstrated an impressive range of protection from 86% to 100% (Garland et al., 2007; The FUTURE II Study Group, 2007; Villa et al., 2005; Villa, Ault, et al., 2006; Villa, Costa, et al., 2006). Despite the strong efficacy of the HPV vaccine, it does not protect against all types of HPV; therefore, condom use may still play a role in reducing infection transmission for both men and women. Although review of the literature contains no comparative studies of the efficacy of condoms versus the HPV vaccine, or both methods used concomitantly, the evidence is clear that the HPV vaccine is superior to condoms in preventing HPV infections. However, additional factors support condom use in addition to HPV vaccine for prevention of cervical cancer, protection against strains of HPV not in the vaccine, and protection against other sexually transmitted infections including HIV.

Rationale for Condom Use

Despite the variability of condom use in preventing HPV infections, condoms have other benefits related to HPV infections and other sexually transmitted infections. There are two main considerations for the use of condoms. The first consideration is that only women are being vaccinated for HPV at the present time. However, men are also at risk for acquiring HPV, including genital warts, and although rare, men can also develop HPV-related penile and anal cancers. Bleeker et al. (2003) demonstrated that condom use promotes regression of HPV-associated penile lesions in men whose partners have CIN. The median time for regression of flat penile lesions was 7.4 months for condom users versus 13.9 months for noncondom users (95% CI, 1.2-3.7). This effect is likely related to blocking viral transmission between sexual partners. Therefore, condoms can help provide protection for men in addition to protection against other sexually transmitted infections, such as HIV (Bleeker et al., 2003; Davis & Weeler, 1999; DeVincenzi, 1994; Holmes et al., 2004).

The second consideration is that evidence has shown that in women who have already been infected with HPV, condom use may also help facilitate CIN regression (Coker, Sanders, Bond, Gerasimova, & Pirisi, 2001; Hogewoning et al., 2003). For example, Hogewoning et al. (2003) randomly allocated 135 women not using condoms who had untreated CIN and their male partners either to use condoms or not to use condoms for all instances of vaginal intercourse. Those couples randomized to use condoms had a significantly higher cumulative 2-year rate of disease regression (53% vs. 35%; 95% CI, 1.4-7.1) as well as a higher cumulative 2-year rate of HPV clearance (23% vs. 4%; 95% CI, 1.5-97.2) than controls. Researchers hypothesize that consistent protection of the cervix by a barrier method, primarily a condom, may provide protection even when the woman is already HPV positive because the cervix is not repeatedly exposed to an HPV-positive partner. This finding is important as it implies that consistent condom use may protect a woman from developing CIN perhaps by decreasing the chances of additional

HPV exposure (Coker et al., 2001). These results suggest that condoms may prevent progression to lesions (warts and low- and high-grade intraepithelial neoplasia) but perhaps not actual HPV infection.

Rationale for Vaccination

Several valid reasons for utilization of the HPV vaccine are clear. Studies have suggested that complete protection from genital HPV infection with condoms may be impossible because infections may occur at epithelial sites not covered by the condom. Winer et al. (2003) showed that 9.7% of women who reported nonpenetrative sexual contact tested positive for HPV DNA. It has been hypothesized that when condoms are used primarily for contraceptive purposes, the condom may not be put on until after external genital contact has occurred, thus increasing the risk of HPV acquisition. Similarly, several studies have found that condoms for contraception only have been found to provide the least protection for cervical intraepithelial lesions, genital warts, and invasive cervical cancer (Kataja et al., 1993; Kjaer et al., 1991; Syrjanen et al., 1984; Wang & Lin, 1996; Zondervan, Carpenter, Painter, & Vessey, 1996).

With an HPV prevalence rate of up to 44%, sexually active young adults, particularly 15- to 25-year-olds, are at the greatest risk for acquiring HPV (Dunne et al., 2007). Several well-documented risk factors for this increased risk of HPV acquisition include young age at sexual debut, multiple sexual partners, smoking, oral contraceptive use, and inconsistent condom use (Winer et al., 2003). In 15- to-19-year-olds, 66.4% of women and 70.9% of men report using condoms at their sexual debut. However, only 35% of men and 25% of women aged 15 to 24 years report using condoms consistently thereafter (CDC, 2004b). This degree of inconsistency may provide an increased opportunity for HPV infection. The quadrivalent vaccine's known efficacy of at least 5 years would provide protection against the most oncogenic strains of HPV and genital warts for a population at the greatest risk for infection.

From a public health perspective, vaccinating adolescents and young adults could greatly reduce the burden of cervical and genital cancers, precancerous dysplasia, and genital warts. Sanders and Taira (2003) estimate that vaccination of the entire U.S. population of 12-year-old girls would prevent more than 200,000 HPV infections, 100,000 abnormal cervical cytology examinations, and 3,300 cases of cervical cancer. It has also been estimated that by vaccinating a cohort of 12-year-olds who receive 100% vaccination coverage, there would be a 70% reduction in the prevalence of high-grade cervical dysplasia and a 76% reduction in cervical cancer deaths throughout their lifetime (Villa, Costa, et al., 2006). This would result in a reduction in lifetime risk of cervical cancer at a cost of $23,000 (2002 dollars) per quality-adjusted life year compared with no vaccination (Sanders & Taira, 2003). Hence, these findings are compelling reasons for vaccination.

More than 9% of virginal women with history of nonpenetrative sexual contact test positive for human papillomavirus DNA.

Rationale for Condoms and Vaccine

The quadrivalent HPV vaccine is highly effective in providing protection against HPV types 6, 11, 16, and 18, including some cross protection against types 31 and 45. However, over 100 different types of HPV exist, 40 of which can infect the genital tract. Therefore, vaccination does not offer 100% protection against HPV. Condoms may offer some additional protection, although variable, against other types of HPV. It has been hypothesized that even with use of the quadrivalent vaccine, consistent condom use may protect women against infection with other high-risk types of HPV that put them at risk for cervical cancer (Winer et al., 2006).

It is important to consider that HPV is transmitted through skin-to-skin contact. A study of college students found that any type of nonpenetrative sexual contact (finger-vulvar, penile-vulvar, or oral-penile) was associated with an increased risk of genital HPV infection in virginal women. Of 72 virginal women reporting nonpenetrative sexual contact, 7 tested positive for HPV DNA (9.7%), whereas only 1 of 76 women (1.3%) reporting no such contact tested positive (Winer et al., 2003). Therefore, wearing condoms in combination with the HPV vaccine will provide the greatest degree of protection, even for those without a history of penetrative intercourse.

Implications for Practice

Human papillomavirus is the most common sexually transmitted infection in the world and causes significant burden of disease with cervical and genital cancers, precancerous dysplasia, and

The greatest degree of protection against human papillomavirus infection is with the simultaneous use of both condoms and the human papillomavirus vaccine.

genital warts. The quadrivalent HPV vaccine is a significant advancement in women's health care and cancer prevention. Strong evidence supports the efficacy of the HPV vaccine against HPV types 6, 11, 16, and 18 with minimal adverse events. Although studies of condom use have shown wide variation in the ability of condoms to protect against HPV infection, condoms have the additional advantage of protection against other sexually transmitted infections. In addition, condoms may help facilitate regression of CIN in women and penile lesions in men who have already been infected with HPV. Reducing the cost, morbidity, and mortality of HPV-related disease through primary prevention is paramount. After evaluating all the relevant data, the evidence suggests that the greatest degree of protection from the untoward effects of HPV infection is with the simultaneous use of both condoms and the HPV vaccine.

When HPV vaccine is being considered, the implications for practice go beyond providing a clear message about the efficacy of the HPV vaccine in preventing cervical cancer. For example, nurses must be prepared to address some of the controversial issues surrounding the HPV vaccine as it involves adolescents, a sexually transmitted infection, and possible state mandates for entry into school. Nurses play a critical role in educating young patients and their parents about vaccine recommendations including the findings presented in this article. Emphasis must be placed on the fact that although the HPV vaccine is a useful tool for disease prevention, it does not protect against all strains of HPV and does not replace the need for condom use. In addition, it does not replace the need for regular Pap screening since it is still possible to have an abnormal Pap smear or develop genital warts from HPV strains not covered in the vaccine. Therefore, routine Pap and sexually transmitted infection screening should be stressed for women who are sexually active.

When women elect to receive the vaccine, compliance with completion of the three-dose vaccination regimen may present a challenge. The importance of completing the entire vaccination series must be stressed since an effective immune response will not develop until after the third injection is administered (Villa, Ault, et al., 2006). According to Garland et al. (2007), at least 99.5% of patients will demonstrate an immunogenic response 1 month after the third injection. A plan should be developed with each patient in order to help facilitate completion of the vaccination series. In summary, it is imperative for nurses to have a clear understanding about HPV and the vaccine, be aware of the implications of infection, be prepared to educate patients and their parents, and be ready to address potential controversies and parental concerns surrounding the vaccine.

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