



Research Paper

Implementation of a targeted HPV educational program in a population with HIV

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Abstract Patients living with human immunodeficiency virus (PLWH) are at higher risk of developing human papillomavirus (HPV)-associated malignancies. This prospective, longitudinal study evaluated the baseline knowledge of PLWH regarding HPV infection and its association with head neck cancer, and it aimed to determine whether a focused educational session could promote both short- and long-term knowledge acquisition in this population. Twenty-seven subjects participated in an interactive educational session and completed pre-test and immediate and delayed (4-month) post-test questionnaires. When compared to their pre-test answers, subjects demonstrated significant improvements in all 28 questions immediately following education. Knowledge preservation was demonstrated 4 months after initial evaluation, with subjects performing significantly better than their pre-test scores in 24 of the original 28 questions. These results suggest that short, focused, educational programs for PLWH may promote a better understanding of HPV's association with human immunodeficiency virus (HIV) and HPV risk factors, methods of transmission, and prevention.

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Introduction

There are an estimated 36 million individuals living with human immunodeficiency virus (HIV) worldwide, with over 2 million new cases per year.¹ Patients living with HIV (PLWH) are at risk of developing numerous malignancies, including acquired immune deficiency syndrome (AIDS)-defining cancers such as Non-Hodgkin lymphoma, invasive cervical carcinoma, and Kaposi's sarcoma.² While the incidence of AIDS-defining malignancies has decreased over time, the frequency of non-AIDS-defining cancers has increased compared to the general population.^{3,4} Further, the dramatically improved efficacy of antiretroviral therapy (ART) has allowed patients to live longer, resulting in fewer patients dying from acute complications and more from longer-term consequences of HIV. The proportion of patients dying from HIV-related malignancies, for example, has increased from 10% prior to the introduction of potent ART to 28% in 2000.³⁻⁵

Over 550,000 people worldwide are diagnosed with head and neck cancer each year, and 380,000 die from these malignancies annually.⁶ Risk factors for head and neck cancer include tobacco use, alcohol consumption, viral infection (e.g. human papilloma virus (HPV) and Epstein-Barr virus), radiation exposure, and immunodeficiency. Associations between HIV and HPV have also been extensively documented in the existing literature.⁷⁻¹⁰ Epidemiologic studies comparing individuals with and without HIV have shown a higher incidence of HPV detection among HIV-infected men and women, decreased rates of HPV clearance, and concordance of like HPV genotypes between partners. Co-infection with multiple HPV genotypes has also been associated with greater likelihood of HIV seroconversion.¹¹

As advancements in HIV treatment continue to improve the life expectancy such that patients are more commonly experiencing longer-term manifestations of HIV, patients must become more aware of the increasingly prevalent and life-threatening complications of the infection. Although there is a substantial link between HIV and HPV, the knowledge base of HIV-infected patients relative to the epidemiology, signs, symptoms, risk factors, and complications of HPV co-infection is not well understood.¹² With the perpetually increasing breadth of medical knowledge, significant advancements have been made toward patient education, shared patient-provider decision-making, and improved access to knowledge for all. This study sought to assess the relative knowledge base in a subset of patients at higher risk of acquiring HPV infection and HPV-associated malignancies, and additionally aimed to evaluate whether a short, directed, and patient-focused educational session performed in clinic can engender immediate and sustained knowledge acquisition.

Materials and methods

Recruitment and data collection

Approval was obtained from the Stanford University Research Compliance Office (the Institutional Review Board) prior to data collection (eProtocol #36152). Patients

were recruited at the Stanford Positive Care Clinic, a multidisciplinary clinic located in Atherton, California that provides comprehensive primary and HIV specialty care. Patients were eligible if they were English-speaking individuals previously diagnosed with HIV and above the age of 18 years old. The attending physician directed the author to the eligible patients.

The implementation of a patient education program requires selection of an appropriate medium. For this study, we chose to approach patients in the waiting room as, on average, a patient may wait over 40 min before seeing a physician.¹³ During this time, patients are often heavily focused on their reasons for seeing the physician, making this period opportune for patient education. Patients were approached during their routine clinic visits with their infectious disease physician during the National Oral, Head and Neck Cancer Awareness Week (April 11-15, 2016) and asked whether they would like to partake in an experimental patient education program.¹⁴ Informed consent was obtained from all individual participants included in this study. Afterward, subjects completed a basic demographics and family history questionnaire, in addition to a 28-item knowledge-based questionnaire (pre-test). Possible answer choices for the knowledge assessment were either "yes", "no", or "unsure". Subjects then participated in a one-on-one, focused, interactive, verbal educational session with one of the authors (NA) that discussed the signs, symptoms, risk factors, and precautionary measures for HPV and head and neck cancer. The association between HPV and HIV was also examined in detail. Immediately after the educational session, subjects were asked to complete an identical knowledge-based questionnaire (immediate post-test).

Four months after study enrollment, subjects were asked to complete the same questionnaire (delayed post-test). All subjects were contacted 3 times over a span of 3 weeks via either traditional mail or email. Subjects who did not respond after 3 contact attempts were considered lost to follow-up. Responses were compared across time, with the pre-test serving as the control and the delayed post-test as a measure of longer-term knowledge retention. All questionnaires were completed independently by the subjects without any assistance or interaction with others.

Statistical analysis

Statistical analysis was performed using Prism (version 7.0; GraphPad Software, La Jolla, CA). The baseline characteristics and questionnaire responses were compared across treatment groups using categorical statistical tests. For ease of analysis, all incorrect answer choices (either yes/unsure or no/unsure) were grouped together and compared against the frequency of correct answer choices. All data were treated as nonparametric, and paired sample *t*-tests were performed to compare the pre- and post-test scores. A standard alpha level 0.05 was used to determine significance for all calculations. Data was recorded and stored on Research Electronic Data Capture (REDCap), a secure, web-based application. Each subject was given a numerical patient identifier that permitted secure coding of data.

Results

Demographics and baseline characteristics

Twenty-nine patients were approached, and of those, 27 enrolled in the study. Of these 27 who participated, 24 (89%) were male and 20 (75%) were Caucasian (Table 1). The average age of participants was 48 years old (range 29–74). Fourteen (52%) had a history of tobacco use, 23 (85%) a history of alcohol consumption, and 6 (22.2%) a previous diagnosis of cancer. None had a personal history of head and neck cancer, but 3 (11%) had a family history of head and neck cancer. Of the 27 total subjects, 3 (11%) had previously received the HPV vaccination.

Pre-test analysis

Pre-test results were recorded immediately prior to patient education and revealed limited knowledge related to the clinical aspects of HPV within this cohort of patients (Table 2). All subjects were literate in English and completed the pre-test independently without the help of the interviewer and without the ability to ask the interviewer questions. Subjects had the option to choose “yes/true”, “no/false”, or “unsure”. All incorrect or “unsure” answers were combined and compared to the number of correct responses. Seventeen (65%) had previously heard of HPV, while 6 (23%) had not and 3 (12%) were unsure if they had. Five patients (19%) correctly answered that HPV is associated with head and neck cancer and two (7%) that there was an association between HIV and HPV infections.

Immediate post-test analysis

Subjects demonstrated a statistically significant improvement in all 28 knowledge-based questions immediately after the educational session (Table 2). Notably, the ability to recognize that HPV is common in adults increased from 37 to 100% ($P < 0.0001$), the ability for HPV to cause head and neck cancer increased from 19 to 100% ($P < 0.0001$), the ability to transmit HPV despite absence of visible genital warts improved from 33 to 93% ($P < 0.0001$), and the recognition of an association between HIV and HPV increased from 7% to 93% ($P < 0.0001$).

Table 1 Demographics and baseline characteristics.

Characteristic	n (%)
Age, mean (SD)	48.1 (13.9)
Gender, n female (%)	3 (11.1)
Ethnicity	
Caucasian/White	20 (74.4)
Hispanic/Latino	5 (18.5)
Asian	0
Black	2 (7.4)
Any current or prior tobacco use	14 (51.9)
Any current or prior alcohol consumption	23 (85.2)
Family history of head and neck cancer	3 (11.1)
Personal history of cancer	6 (22.2)

Despite completing the post-test questionnaire immediately following education, a noteworthy number of subjects answered some questions incorrectly. For example, 52% of subjects incorrectly answered that HPV-associated cancers are usually seen in people who also drink alcohol and/or use tobacco products, and 63% of subjects stated that HPV is commonly transmitted through kissing. Both of these questions, however, had significant improvement compared to pre-test evaluation.

Delayed post-test analysis

The delayed post-test questionnaires were completed 4 months after initial evaluation by 14 (52%) of subjects (Table 3). The average age of these patients was 49 years old (range 29–71). Twelve (86%) were male and 10 (71%) were Caucasian, 3 (21%) Hispanic, and 1 Asian (7%). Two (14%) had a family history of head and neck cancer. Patients showed significant improvement when compared to pre-test responses in 24 of the 28 questions (86%). For 4 of the 28 questions, subjects did not show significant improvement at 4 months compared to baseline, although they did during the immediate post-test assessment. These questions asked about pain as a common symptom of head and neck cancer ($P = 1.0000$), the association between HPV-associated cancers and age ($P = 0.1201$), asymptomatic HPV infections ($P = 0.0542$), and whether HPV is commonly transmitted through kissing ($P = 0.6776$). This illustrates some loss of knowledge during the 4-month period between education and the delayed assessment.

Discussion

HPV has been associated with anogenital (cervical, vaginal, penile, anal) and head and neck (base of tongue and oropharyngeal) cancers.² The relationship between HIV infection and HPV-associated cancers stems from multiple fronts: lifestyle factors may increase the risk of contracting both infections, altered T cell function may limit complete and timely eradication of HPV, and the likelihood of persistent HPV infection may increase concomitantly with greater immunosuppression.¹⁵ Despite the relative prevalence, head and neck malignancies do not typically receive as much media attention as other cancers, resulting in a limited understanding of these cancers among the general public.¹⁶

The exponential increase in medical knowledge, coupled with progressively shortened patient visits, has burdened patients and health professionals alike.¹⁷ In order to adhere to their overstretched daily schedules, health professionals often must speak quickly and concisely, and then schedule a follow-up appointment to discuss lingering questions or concerns. This has made it nearly impossible for physicians and other medical professionals to thoroughly educate patients and provide a full discussion of the disease at hand. Given these clinical limitations, there is a need to identify new strategies for information dissemination. To promote awareness, health professionals must ensure that patients understand the potential short- and long-term complications, signs and symptoms of any local or systemic manifestations of disease, and preventative measures. This is

Table 2 Comparison of pre-test and immediate post-test questionnaire responses (n = 27, n (%)).

Questions	Pre (correct responses)	Immediate post (correct responses)	P-value
Is HPV common in adults? (yes)	10 (37)	27 (100)	<0.0001
Do you think HPV is associated with head and neck cancer? (yes)	5 (19)	27 (100)	<0.0001
One of the signs and symptoms of head and neck cancer is pain (true)	16 (59)	23 (85)	0.0091
If detected early ^a , the survival rate of head and neck cancer is >80% (true)	8 (30)	25 (93)	<0.0001
People with HIV are more likely to develop head and neck cancer than people without HIV (true)	5 (19)	27 (100)	<0.0001
HPV is the most common sexually transmitted infection in adults (true)	4 (15)	25 (93)	<0.0001
People with HIV are more likely to have HPV-associated cancers (true)	7 (26)	27 (100)	<0.0001
HPV-associated cancers have a higher survival rate than non-HPV cancers (true)	7 (26)	26 (96)	<0.0001
HPV can cause cervical cancer (true)	15 (56)	23 (85)	0.0352
HPV can cause penile cancer (true)	6 (22.2)	25 (93)	<0.0001
HPV can cause anal cancer (true)	14 (52)	27 (100)	<0.0001
HPV can cause oral cancer (true)	8 (30)	27 (100)	<0.0001
There is no association between HPV and HIV (false)	2 (7)	25 (93)	<0.0001
HPV-associated cancers more commonly occur in older adults (false)	3 (11)	23 (85)	<0.0001
HPV-associated cancers are more commonly seen in people who also drink alcohol and/or use tobacco products (false)	5 (19)	13 (48)	0.0418
In general, HPV-associated cancers are harder to treat than non-HPV cancers (false)	5 (19)	25 (93)	<0.0001
HPV is transmitted through sexual intercourse (true)	14 (52)	27 (100)	<0.0001
With more sexual partners, I have increased risk of infection with HPV (true)	13 (48)	25 (93)	0.0007
Using condoms correctly reduces the risk of acquiring HPV infection (true)	13 (48)	25 (93)	0.0007
Someone can be infected with HPV and show no symptoms (true)	7 (26)	24 (89)	<0.0001
I can only be infected with HPV if my partner has genital warts (false)	9 (33)	25 (93)	<0.0001
If I have been vaccinated for HPV, I cannot be infected with HPV (false)	6 (22)	26 (96)	<0.0001
HPV is commonly transmitted through kissing (false)	3 (11)	17 (63)	0.0002
HPV is commonly transmitted through sneezing/coughing (false)	7 (26)	25 (93)	<0.0001
HPV is commonly transmitted from toilet seats (false)	5 (19)	22 (82)	<0.0001
HPV is commonly transmitted due to poor hygiene (false)	3 (11)	24 (89)	<0.0001
HPV is commonly transmitted through blood transfusions (false)	3 (11)	22 (82)	<0.0001
Sharing food and utensils puts me at risk for HPV infection (false)	6 (22)	25 (93)	<0.0001

HIV, human immunodeficiency virus; HPV, human papillomavirus.

^a "Early" here refers to "early-stage" cancers.

especially evident for certain disorders in which increasing life expectancy can lead to a higher prevalence of secondary complications of disorders. Additionally, given the increasing amount of information available to patients, it is necessary to ensure that patients receive education through reliable sources such as their healthcare providers. Patient education programs similar to the one employed in this study may help patients better understand their diagnosis and treatment options, and this interaction may prompt more substantial discussion and collaboration between patients and providers. Such educational endeavors may also be beneficial in underserved areas where information may not otherwise be readily available.¹⁸ Additional studies would need to be performed to help verify this.

Prior research has shown that patients cannot recall significant portions of their typical discussions with a physician, including surgical consent and preventative health measures.^{19–21} Patient-centered educational programs, however, can help patients learn more about their illness, identify worrisome risk factors or progression of disease, and better comprehend methods of prevention.^{22,23} In the age of the internet and easy access to

endless amounts of potentially inaccurate information, a healthcare professional-directed educational format provides patients with standardized, evidence-based, and trustworthy information that patients can consume at their own pace.

Although many patients showed an increase in knowledge following education, the pre-test responses demonstrated that HPV-associated knowledge was very limited at baseline. This is especially worrisome given the increased risk of HPV-associated malignancies in this patient population. A number of studies have previously illustrated the benefits of head and neck cancer screenings, in addition to awareness and prevention programs.^{24–26} Some studies involved general screenings, while others have targeted specific subgroups in which there may be a higher prevalence of habits that increase the risk for head and neck cancer, such as NASCAR events.^{26,27} While these endeavors have proven successful, this study demonstrates the need for more extensive and creative forms of patient education, especially within high-risk patient populations such as those with HIV. However, it must be noted that not all screenings have been shown to be beneficial, and they in contrast may

Table 3 Comparative analysis of the pre-test and delayed (4-month) post-test responses (n = 14^a, n (%)).

Questions	Pre (correct responses)	Delayed Post (correct responses)	P-value
Is HPV common in adults?	6 (43)	14 (100)	0.0019
Do you think HPV is associated with head and neck cancer?	4 (29)	13 (93)	0.0013
One of the signs and symptoms of head and neck cancer is pain	9 (64)	9 (64)	1.0000
If detected early ^b , the survival rate of head and neck cancer is >80%	5 (36)	13 (93)	0.0044
People with HIV are more likely to develop head and neck cancer than people without HIV	4 (29)	14 (100)	0.0002
HPV is the most common sexually transmitted infection in adults	3 (21)	12 (86)	0.0018
People with HIV are more likely to have HPV-associated cancers	5 (36)	13 (92.9)	0.0044
HPV-associated cancers have a higher survival rate than non-HPV cancers	4 (29)	12 (86)	0.0063
HPV can cause cervical cancer	8 (57)	14 (100)	0.0159
HPV can cause penile cancer	6 (43)	12 (86)	0.0461
HPV can cause anal cancer	5 (36)	13 (93)	0.0044
HPV can cause oral cancer	8 (57)	14 (100)	0.0159
There is no association between HPV and HIV	2 (14)	13 (93)	0.0001
HPV-associated cancers more commonly occur in older adults	3 (21)	8 (57)	0.1201
HPV-associated cancers are more commonly seen in people who also drink alcohol and/or use tobacco products	3 (21)	10 (71)	0.0213
In general, HPV-associated cancers are harder to treat than non-HPV cancers	4 (29)	11 (79)	0.0213
HPV is transmitted through sexual intercourse	9 (64)	14 (100)	0.0407
With more sexual partners, I have increased risk of infection with HPV	8 (57)	14 (100)	0.0159
Using condoms correctly reduces the risk of acquiring HPV infection	8 (57)	13 (93)	0.0768
Someone can be infected with HPV and show no symptoms	5 (36)	11 (79)	0.0542
I can only be infected with HPV if my partner has genital warts	6 (43)	13 (93)	0.0128
If I have been vaccinated for HPV, I cannot be infected with HPV	3 (21)	13 (93)	0.0003
HPV is commonly transmitted through kissing	3 (21)	5 (36)	0.6776
HPV is commonly transmitted through sneezing/coughing	6 (43)	13 (93)	0.0128
HPV is commonly transmitted from toilet seats	4 (29)	12 (86)	0.0063
HPV is commonly transmitted due to poor hygiene	2 (14)	11 (79)	0.0018
HPV is commonly transmitted through blood transfusions	0	9 (64)	0.0006
Sharing food and utensils puts me at risk for HPV infection	5 (36)	13 (93)	0.0044

HIV, human immunodeficiency virus; HPV, human papillomavirus.

^a Subjects lost to follow up were excluded from this analysis.

^b "Early" here refers to "early-stage" cancers.

have unintended harmful consequences, including false positives, over-diagnosis or over-treatment of benign lesions, and increased psychological stress.²⁸ These potential harms and benefits must be weighed against each other.

Providing in-person education has obvious pitfalls, including scalability and sustainability due to limited personnel. Another, less employee-intensive, medium is a video. Educational programs like Khan Academy have had immense success using relatively short, interactive, and focused videos.²⁹ Similar videos have also been used in the medical profession, with Pathoma already educating thousands of medical students.³⁰ A number of studies have also illustrated the benefit of video-based patient education on raising awareness, promoting prevention, and improving overall understanding.^{31–34} A direction for future action would be development of educational videos that could substitute for one-on-one in person education. Such an educational model has the benefit of scalability, implementation in resource limited environments, and review by patients in the future.

This study has a number of limitations. In addition to loss to follow-up, this study evaluated a relatively small sample

of the entire HIV population in the United States. Epidemiologic studies have shown that HIV disproportionately affects some segments of the population. In 2014, for example, 49 and 18% of new HIV diagnoses in the United States occurred in African Americans and Latinos, respectively.³⁵ The demographic characteristics of this study's participants (74% Caucasian) did not correlate with those of general population being diagnosed with HIV. While no separate control group was used for the delayed post-test questionnaire, the subjects served as their own controls, as the purpose was to demonstrate a sustained transfer of knowledge over time. It remains to be seen whether larger-scale, patient-directed videos are capable of imparting substantial and enduring knowledge. Further studies are also necessary to determine the optimal interface (i.e. in-person, video, etc.) that is sustainable and scalable while generating long-term knowledge acquisition.

Conclusions

The association between HIV and HPV infection, in addition to the diverse set of longer-term complications of

concomitant infection, has been well documented in the literature. Patients with HIV are at higher risk of developing HPV-associated cancers and thus require extensive education on the subject. Although the patients in this study did not have high baseline knowledge of the association between HIV and HPV, they demonstrated the ability to retain a wealth of information. This suggests that similar, patient-focused educational programs can significantly augment patient knowledge and promote awareness. A greater push to perform these educational sessions by primary providers has the potential to dramatically improve patient understanding of their condition.

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Conflicts of interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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