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Can HPV Vaccination Prevent Oral Cancer? Current Evidence and Clinical Implications

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Abstract

Introduction: Benign and malignant neoplasms in humans have been causally related with HPV (Human papillomavirus), and specifically in locations such as the cervix, vagina, penis, anus, and oropharynx. Current evidence indicates an increased incidence of Oropharyngeal Squamous Cell Carcinoma (OPSCC), underscoring the need for an effective preventive vaccination strategy.

Methods: The current evidence was reviewed in the literature to investigate the impact of the HPV vaccine as a preventive measure for OPSCC, mainly by reducing the incidence of HPV infection of the oropharynx. Previous studies whose objective was the clinical efficiency of the immunological response to the vaccination have been reviewed.

Results: HPV vaccination targets specific oncogenic genotypes, such as HPV-16 and HPV-18, and prevents infectious, precancerous, and malignant lesions of anogenital and oropharyngeal location. Anti-HPV antibodies have been isolated from oropharyngeal secretions and play a pivotal role as mucosa-protecting substances.

Conclusions: HPV-positive OPSCC cases could be eliminated by the widespread implementation of HPV vaccination in female and male adolescents, even though carcinogenesis is a long-term process. Clinical evidence-based perspectives are delineated in this review, as future modalities should nevertheless be investigated.

Keywords: HPV; Oral cancer; Hpv vaccination; Oral pathology; Oral surgery

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Introduction

HPV infection of the anogenital tract is characterized as a global public health issue, with over 200 genotypes isolated, and a subset of high-risk genotypes responsible for various malignant neoplasms [1]. The oncogenic HPV16 genotype primarily causes OPSCC, as its protein p16 is consistently found in these tumor cells [2]. Longitudinally, the focus of public health providers was shifted to the cancer of the cervix due to the higher incidence observed with screening strategies and vaccines [3]. As a result, the incidence of cervical cancer decreased globally [4]. On the other hand, HPV-positive OPSCC has resumed an upward trend nowadays in Europe and the USA, hereby recommending a rising public health issue [4]. Oral cavity cancer has a distinct biological substrate from oropharyngeal cancer; however, they are often grouped under oral cancer [5]. Tobacco and alcohol consumption are strongly related to oral cavity cancer, whereas HPV indicates an oncogenic behavior mainly in the oropharynx (HPV-positive OPSCC) [6].

Secondary prevention programs for early diagnosis of HPV-positive OPSCC are not implemented as a screening process in the general population [7]. Therefore, an efficient vaccination strategy is an important measure for controlling and reducing the incidence of malignant transformation [8]. In a global context, HPV vaccination rates are rising, more efficiently in female and male adolescents, making it a necessity to investigate also the efficacy in preventing HPV-positive OPSCC [9,10]. Clinical perspectives of evidence-based literature in daily practice and public health are discussed in this review.

Methods

Oral cavity squamous cell carcinoma related to tobacco and alcohol consumption has a worse clinical prognosis, distinct pathogenetic and epidemiologic pattern than HPV-positive Oropharyngeal Squamous Cell Carcinoma (OPSCC) [11]. HPV-positive OPSCC's main cause is the infection from HPV16 genotype involved in carcinogenesis [12]. In the vast majority of cases,

the host's naïve immunological response mechanisms clarify a parodic HPV infection when there is no immunosuppression [12]. Over time, molecular errors accumulate in a pattern that enhances the development of a malignant neoplasm [13]. HPV oncoproteins E6 and E7 have a well-established oncogenic action, disactivating p53 and pRb (retinoblastoma protein), which normally function as tumour suppressor proteins [14,15]. The persistence of HPV16 infection is a necessary but not sufficient condition to develop HPV-positive OPSCC, as malignant transformation occurs in multiple steps, with factors such as immunosuppression, sexual practices, tobacco consumption, and genetics having an additional impact on oncogenesis [8,16]. A long-term interval may be evident from infection to neoplasm transition, highlighting the difficulty of determining the influence of vaccination on oral cancer prevention, with researchers investigating a reduction in the incidence of oral HPV infection as an indicator of effective vaccination policy [17].

The preventive, but not the therapeutic nature of HPV vaccination programs, has been shown in previous studies [18,19]. Nowadays, protection against 9 HPV genotypes (HPV-6, 11, 16, 18, 31, 33, 45, 52, 58), which include the high-risk genotypes HPV16 and HPV18 involved in malignancies of various locations, is ensured with the current HPV vaccination policy [19,20]. VLPs are virus-like particles similar to HPV's capsid, but lacking viral DNA, highly immunologically responsive, without inducing HPV infection [21]. Recent studies have shown that post-vaccination antibodies are circulating in serum and oral fluids, enabling immunologic defense also at the level of oropharyngeal mucosa [22,23]. The greatest potential of immunization can be achieved by individuals not previously exposed to HPV (Kreimer et al.). Vaccination is suggested to be undertaken preferentially by sexually inactive female and male adolescents as a routine [21,24].

Results

A study published in 2015 from Costa Rica as a Vaccine Trial highlighted a beneficial impact of HPV vaccination strategy on the prevention of oral HPV infection with a lower prevalence of HPV16 and HPV18 oral infection rates in vaccinated versus unvaccinated females in the years following immunization, investigating the preventive potential of HPV vaccination beyond the anogenital tract [25]. The prevention of HPV infection, as shown in this study, only in female patients, though, expands the limits of an efficient vaccination strategy beyond the cervical cancer malignancies associated with HPV [25]. Observational studies based on real-world databases supported this statement in a wider pool of patients [26,27]. In the USA, the database of the National Health and Nutrition Examination Survey has been used in large population-based studies demonstrating a decrease in oral HPV infection following vaccination at an early age [16,21]. Consistency in these findings has been noted in the observational studies, despite their limitations, such as the vaccination status report and the variety of sexual practices [28,29].

Anti-HPV antibodies have been isolated after HPV vaccination in oral secretions, reflecting a decrease in the host potential of the oropharynx in immunized individuals [15,30]. The future perspectives are promising; nevertheless, researchers should focus on the long road of carcinogenesis post-HPV infection and the impact of HPV vaccination. Evidence from systematic reviews indicates that high-risk for OPSCC oncogenesis HPV16 and HPV18 genotypes are isolated less often in the vaccinated population [31,32]. Therefore, a single test was performed in the vast majority of studies without proving a difference between transient and persistent oral infections with potential oncogenic impact [33,11]. The value of HPV vaccination strategies, specifically in preventing HPV-positive OPSCC, will be strongly supported by researchers as a public health measure when standardization of sampling methods is established, and long-term results of infection in malignant transformation are researched meticulously [34,35].

Discussion

Cervical cancer in women has been used as a strong example of HPV vaccine-mediated preventive measures for malignant neoplasms of other locations [24]. Not only females but also males should be vaccinated through the national vaccination program to decrease the incidence of HPV-positive OPSCC in the future [8]. HPV-positive malignancies of the anogenital and upper airway tract could be potentially eliminated by the widespread use of the HPV vaccine, as supported by recent studies with emerging clinical information [36,37]. The context of the HPV vaccination should shift towards a multi-locational cancer prevention strategy, rather than a vaccine only against cervical cancer, referring falsely only to women [38]. Public health programs should encourage men's HPV immunization who are also adversely affected by HPV-positive OPSCC globally, with direct protection and herd immunity indirectly preventing cervical cancer in women, resulting in a total decrease in HPV infection rates [39,40].

Before an individual is exposed to HPV infection, the maximum efficacy of HPV vaccination is noted, a fact that names adolescents as the most suitable vaccination candidates for HPV-positive cancer prevention [41]. Elder adults can also be vaccinated with a notable value as a cancer preventive strategy, with a decrease in efficacy in individuals previously exposed to high-risk HPV genotypes [29]. Head and neck surgeons, and generally, healthcare providers, can initially detect HPV-associated lesions, especially in their patients' oropharynx [12]. Additionally, they should encourage their patients to participate in HPV vaccination programs, providing evidence-based information about the preventive, but not therapeutic, nature of the HPV vaccine [42,43]. Concomitantly, the conventional risk factors should be addressed as part of a multifactorial strategy for oral cancer prevention, such as tobacco and alcohol consumption [10,11,44].

There is strong evidence that the HPV vaccination protects an individual against oral HPV infection. Nevertheless, the remaining fields should also be investigated to establish the HPV vaccine as a preventive measure of oropharyngeal carcinogenesis, as a long-term process is usually required. Sampling and laboratory assessment modalities vary between studies, leading to inconsistent oral HPV detection methodology, which serves as a substitute for HPV-positive OPSCC incidence [17,28]. Researchers in the future should focus on identifying the persistence of oral HPV infections, a condition that mainly leads to malignant transformation [23]. Standardization of sampling modalities, especially in immunocompromised patients, should be implemented, aiming to prove the long-term protective capacity of HPV vaccination [12,34].

Conclusion

The central concern for clinicians is whether the documented decline in oral HPV infections will ultimately translate into fewer cases of Oropharyngeal Squamous Cell Carcinoma (OPSCC) [12]. Longitudinal data confirming a reduction in cancer incidence remain

scarce, but this is expected given the disease's natural progression rather than a lack of vaccine efficacy [45]. Because OPSCC typically emerges decades after initial viral acquisition and mass immunization is a relatively recent development, most vaccinated cohorts have not yet reached the high-risk window for these malignancies [43,46]. Despite the challenges of long-term tracking, the biological rationale for the vaccine's protective role is strong. Persistent high-risk HPV16 is the primary driver of oropharyngeal cancers; therefore, preventing initial infection logically disrupts the oncogenic pathway [47,48]. A broad body of evidence from clinical trials and systematic reviews confirms that the vaccine elicits a robust immune response in oral tissues, significantly reducing the types [9,8]. Consequently, expanding vaccine accessibility and public awareness for both sexes remains a vital public health objective to mitigate the future global burden of head and neck cancers [40,37].

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