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Review Article

HUMAN-PAPILLOMA VIRUS IN ORAL MUCOSA: AN OVERVIEW

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ABSTRACT

Since 20 years there been an ever-increasing interest in human papillomaviruses HPV for the reason that of their impending character in the pathogenesis of malignant tumors. HPV was undeniably confirmed as an independent risk factor which leads to oral carcinoma. Up to now, totally more than 200 different strains and 170 types of HPV have been identified with their genomes and of them generally very less leads to the cancerous stage. As in HPV type 16 is the most prevalent type in oral carcinomas. The benign oral lesions, related with HPV infection, include Oropharyngeal squamous cell carcinoma, verrucca vulgaris and focal epithelial hyperplasia (FEH) and benign warts (genital, plantar and flat warts). These Oral benign HPV lesions are mostly asymptomatic as they may persist or regress spontaneously.

Keywords: Human papilloma viruses, malignant tumors, oral carcinoma, HPV infection

INTRODUCTION

Human papillomavirus (HPV) is a DNA virus from the papillomavirus family that is capable of infecting humans[1-2]. The first visualization of papillomavirus particles in human warts by electron microscopy was reported in 1949[3]. The structure of papillomavirus genomes was unraveled by Crawford and Crawford in 1963. The unavailability of tissue culture systems and the apparent benign nature of human warts led to few additional experimental approaches in subsequent years. Gradually interest in papillomaviruses evolved in second part of the 1970s, evidenced by the first papillomavirus workshops, commonly attended at that time by 15 to 30 participants. This developed in part from the hypothesis that papillomavirus may play significant role in etiology of cancer of the cervix[4,5]. Meisels and Fortin proposed a papillomavirus origin of koilocytotic atypias, separating them from 'true' pre-neoplastic lesions. In the 1980s the situation changed almost abruptly; the isolation of new HPV types HPV 6 and 11 from genital warts[67] and subsequently directly from cervical cancer biopsies HPV type 16 and 18[8] resulted in a rapid expansion of experimental work and also in early epidemiological approaches. HPVs establish productive infections only in keratinocytes of the skin or mucous membranes. There are two types of sexually transmitted HPV infections:

1. Low risk viruses that can cause skin warts like Condylomata acuminata
2. High risk or cancer producing viruses are Type 16 and 18. HPV 16 and 18 infections are a cause of a unique type of oropharyngeal throat cancer [9,10].

Various scientists have identified that there are two major variants of HPV16, European HPV16-E and Non-European HPV16-NE[11]. The casual link between human papillomavirus HPV infection and the growth of head and neck carcinomas (HNCs) particularly in the oropharynx are becoming more firmly established[12-14]. Still there are number of unanswered questions remain. Unlike cervical cancer, with high risk HPVs in HNC are neither an obligatory nor an adequate cause of cancer and only of these 20 % malignancies are associated with the transmission[12]. There is a need to conclude whether a test based on oral exfoliated cells can be used to provide a sensitive method for predicting oncogenic mucosal HPV types in head and neck tissues[15]. This review tries to summarize our present understanding of papillomavirus infections by emphasizing their role in human cancers.

The current review was conducted by means of a search of various articles and various websites associated with the HPV. The search terms used were: 'History Associated with HPV," 'Structure of Human Papillomavirus,' 'Types of HPV Has Been Identified Up to The Date,' 'Physiological Basis Of Human Papillomavirus,' 'Preventive Measures Associate With Human Papillomavirus.' Based on these review and considering only published information, this article is constructed.

Structure of Viral Particles

The diameter of HPV particles amounts to approx 55 nm. Full particles contain the double-stranded closed circular DNA genome. The viral DNA is associated with histone-

like proteins[16,17] and encapsulated by 72 capsomeres[18]. The major capsid protein is coded by the L1 open reading frame seems to contain reactive epitopes for type-specific neutralization. The L2 open reading frame codes for an additional structural component of the viral capsid. Antigenic domains of this protein appear to be responsible for a group-specific reactivity of antisera. Virus like particles containing the structural components of various types of HPV can however be obtained by the expression of these proteins in recombinant vectors[19,20]. Obviously the L1 protein suffices for this particle formation. This protein has a molecular weight of approx 55000 and is highly conserved among different papillomavirus types. The second structural protein, L2 is less conserved and possesses a molecular weight of about 75000. The non-enveloped structure renders papillomaviruses relatively resistant to heating and to organic solvents[21].

Table 1: Characterized HPV types from

HPV TYPES	GENOMES
HPV-1	Mu papillomavirus 1
HPV-2,27,57	Alpha papillomavirus 4
HPV-3,10,28,29,77,78,94,117,125,160	Alpha papillomavirus 2
HPV-41	Nu papillomavirus 1
HPV-5,8,12,14,19,20,21,24,25,36,47,93,98,99,105,118,124,143	Beta papillomavirus 1
HPV-6,11,13,44,55,74	Alpha papillomavirus 10
HPV-7,40,43,91	Alpha papillomavirus 8
HPV-9,15,17,22,23,37,38,80,100,104,107,110,111,113,120,122,145,151	Beta papillomavirus 2
HPV-16,31,33,35,52,58,67	Alpha papillomavirus 9
HPV-18,39,45,59,68,70,85,97	Alpha papillomavirus 7
HPV-26,51,69,82	Alpha papillomavirus 5
HPV-30,53,56,66	Alpha papillomavirus 6
HPV-32,42	Alpha papillomavirus 1
HPV-34,73	Alpha papillomavirus 11
HPV-96,150	Beta papillomavirus 5
HPV-46	Subtype of HPV 20
HPV-49,75,76,115	Beta papillomavirus 3
HPV-91	Alpha papillomavirus 8
HPV-64	Subtype of HPV 34
HPV-92	Beta papillomavirus 4
HPV-61,62,72,81,83,84,86,87,89,102,114	Alpha papillomavirus 3
HPV-63	Mu papillomavirus 2
HPV-54	Alpha papillomavirus 13
HPV-71,90,106	Alpha papillomavirus 14
HPV-79,152,157,158,167,168	Not known
HPV-4,65,95	Gamma papillomavirus 1
HPV-48	Gamma papillomavirus 2
HPV-50	Gamma papillomavirus 3
HPV-60	Gamma papillomavirus 4
HPV-88	Gamma papillomavirus 5
HPV-101,103,108	Gamma papillomavirus 6
HPV-109,123,134,149,155	Gamma papillomavirus 7
HPV-112,119	Gamma papillomavirus 8
HPV-116,129	Gamma papillomavirus 9
HPV-121,130,133	Gamma papillomavirus 10
HPV-126,136,140,141	Gamma papillomavirus 11
HPV-127,132,148	Gamma papillomavirus 12
HPV-128,153	Gamma papillomavirus 13
HPV131	Gamma papillomavirus 14
HPV-135	Gamma papillomavirus 15
HPV-137	Gamma papillomavirus 16
HPV-144	Gamma papillomavirus 17
HPV-138,139,142,146,147,154,156,161,162,163,164,165,166,169,170	Gamma papillomavirus
HPV-159	Beta papillomavirus[22-24]

Patho-physiology

HPV infects the basal cells of stratified squamous epithelium tissue, where they replicate[25]. They infect epithelial tissues through expose segments (abrasions or trauma) of the basement membrane or during human sexual behavior[25]. The infection is having slow course of action, takes around 12–24 hours for initiation of transcription process. HPV lesions and infections arise from the proliferation of cells in the epidermis (Infected basal keratinocyte). HPVs are released as a result of deterioration of desquamating cells. Individuals with plantar warts spread virus by walking barefoot which shows that virus can survive without host for long[26]. Studies have showed that HPV is a small DNA virus with a genome of approximately 8000 base pairs[27]. The development and history of the various strains of HPV usually shows the relocation patterns of modern humans (Homo sapiens) and suggested that HPV may have become more varied among humans. It has been showed in many studies that HPV evolved along the five major branches that would be a sign of the civilization of human hosts, and varied along with the human population[28].

Symptoms and Lesions associated

Oral HPV is mostly asymptomatic and may persist or relapse spontaneously. The similarity of the morphologic features of genital and oral HPV- associated lesions was one of the early findings that suggested HPV might be involved in oral and laryngeal squamous cell carcinomas SCCs[29]. DNA HPV has been found in 25-30 % of the cases of oral carcinomas. HPV-related cancers arise mainly from the tonsils and base of the tongue, gingivae, cheek, palate and floor of the mouth[30-31]. HPV-related diseases are increased in oral cavity of immune-suppressant individuals, such as that of HIV. Studies have demonstrated an increase in the incidence of oral warts related to HPV infection since the advent of antiretroviral therapy. Smoke contains several carcinogenic pyrolitic products that bind to DNA and cause genetic mutations.

Diagnostic measures

These studies used a variety of detection techniques, including:-

- Lower- sensitivity methods in situ hybridization and Southern blot hybridization
- High-sensitivity methods polymerase chain reaction PCR.
- Several sampling methods were employed, including biopsies, scrapes, brushes, and oral rinses.
- Fresh, frozen or formalin-fixed paraffin-embedded samples were used.
- Screening methods such as Pap Smear and HPV DNA Test
- The acetic acid test: This test can be used in conjunction with colposcopy to examine cervical lesions; however, it is reserved for suspicious lesions and should not be used for routine screening.

Treatment / Vaccination

The use of vaccination for the prevention of oral cancer has been suggested and is currently being researched or is under clinical trials. The arrival of HPV vaccination in women may lead to a decreased incidence of oropharyngeal cancer in the future. Drugs designed firmly for the deterrence of cervical cancer and vulvar genital warts which had been introduced within a few years. The two materialistic accessible vaccines are Gardasil which protects against HPV types 6, 11, 16 and 18 and Cervarix which targets HPV types 16 and 18[32-33] are commercially available. As the impact of these vaccines on the occurrence of persistent oral HPV infection not determined so far, so for these vaccines to be efficient, they should be given before the patient begins with human sexual behavior. Clinical trials which are regulating the efficacy of the Gardasil HPV are under progress and are evaluating it for fight against oral cancer and HPV infection. Surgery and radiation therapy can also be the line of treatment for oropharyngeal cancer (Electro-cauterization of benign warts) and (Intensity modulated radiation therapy for HNCs) and chemotherapy can also be used as it is more superior to radiation therapy.

CONCLUSION

In this study we detailed about types of HPV, its physiology and various preventive measure. It is seen that younger age cases with cancers of oral cavity/oropharynx may have higher prevalence of HPV in tumors because of behaviors linked to sexually transmitted diseases. The observation is consistent with data on cancers of the cervix and anogenital areas that involve viral transmission through direct physical contact[34]. Although much speculation has been made about sexual transmission of the virus in HPV-HR HNC, few large scale investigations have been conducted. A study by Schwartz *et al*, found a higher odds of HPV-16 in oral cancer patients with 15 or more sex partners adjusted OR-2.5; 95 % CI- 1.1-5.6, but the data were not presented by age group. The risk of HPV-HR was greater among men whose female partners had a history of either an abnormal pap smear or a cervical dysplasia, is consistent with data from a large Swedish cancer databases.

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