Human Papillomavirus in the Oncogenesis of Oral Squamous Cell Carcinoma: a Narrative Review

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Abstract. Squamous Cell Carcinoma (SCC) is characterized by being a tumor that affects the structures of the mouth, with risk factors including smoking, alcohol consumption, poor dietary habits, as well as genetic factors and Human Papillomavirus (HPV) infection. HPV, belonging to the Papillomaviridae family, has a non-enveloped structure, with its protein capsid containing a single molecule of double-stranded DNA. There are over 200 types of HPV described, classified as high and low oncogenic risk, with HPV-16 and HPV-18 being highly oncogenic types. The aim of this work is to associate SCC with positive HPV infection. This work is a narrative literature review, using scientific databases PubMed, Google Scholar, SciELO, and INCA from 2015 to 2021. In conclusion, it was possible to verify that HPV-positive oral carcinoma is directly linked to unprotected sexual practices with or without associated alcohol and smoking, due to HPV being a virus primarily transmitted through sexual contact.

Keywords. Human Papillomavirus, Squamous Cell Carcinoma, Prevalence, Oral Cancer.

1. Introduction

Squamous cell carcinoma (SCC) is a common oral cancer, especially in men over 40 years old, with risk factors such as smoking, alcohol consumption, and Human Papillomavirus (HPV) infection. HPV, a virus primarily transmitted through sexual contact, is associated with various conditions, including cervical, oral, and oropharyngeal cancers [1].

There are different types of HPV, some of which are high-risk oncogenic types that can lead to cellular transformation and cancer. HPV infection mainly occurs in basal cells of the squamous epithelium and can be detected through clinical and laboratory tests [2].

Prevention of HPV is mainly achieved through vaccination, with immunization programs in place in many countries. Diagnosis and treatment of oral cancer vary depending on the stage of the disease, with options including surgery, chemotherapy, and radiation therapy [3].

Oral lesions associated with HPV may include warts, papillomas, and focal epithelial hyperplasia, which are treated by removing visible lesions and, in some cases, clinical treatment to destroy infected tissue [4].

Due to its medical significance, it is necessary to describe and discuss the current scenario of HPV-related cancer in the oncogenesis of oral SCC.

2. Research Methods

This is a narrative literature review study that examines the role of HPV in the oncogenesis of oral Squamous Cell Carcinoma.

A variety of bibliographic and electronic sources are used to describe and discuss the current scenario of this relationship.

Articles published in the last 5 years in English, Portuguese, and Spanish were examined, selected based on title and topic. Keywords included terms related to squamous cell carcinoma, HPV, prevalence, and oral cancer.

The databases used included PubMed, Google Scholar, SciELO, and INCA. Inclusion criteria considered the publication year (2015-2021), relevance of the title, related abstracts, and specific languages.

3. Results

3.1 Epidemiology

HPV is globally prevalent and is primarily transmitted through sexual contact. Its presence is common in cervical cancers, with approximately 95% of biopsies showing HPV viral genomes [3].

In Brazil, the Epidemiological Study on the National Prevalence of HPV Infection (POP-Brasil) revealed a high prevalence of HPV, around 53.6%, with the presence of at least one of the types of HPV analyzed [5].

HPV infection is associated with 20 to 60% of oropharyngeal squamous cell carcinomas, with varying rates between countries [6].

3.2 Taxonomy and classification

HPV belongs to the viral family Papillomaviridae and has a double-stranded DNA structure within a protein capsid. Its genetic structure is divided into three regions: initial, which encodes proteins necessary for viral replication and regulation; late, which encodes viral capsid proteins; and the long one, which contains the sequences that control the replication and transcription of the virus [7].

There are over 200 types of HPV grouped into five main genera, with tropism for mucous membranes and cutaneous epithelia, causing a variety of diseases, including head and neck cancers [8].

Different HPV types can be classified according to their oncogenic potential, thus divided into low-risk or high-risk. Low-risk viruses generally produce benign clinical manifestations associated with warts or low-grade squamous intraepithelial lesions but tend to progress to malignant lesions. However, 85% of low-grade lesions contain HPV from the oncogenic group, which can evolve into malignant lesions. On the other hand, those from the high-risk or oncogenic group are associated with high-grade squamous intraepithelial lesions, causing intraepithelial neoplasia that may progress to invasive carcinoma [7].

3.3 Risk factors

The main risk factors for the development of HPV-related lesions include smoking, alcohol consumption, immunodeficiencies, malnutrition, cancers, and the use of immunosuppressive medications [2].

Studies indicate that smoking and alcohol consumption are significant risk factors for persistent oral and genital HPV infections, increasing viral load and the likelihood of cancerous transformation of infected cells. Additionally, prior HPV infection may increase the chances of acquiring another HPV infection [3].

3.4 Viral life cycle

The infectious cycle of HPV exhibits evolutionary adaptations and is closely linked to the differentiation of the host's squamous epithelium. The virus infects undifferentiated basal epithelial cells, and viral progeny is produced in differentiated daughter cells in the upper layers of the epithelium [7].

Viral particles suppress cellular control mechanisms, allowing viral replication. Replication of the viral genetic material can occur during cell replication, keeping the virus in a latent state for years and ensuring infection of basal cells [8].

3.5 Diagnosis

Most HPV infections are asymptomatic, but clinical manifestations can vary in size, color, and shape, and may be asymptomatic or cause symptoms such as itching, pain, or bleeding. Diagnosis can be made through clinical and laboratory examinations, including cytopathological, histopathological, and biopsy analyses [10].

The Southern Blot technique is considered the gold standard, despite being laborious. The technique consists of collecting genetic material for analysis using a DNA or RNA probe. In addition to this method, the PCR test can also be performed, which will replicate genetic copies of the viral DNA or RNA, allowing cytological analysis. This test should be associated with oncotic cytology to reduce errors in cytological diagnoses [11].

3.6 Treatment and prophylaxis

Treatment of symptomatic lesions caused by HPV focuses on eliminating condylomas, as there is no definitive treatment for the infection. Various clinical and surgical options are available for anogenital warts [2].

The primary prevention is through vaccines, such as the nine-valent vaccine, effective against approximately 90% of HPV-associated cancers[3]. In Brazil, the National Immunization Program provides free HPV vaccines for specific age groups, with vaccination recommended for both girls and boys [12].

3.7 Oropharyngeal Squamous Cell Carcinoma

Squamous cell carcinoma of the head and neck is a type of cancer that is common around the world and has a very poor prognosis. It progresses as a fast-growing and very aggressive malignant neoplasm. The risk factors for this type of cancer vary greatly, with particular emphasis on smoking and alcohol consumption [13].

In the last 10 years, the scientific community has detected a considerable change in cases of oropharyngeal cancer, as a decrease in cases caused by smoking, characteristic of males and patients with an average age of 60 years, has been noticed, and an increase in the number of cases related to HPV infection, whose patients are younger [14].

This change created three patient profiles and, consequently, three prognosis profiles: the classic profile, alcoholic and smoker, whose prognosis is the worst; smokers and HPV positive, who have a median survival compared to the other two profiles; and non-smokers and HPV positive, whose prognosis is the best of the three, with less aggressive manifestations and more responsive to treatment

[13].

Symptomatic manifestations are also different. In patients with HPV-related oropharyngeal carcinoma, the most common symptom is a neck mass, and they are more likely to develop early-stage tumors and cervical nodal disease. Furthermore, patients have better survival results and response to treatment [16].

The main form of transmission observed in oropharyngeal carcinomas is oral sex and some studies indicate the possibility of transmission via sharing cigarettes, if the lesion already exists. Transmission through kissing is still widely discussed, since the virus is mainly found at the base of the tongue and in the tonsils, but finds a barrier in the defense mechanisms present in saliva [14].

Treatment of oropharyngeal carcinoma consists of surgical excision of the lesion, chemotherapy and/or radiotherapy. However, chemotherapy and radiotherapy cause serious adverse effects for patients due to high toxicity rates. This shows that the search for new treatments is still a challenge for academia [17].

4. Conclusions

This review study highlighted the association between HPV-positive oral carcinoma and unprotected sexual practices, along with smoking and alcohol consumption. HPV is primarily transmitted through sexual contact, and smoking and alcohol increase the viral load and the likelihood of malignant transformation of infected cells. The presence of HPV in oral carcinoma improves the prognosis, making the tumor more sensitive to radiotherapy and chemotherapy. However, limitations in the understanding of risk factors and diagnostic methods were identified as challenges. Further research is needed to better understand oral HPV transmission, develop new treatments, and increase awareness about prevention, including safe sexual practices and vaccination.

5. References

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