HUMAN PAPILLOMAVIRUS AND OROPHARYNGEAL CARCINOMA

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HUMAN PAPILLOMAVIRUS AND OROPHARYNGEAL CARCINOMA

INFORMATION FOR DENTAL PRACTITIONERS

Human Papillomavirus

Human Papillomavirus (HPV) comprises of multiple subtypes and variants (over 200) with varying infective potentials. Its emerging recognition can be attributed to the rapidly increasing number of cases reported in association with oropharyngeal cancer. According to oncoepidemiologic studies, HPV is broadly divided into two types – high risk and low risk. It is well established that HPV is linked to the majority of cervical cancer cases and is considered a prime aetiologic agent of cervical cancer. HPV has also been correlated with anal, vulvar, penile and oropharyngeal carcinomas. The incidence of HPV and related cancers and precancers lesions are governed by many risk factors such as onset of sexual activity and multiple sexual partners.

Anatomy of the Oropharynx

According to the anatomy, the posterior part of the oral cavity comprises of the pharynx which is broadly divided into 3 compartments, namely, nasopharynx, oropharynx and hypopharynx (laryngopharynx).

The contents of the oropharynx are the base of the tongue, palate tonsils, soft palate and oropharyngeal mucosa; anatomical boundaries of the oropharynx are as follows:

- Anteriorly, circumvalate papillae of tongue and anterior tonsillar pillars
- Posteriorly, pharyngo constrictor muscles
- Superiorly, soft palate
- Inferiorly, epiglottis and glossoplatygotic fold.

HPV and Oropharyngeal Cancer (OPC)

Cancer involving the oropharynx including base of the tongue, palate tonsils, soft palate and oropharyngeal mucosa is called oropharyngeal cancer (OPC). Cancers involving the oral cavity and oropharynx constitute the sixth most common cancer worldwide. Five-year survival rates of oral and oropharyngeal cancers are approximately 50%.

Until recently, oral cavity and oropharyngeal cancers were considered a combined entity and therefore separate statistics for OPHC are not yet available. Nearly 30% of OPCH are HPV related.

The prevalence of HPV related OPC has been increasing among white middle-aged males in developed countries such as UK, USA and Australia. A decline in the incidence of lip and oral cavity cancer has been reported in Australia in the past decade; however, a rise in the incidence of oropharyngeal cancer has also been noted. The symptoms of OPC

- The most common symptom is sores in the throat or on the palate that do not heal for more than 2 weeks.
- Red or white patch on the back of the throat or tonsils.
- Lump in the throat which could lead to swallowing and breathing difficulties.
- Persistent sore throat or feeling that something is caught in the throat like a thread or a lump.
- Hoarseness or change in voice, changes in speech delivery.
- Number of the throat and compromised swallowing capabilities.
- Spontaneous pain or bleeding from the throat which can be observed when a person spits or coughs.
- Difficulty in chewing, swallowing, or moving the jaws or tongue.
- Ear and/or jaw pain.
- Unexplained weight loss with feelings of fatigue.
- Loss of appetite, especially when prolonged.

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Risk Factors for HPV and OPC

- Early onset of sexual activity
- Multiple sexual partners
- History of non-specific sexual behaviours
- Avoiding use of protected sexual practices e.g. condoms, dental dam.
- Tobacco smoking
- Immune suppressed states
- Alcohol consumption

Why does HPV positive oropharyngeal cancer have a better prognosis?

- HPV-positive tumours may harbour fewer or different genetic alterations that can be associated with better response to therapy.
- HPV-positive tumours have higher radio sensitivity, probably due to intact apoptotic response to radiation.
- The development of an abnormal area of epithelium where cells show a collection of early changes in the process of transformation towards malignancy is known as field carcinoma. It has been shown that the absence of field carcinoma in HPV-positive tumours contributes to their better prognosis.
- Immuneologic response may play a role in the improved response to radio- and chemotherapy in HPV-positive tumours (due to the stimulation of immune response directed to viral specific tumour antigens).
- Younger age, good performance status, fewer comorbidities of HPV-positive oropharyngeal cancer patients may also contribute to improved survival.

Preventive Measures against HPV Infection

1. Safe sexual practices, using protective measures like condoms and dental dams.
2. Regular Pap testing for women, to observe any irregularities.
3. Stop smoking and limit alcohol consumption.
4. Vaccinations – two commercial vaccines are available (Cervarix and Gardasil), although many countries now have a national vaccination program in schools for both girls and boys.

Vaccinations against HPV Infection

Two commercially available vaccines are on the market for HPV infections and prevention against cervical and oropharyngeal cancer, Cervarix and Gardasil 9. Popularising vaccinations against HPV infection has been challenging as there has been a lot of controversy regarding the side effects of HPV vaccination, which were not categorised as life threatening. Some side effects included syncope, dizziness and headaches while only 6% of the papers reviewed in a systematic review observed pulmonary emboli and death as side effects. However, in most of the case, pulmonary emboli and death were explained by factors other than the vaccination.

The HPV vaccine provides almost 100% protection from nine HPV types (6, 11, 16, 18, 31, 33, 45, 52 and 58), if all doses are received at the correct intervals, and if it is correctly administered before contact with HPV.

The Advisory Committee on Immunization Practices (ACIP) and the Centers for Disease Control and Prevention (CDC) recommends that:

- Routine vaccination of girls aged 11 or 12 years that can be started at 9 years of age;
- Catch up vaccination for females aged 13-26 years;
- Routine vaccination of boys aged 11 or 12 years;
- Routine vaccination for men who have sex with men (MSM) and immunocompromised individuals aged 22 through 26 years;
- Men aged 13 to 21 years who were not previously vaccinated;
- Men aged 22 to 26 years may also receive the vaccine;
- Vaccinating lactating women, patients with minor acute illnesses such as diarrhoea or upper respiratory tract infection (with or without fever) and women with equivocal or abnormal Pap test.

Everyone aged 26 years and older, is not recommended for vaccination. However, adults aged 27 to 45 years who are not vaccinated may discuss with their doctor about the market for HPV infections and prevention as well as the potential benefits of vaccination and decide to get the HPV vaccine. Given that many people in this age range have already been exposed to HPV, vaccination provides less benefit for them.

Vaccination in Australia

- 2007 - Australia started a National HPV Vaccination Program only for girls, one of the first countries to do so.
- 2013 - The government initiative was expanded to boys (aged 12-13 years), with catch-up for 14-15-year-olds available till end-2014 implementing a gender-neutral HPV vaccination program.
- 2018 - Four valent vaccine (Gardasil 4) was replaced by Gardasil 9 which gives protection against 9 subtypes of HPV (6, 11, 16, 18, 31, 33, 45, 52 and 58).
- The National Immunization Scheme in Australia has included HPV vaccination, which is now provided free of cost in schools and health care centres.

Vaccination in New Zealand

- 2008 - New Zealand began their HPV vaccination programme.
- 2008-2016 – HPV immunisation was provided free for females up to 20 years old, including non-residents up to 16 years old and living in New Zealand for 8 months.
- 2017 – HPV immunisation became free for everyone – both male and female - aged 9 to 26 years or living in New Zealand for 8 months.

HPV vaccination is offered to children who are aged 9 in year 8 at school via a school-based immunisation programme or through their family doctor, in the absence of such a programme.

Diagnosis, Treatment and Management Strategies

Based on signs and symptoms, age and general health, the findings of associated medical investigations and the type of the cancer suspected the following tests may be used to help diagnose HPV related OPC after conducting a physical examination.

Endoscopy of the oropharyngeal area

HPV testing

Cervical screening/Pap test for females

Oral brush biopsy: A sample of cells from the suspected area is taken using a small brush in the dentist’s chair with little or no pain.

If the above tests suggest the presence of a cancer, a biopsy is performed to confirm the diagnosis.

Nationwide surveys are currently underway to record the actual prevalence of this virus and its consequences. According to a survey, the high risk types of HPV were the most common sexually transmitted infection in Australia with an estimated 4 out of 5 Australians having a high risk (HPV) infection at some point in their lives. It affects both males and females although the rates of the HPV associated oropharyngeal cancers are higher in men than in women. In New Zealand, HPV related cervical cancer is the fourth most common cause of cancer in women aged 15-44 years.

Figure 1: Human Papillomavirus

Figure 2: Oropharynx anatomical position

Epidemiology of Oropharyngeal Cancer (OPC)

The HPV has shown an increased tendency for residing and proliferating in those areas of the human body which show a transition in the type of lining mucosal epithelium. The oropharynx is one of those sites which has now come to light and is showing high rates of HPV and consequently leading to pre-malignant and malignant changes. HPV related OPC has been declared as the most common sexually transmitted infection by the World Health Organisation in 2013. HPV-associated oropharyngeal squamous cell carcinoma (OPSCC) is one of the most rapidly increasing incidences of any cancer in high income countries. It disproportionately affects men and younger people.
Most HPV infections are spontaneously cleared within the first two years and remain asymptomatic, however, certain strains (HPV 16/18) and risk factors predispose an individual to retaining the virus leading to benign, precancerous or cancerous changes. Benign growths include warts which can be treated by medications (systemic and topical), burned by electric currents (electrocautery) or frozen off by liquid nitrogen (cryotherapy).

For the management of precancerous and cancerous changes, there is no specific treatment modality available to date except surgical removal of affected areas, chemotherapy and radiotherapy.

Summary

- HPV related OPC is one of the cancers which is increasing rapidly in prevalence worldwide.
- Nearly 70% of the cancers of the oropharynx are related to HPV.
- Oral and oropharyngeal cancers combined are the sixth most prevalent types of cancers in the world.
- Sore throat, lump in the throat, change in voice or hoarseness, persistent ear and throat pain and difficulty in chewing and swallowing are some of the symptoms of oropharyngeal carcinoma.
- HPV is a sexually transmitted infection which can be easily prevented via safe sexual practices and timely vaccination.
- Two vaccines against HPV Infection (Cervarix and Gardasil 9) are commercially available.
- Girls and boys should ideally be vaccinated before they become sexually active in their early teen years (11-13 years).
- The human body usually gets rid of the HPV infection over time although risk factors could predispose an individual to retain the virus and manifest symptoms.
- A biopsy confirms the diagnosis of HPV/OPC. Surgical removal of affected areas, chemotherapy and radiotherapy are currently available for management of precancerous and cancerous lesions of HPV related OPC while benign growths can be treated by medications, electrocautery and cryotherapy.

References:


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FOR FURTHER ENQUIRIES

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