Oral Cancer Screening in Dental Set Up

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Abstract

Cancer is a major public health problem in the United States and many other parts of the world. One in 4 deaths in the United States is due to cancer. Oral cancer (OC) is the sixth most common cancer worldwide. Oral cancer can be divided into three clinic-pathological categories: carcinoma of the lip vermilion, carcinoma of the oral cavity proper, and carcinoma of the oropharynx. The chief predisposing factors are tobacco use, alcohol consumption, and persistent viral infections such as HPV 16. Oral cancer is particularly dangerous because in its early stages it may not be noticed by the patient, as it can frequently prosper without producing pain or symptoms they might readily recognize, and because it has a high risk of producing second, primary tumors. The incorporation of OralID in the first-line practice settings, such as dental offices and primary health care settings may be a boon to population for their regular check up for early detection of premalignant lesions.

Keywords: Oral Cancer, OralID, Dental, HPV16

1. Introduction
1.1 Incidence and Occurrence

Oral cancer (OC) is the sixth most common cancer worldwide[1]. It affects anterior tongue, cheek, floor of mouth, gingiva or any other part of the oral cavity. Worldwide, there is a great variation in the incidence of cancer of the oral cavity. It accounts for less than 5% of all cancers in United States, Western Europe and Australia. India, few pockets in France, Brazil, central and eastern Europe have few of the highest rates of cancer of the oral cavity in the world. The differing social customs are likely to be responsible for regional variations in the disease incidence. The high rate of OC in France and Eastern Europe has historically been linked to the heavy consumption of alcohol and tobacco in these countries.[2] Cancer is a major public health problem in the United States and many other parts of the world. One in 4 deaths in the United States is due to cancer. A total of 1,660,290 new cancer cases and 580,350 cancer deaths are projected to occur in the United States in 2013.[3] Cancers of the oral cavity and oropharynx are among the most common cancers worldwide, with an estimated 400,000 incident cases and 223,000 deaths during 2008.[4] It is estimated that there will be 45,780 new cases of oral cancer diagnosed in the United States in 2015 and 8,650 deaths due to this disease.[5] The estimated age-standardized (World Standard Population) worldwide incidence and mortality rates of oropharyngeal cancer in 2008 were 5.9 and 3.3 per 100,000 persons per year, respectively.[6] Primarily due to differences in tobacco and alcohol use, there is wide variation in rates across the world.[7] South central Asia and Melanesia have particularly high rates of oral cancer attributable to betel quid chewing, and Australia has a high rate of lip cancer attributed to solar irradiation.

Oral cancers are part of a group of cancers commonly referred to as head and neck cancers, and of all head and neck cancers they comprise about 85% of that category. Oral cancer can be divided into three clinic-pathological categories: carcinoma of the lip vermilion, carcinoma of the oral cavity proper, and carcinoma of the oropharynx. Squamous cell carcinoma, which arises from the oral mucosal lining, accounts for more than 90% of the tumors in the oral cavity and oropharynx. Other types of primary
tumors arising in this area include lymphoma, sarcoma, melanoma, and minor salivary gland tumors. In the Western world the most common locations of tumor development are the tongue and floor of the mouth; however, in parts of the world where tobacco or betel quid chewing is prominent, cancers of the retromolar trigone and buccal mucosa are common. Oral squamous cell carcinomas are sometimes preceded by oral preneoplastic lesions, which are often present as visible alterations of the mucosal surface and include leukoplakia and erythroplakia.[8]

### 1.2 Risk Factors

Understanding the causative factors of cancer will contribute to prevention of the disease. Age is frequently named as a risk factor for oral cancer, as historically it occurs in those over the age of 40. The age of diagnosed patients may indicate a time component in the biochemical or biophysical processes of aging cells that allows malignant transformation, or perhaps, immune system competence diminishes with age. However, it is likely that the accumulative damage from other factors, such as tobacco use, alcohol consumption, and persistent viral infections such as HPV, are the real culprits. Factors associated with increased risk of oral cancer are illustrated in Table 1.

#### Table 1: Potential Risk Factors for Oral Cancer

| Category            | Risk Factor | Progression |
|---------------------|-------------|-------------|
| **Chemical Factor** | Tobacco     | There are ample evidences suggesting that tobacco in various forms, including smoking, chewing and in betel quid etc., have carcinogenic impact in oral cavity. Tobacco use is responsible for more than 90% of tumors of the oral cavity among men and 60% among women[9]. While tobacco confers the highest risk for cancer of the floor of the mouth[10] it is associated with an increased risk for all sites of oral cancer. |
| Alcohol             | Numerous studies have suggested alcohol to be a major risk factor for OC. Studies have shown that individuals consuming more than 170 g of whisky daily have ten times higher risk of OC than the light drinkers.[11] The combined use of alcohol and tobacco increases the risk for oral cancer far greater than either independently. |
| **Biological Factor** | Viruses     | The human papilloma virus, particularly HPV16, has been definitively implicated in oral cancers, particularly those that occur in the back of the mouth (Oropharynx, base of tongue, tonsillar pillars and crypt, as well as the tonsils themselves). There is an association between HPV and oral cancer, particularly HPV type 16 as shown in multiple case-control studies. HPV 16 accounts for 90% to 95% of HPV-positive oropharyngeal cancer (HPV-OPC), but other high-risk subtypes include 18, 31, 33, and 35. The mechanism of HPV in the etiology of oral cancers may be related to its oncoproteins E6 and E7, which bind to and trigger the degradation of the p53 and pRb tumor suppressor proteins, respectively.[12] |
| Candida             | Candida has been suggested to play a role in initiation of OC. Clinical studies have reported that nodular leukoplakia infected with Candida has a tendency for higher rate of dysplasia and malignant transformation. It has also been shown that epithelium of the chick embryo, when infected with Candida albicans show squamous metaplasia and higher proliferative phenotype.[13] |
| **Genetic Factor**  | Susceptibility | Evaluation of specific genetic polymorphism in key genes involved in oral carcinogenesis has been the major area of study. Glutathione S-transferase M1 (GSTM1) null genotype appears to be the most consistent polymorphic susceptibility marker for head and neck cancer including OC. |
| Oral Health         | Poor Oral Hygiene | There is inverse association between oral hygiene and incidence of OC. Poor oral hygiene and prolonged irritation from sharp teeth have been viewed for their possible role in the development of OC. Poor oral hygiene and dental sepsis is thought to promote carcinogenic action of tobacco.[14] |
| Environmental       | Sun Light    | The majority of cases of carcinoma of the lip occur on the lower lip, which has greater sun exposure than the upper lip. While tobacco has been strongly associated with lip cancer, sun exposure may be a factor as well. Sunscreen use has been associated with a lower incidence of skin cancers[15][16] and thus may lower the incidence of lip cancer |
1.3 Clinical Picture

Oral cancer can be divided into three clinic-pathological categories: carcinoma of the lip vermilion, carcinoma of the oral cavity proper and carcinoma of the oropharynx. Squamous cell carcinoma, which arises from the oral mucosal lining, accounts for more than 90% of the tumors in the oral cavity and oropharynx. Oral squamous cell carcinomas are sometimes preceded by oral preneoplastic lesions, which are often present as visible alterations of the mucosal surface and include leukoplakia and erythroplakia. The earliest signs of oral cavity and oropharyngeal cancer may be mistaken for other problems and some of the most common oral cancer symptoms and signs are illustrated in Table 2.

### Table 2: Common Oral Cancer Symptoms

| No. | Symptom Description                                                                 |
|-----|-------------------------------------------------------------------------------------|
| 1   | Persistent mouth sore- A sore in the mouth that does not heal is the most common symptom of oral cancer |
| 2   | Persistent mouth pain                                                               |
| 3   | A lump or thickening                                                                 |
| 4   | A white or red patch in the oral cavity                                             |
| 5   | Difficulty swallowing                                                               |
| 6   | Difficulty moving the jaw/tongue                                                    |
| 7   | Jaw swelling that makes dentures hurt or fit poorly                                 |
| 8   | Numbness in oral cavity                                                             |
| 9   | Voice Changes                                                                        |
| 10  | Weight Loss                                                                          |

2. Diagnostic

Despite recent diagnostic and therapeutic advances, the 5-year survival rate for oral cancer has remained less than 50% over the last 50 years owing to the following reasons; i) The majority of oral cancer cases (60%) present with advanced stages (III and IV) at diagnosis and ii) Oral cancer has the highest risk for the development of second primary tumors (‘field cancerization phenomenon’) of any cancer.

Often oral cancer is only discovered when the cancer has metastasized to another location, most likely the lymph nodes of the neck. Prognosis at this stage of discovery is significantly worse than when it is caught in a localized intra oral area. Besides the metastasis, at these later stages, the primary tumor has had time to invade deep into local structures. Oral cancer is particularly dangerous because in its early stages it may not be noticed by the patient, as it can frequently prosper without producing pain or symptoms they might readily recognize, and because it has a high risk of producing second, primary tumors. This means that patients who survive a first encounter with the disease, have up to a 20 times higher risk of developing a second cancer. This heightened risk factor can last for 5 to 10 years after the first occurrence. There are several types of oral cancers, but around 90% are squamous cell carcinomas.[17]

Currently available and developing tools are Biopsy and histopathological examination, Vital staining, Biomarkers, DNA ploidy (chromosomal polysomy), Brush biopsy and Optical techniques. Conventional oral examination (COE) is the standard method of revealing potential malignant lesions (PML) and oral squamous cell carcinoma (OSCC), confirming the clinical suspicion by biopsy and histopathological examination. Histopathology has for many years been the gold standard in the diagnosis of OSCC; however, it is a rather slow process, requiring several days to fix, embed and stain the biopsy specimen before results can be available. It is subject to interpretation of pathologists, and although it can detect cellular changes, it can only detect molecular changes if special techniques are employed.[18]

2.1 Dental-Set Up: To detect oral cancer and its precursors

General dental practitioners do not have the clinical training and experience to distinguish potentially malignant lesions from confounding lesions; hence, many of these patients need to be referred to a specialist clinic for scalpel biopsy for a definitive diagnosis.[19] It should be noted that for patients with oral cancer, delays in diagnosis by even 1 month may contribute to a diagnosis of a later stage disease.[20] Moreover, treatment delays of more than 40 days in early-stage oral cancer were associated with an increased risk of locoregional failure impacting their survival.[21] In addition, scalpel biopsy is time consuming, uncomfortable and stressful for the patient and is a relatively expensive procedure.[19]

In the previously described approaches, clinicians illuminate tissue with white or blue light and observe light that is reflected from the mucosal surface. However, there are a range of light–tissue interactions that can be exploited to improve the visualization of neoplastic lesions. In particular, tissue autofluorescence has recently shown promise as an adjunctive diagnostic tool. Fluorophores within the oral epithelium and stroma absorb UV and visible light and can re-emit some of this light at longer wavelengths in the form of fluorescence. When the reflected illumination light is blocked with an absorbing filter, it is possible to visualize the longer
wavelength fluorescence even with the naked eye. Autofluorescence originates from a variety of fluorophores in the oral cavity, and is sensitive to alterations in both tissue morphology and biochemistry associated with neoplasia.[22][23] Oral cancer and precancer display a loss of autofluorescence across a broad range of UV and visible excitation wavelengths; as described later, this loss of fluorescence is largely attributed to a decrease in fluorescent crosslinks associated with stromal collagen that underlies the neoplastic lesion.[19]

3. OralID Technology: Cost Effective and Result Oriented

OralID is commercially available device to visualize loss of tissue autofluorescence associated with precancer and cancer in the oral cavity. OralID uses a proven, optically based technology called “fluorescence technology.” OralID’s fluorescence technology uses a blue light (435–460 nm) that allows a clinician to identify oral cancer, pre-cancer and other abnormal lesions at an earlier stage. OralID is a battery-operated, hand-held oral examination light used as an adjunctive device for oral mucosal screening. The device emits a visible blue light (435–460 nm) that one shines directly into the oral cavity. OralID is equipped with the necessary eyewear to use the device. Wearing the special OralID eyewear enhances the visual effects of the blue light during the oral exam. When the blue light from OralID shines on healthy oral tissue, it fluoresces green. However, when it shines on abnormal tissue, it appears dark due to a lack of fluorescence.

OralID is the simpler, efficient and more affordable oral screening device. OralID uses the fluorescence technology as other commercially available devices but the main advantage lies under its economic slab. The incorporation of OralID in the first-line practice settings, such as dental offices and primary health care settings may be a boon to population for their regular check up for early detection of pre malignant lesions. Further, there is enormous amount of advantage of this cost effective device (OralID) in the developing countries where financial liability is the main hindrance during oral cancer screening for mass population.

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