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Perspective

Screening for oral cancers: Future perspectives.

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Oral cancer is a condition where malignant cells are formed in the mouth and throat. These types of cancers are more predominant in men than in women, and in the age group of 55-64 years. Oral cancer incidence forms 3% of all the malignancies worldwide, and is highest in Brazil, France and Asian countries. The variation in incidence and pattern of disease can be attributed to the combined effect of ageing of the population, as well as to regional differences in the prevalence of disease-specific risk factors.[1]

Oral cancers usually appear as squamous cells forming a thin flat layer at the lining of lips, oral cavity and oropharynx region. This is known as squamous cell carcinoma (SCC), the commonest cancer type accounting for about 96 % of all the cancers in the oral cavity, followed by oral squamous cell carcinoma (OSCC), oropharyngeal and pharyngeal SCC, which is now ranked 6th amongst other malignancies. The remaining oral cancer types include malignant melanomas, salivary gland tumors, sarcomas of the soft tissues or jaw bones, non-Hodgkin's lymphomas and metastases from extra-oral primary tumors.

The detection of oral cancer is a crucial process because of its tendency to be diagnosed at the later stages, which is detrimental to the patients because of its high mortality and morbidity rates (survival rate 15-50%).[2] The mean survival rate of oral cancer patients is up to five years, much lower than other cancer types.[3] The highest death rate of oral cancers is attributed to the low rate of symptoms at the location of metastasis. Initially, it exerts no symptoms, being painless until it expands deeper into the tissues. Therefore, it is not noticed by the patient in the early stages. Prognosis is very bad as it spreads to neck lymph nodes and due to the development of undetected secondary lesions. Thus, early detection can offer 90% cure and promote long term survival with improved treatment outcomes.[4]

Screening consists of looking for cancer before a person has any symptoms. When abnormal tissue or cancer is found early it may be easier to treat. Because, by the time symptoms appear, cancer may have already begun to spread. Thus, screening for oral cancer should be standardised and applied to the healthy population who are apparently free of disease to identify those who may have oral cancer and to distinguish them from those who may not. It should be able to identify tissue changes that may indicate the likelihood of having or developing the disease in question and provide information about the lifestyle pattern and other environmental

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factors of a patient. Because this would help doctors to recommend who should be tested further for cancer, which tests should be used, and how often the tests should be applied. In addition, such screening program must do no harm and be cost effective to the population. The future of oral cancer screening must be developed as an on-going public health measure for the early detection of the disease.[5]

Current practice includes screening of the oral cavity by a dentist or medical doctor. They examine the site for lesions, including areas of leukoplakia (an abnormal white patch of cells) and erythroplakia (an abnormal red patch of cells) as they may eventually become cancerous.[6] But this type of screening is associated with major risks, due to misdiagnosis, false negative and false positive test results. This calls for an urgent need to develop standard or routine screening protocols to diagnose cancer.

Several lifestyle factors, particularly tobacco use, affect an individual's risk of developing oral cancer. Worldwide, 20 to 30% of oral cancer cases are attributable to cigarette smoking. Thus, a comprehensive assessment of lifestyle status is commonly required, based on demographics (specific consideration to age), previous medical history, cancer-related symptoms, dietary and oral assessment, current medication status, psychosocial behaviour, diet plan and swallowing ability, physical activity, social risk factors such as smoking history, alcohol or drug use, socioeconomic status, availability of a social support system and also assessment of the patient and the family´s cultural and religious belief systems.[7] The pooled analysis should be developed to estimate the effects of lifestyle on cancer development.

Diet or nutrition play an important role in a healthy individual for the maintenance of quality of life and among cancer patients for their survival. Based on literature, it is known that 30% to 87% of cancer patients are diagnosed with malnutrition, and 80% of them correspond to oral cancer patients, with 30–60% of patients having protein-calorie malnutrition. Hence, large numbers of patients from this group develop clinical symptoms involving the gastrointestinal (GI) tract contributing to a compromised nutritional status.[8] Therefore the goal of screening will be to identify patients who present with, or are at a high risk for, malnutrition. Earlier studies have validated few tools for screening nutritional status using markers of serum proteins, anthropometrics data and total body potassium. Though these nutritional assessments have shown good correlation with serum inflammation markers, a standard tool has not been generated for the screening of individual cancer. In addition, saliva is another potential body fluid bearing enormous information to diagnose cancer.[9] Further assessment of protein, vitamins and minerals in serum, saliva and urine samples of an individual will lead for an effective screening technique. Thus, the future of nutritional screening will identify and prioritize those patients at highest nutritional risk that need to be evaluated for cancer.

Emotional suppression, distress through feelings of helplessness/hopelessness and depression with cancer diagnosis can elevate the level of stress markers in an individual. If these stress related markers in serum and saliva are assessed, the cancer status can be established. It is clear that cancer patients experience physical, emotional and social losses during treatment and this has to be differentiated from issues of healthy individuals. Various oxidative stress markers in saliva and serum have been evaluated in different populations around the world. But the techniques are not validated specifically for cancer diagnosis. Stress assessment in conjugation with psychosocial behaviour needs to be studied. Individuals who live alone or who are under social deprivation and isolation are at increased risk of stress. Therefore, it is important to understand the variety and causes of the stress. A boundary line should be developed to separate the cancer-generated from the normal self-generated stress.

The development of tumorigenic disease is associated with genotypic and phenotypic alterations such as activation of protoncogenes and oncogenes along with the inactivation of tumor suppressor genes. These variations in genetic factors are expressed by the affected cells or cancerous tissue. Typical changes in the DNA of dysplastic or cancer cells commonly include point mutations, deletions, translocations, amplifications and methylations, as well as changes in cyclin D1, epidermal growth factor receptor (EGFR), microsatellite instability and HPV presence.[10]

It has been studied that nucleic acids and proteins related to cancer cells can be detected in plasma/serum, urine, saliva and other bodily fluids. Hence, these nucleic acids and proteins can be used as molecular markers for the early diagnosis of the disease and as recurrence markers to deal

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with the treatment of cancer.

The methods presently available in the literature are not ready for immediate clinical use as diagnostic tools. Hence, research to develop a simple, efficient, fast, portable and cost-effective screening tool for oral cancer is the need of the hour.

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