ORAL CANCER & EARLY DETECTION: A REVIEW

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ABSTRACT:

Oral cancer is one of the major global threats to public health. The development of oral cancer is a tobacco-related multistep and multifocal process involving field cancerization and carcinogenesis. In spite of numerous advances in the treatment of oral cancer, 5-year survival rate remains only 50%. This poor prognosis is due to several factors. However, single most effective route to improving the long-term outcome of oral cancer is early diagnosis. Oral cancer is among the 10 most common cancers worldwide, and is especially seen in disadvantaged elderly males. Early detection and prompt treatment offer the best chance for cure. As patient awareness regarding the danger of oral cancer increases, the demand for "screening" is expected to increase. It is critical to detect the oral cancer at a very early stage to prevent mortality and morbidity and achieve optimum results of the treatment.

Keywords: Oral biopsy, Early Detection, Oral diagnosis.

INTRODUCTION:

In our oral cavity, oral cancer is a life threatening disease. It is a part of group of head and neck cancer which may arise as a primary lesion in any part of the oral cavity or oropharynx by metastasis from a distant site of origin. Head and neck cancers are among the sixth most common human cancers [1], and constitute 3% of all types of cancers [2].Oral cancer most commonly involves the tongue, floor of the mouth, buccal mucosa, gingiva and lips. The American Cancer Society's screening protocol for all head and neck cancers (including oral cancers) states that asymptomatic individuals between the ages of 20 and 40 should be screened every three years and asymptomatic patients after the age of 40 should be screened annually. High risk individuals, such as smokers and alcohol users should be examined every year, regardless of their age [3]. In many Asian countries, especially India, chewing betel, paan and Areca are known to be risk factors for developing oral cancer. Several studies have been done in the past regarding the factors behind the diagnostic delay of Oral Squamous Cell Carcinoma (OSCC) but early detection of it still remains disappointingly constant over recent decades. Oral Squamous Cell Carcinoma can be a small problem in numerical terms, but it is considered as a highly lethal disease in world population [4]. An early detection of these cancers helps in better and faster treatment for improving

the prognosis to some extent and the available advanced diagnostic adjuncts aid as a helpful tool for the early diagnosis of

Table 1. Currently available diagnostic technologies.

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Vital staining

Biomarkers

DNA ploidy (chromosomal polysomy)

Brush biopsy

Optical techniques

Saliva-based oral cancer diagnostics

PCR-Based diagnostic aids

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VITAL STAINING:

Tolonuim chloride also known as Toluidine blue, (TB) has been used in the past for the detection of mucosal abnormalities of the cervix and the oral cavity. TB is an acidophilic metachromatic dye that has an affinity to selectively stain the acidic tissue components, sulfate, carboxylate and phosphate radicals such as DNA and RNA, but not normal mucosa. Most studies have shown a high sensitivity for the detection of oral carcinomas. Warnakulasuriya and Johnson [5] for example, stained the oral mucosa of 102 patients with clinically suspicious lesions. Eighteen patients proved to have oral carcinomas and all of their respective malignant lesions stained with toluidine blue (sensitivity = 100% for detection of oral cancer). However, the overall specificity was low at 0.62.

Toluidine blue appears to be good at detecting carcinomas but is positive in only

oral cancer to the medical practitioners in treating patients suffering from it.

50% of lesions with dysplasia. In addition, it also frequently stains common, benign conditions such as non-specific ulcers. Martin et al. [6] stained a series of resection specimens to correlate stain uptake to histological areas of carcinoma or dysplasia. All sites of carcinoma were positive, but only 17 of 40 (42%) areas of dysplasia were positive. Lugol's solution is used for delineation of the malignant change which produces a brown black stain when the iodine reacts with the glycogen content. The use of toluidine blue and Lugol's iodine serves as a useful adjunct in the diagnosis of patients who are at risk and for selecting the site for biopsy with wide field cancers prior to treatment [7]

TUMOUR MARKERS:

Tumor markers are biochemical substances elaborated by tumor cells due to either the cause or effect of malignant process produced by host in response to a tumor that can be used to differentiate a tumor from normal tissue or to determine the presence of a tumor based on measurements in blood or secretions [8] These Tumor markers may be present in blood circulation, body cavity fluids, cell membranes and cell cytoplasm when released by cancer cells or produced by the host in response to cancerous substances. Tumour Suppressor Genes, oncogenes, cell proliferation markers, angiogenic markers and cell adhesion molecules are some of the potential tools which help in prediction for the prognosis of patients with OSCC.

According to a study, use of cytokeratin markers are also used in detecting OSCC by the help of analyzing the altered keratin expression in the oral site especially the buccal mucosa [9].

DNA PLOIDY:

DNA ploidy is the measurement of nuclear DNA content that provide a measurement of gross genetic damage. If the chromosomes are not uniformly distributed to the daughter cells during mitosis or if some parts of chromosomes become detached, the chromosomal segregation becomes unbalanced and aneuploidy is seen which is commonly observed in many cancers. . Cancer progression is contributed by genomic instability, and dysplastic lesions are distinguished by abnormal DNA content [10]. The cytological samples after staining with Feulgen dye are compared against a reference group of cells, and a computer-assisted analysis identifies deviations of cellular DNA content. DNA image cytometry shows high sensitivity and serves as a non-invasive method for cancer detection. [11]

BRUSH BIOPSY:

The Brush Biopsy (CDx Laboratories, Suffren, NY) was introduced as a potential oral cancer case-finding device in 1999. It was designed for the interrogation of clinical lesions that would otherwise not be subjected to biopsy because the level of suspicion for carcinoma, based upon clinical features, was low.

Several studies have shown encouraging results with oral brush cytology for evaluation of oral precancerous lesions. The study by Scuibba et al. [12] was a prospective, multicenter study to determine the sensitivity and specificity of oral brush biopsy (OralCDx) for the detection of pre-cancerous and cancerous lesions of the oral mucosa. Brush biopsy results were recorded as "positive", "atypical", or "negative". Patients with clinically suspicious lesions (Class I) underwent both the OralCDx and the "gold standard" scalpel biopsy (n = 298). The remaining patients, whose lesions were judged to be innocuous (Class II), only underwent OralCDx testing (n = 647). The only exception was for a small number of cases with abnormal OralCDx results that underwent subsequent scalpel biopsy at the investigator's discretion (n = 29). Using a combination of Class I and Class II lesions, a 100% sensitivity with 100% specificity was reported if positive test results were deemed indicative of cancer and 92.9% specificity if atypical or positive results were considered indicative of cancer.

OPTICAL TECHNIQUES:

Tissue reflectance: Tissue reflectance (ViziLite Plus, MicroLux DL) has been used for many years as an adjunct in the examination of the cervical mucosa for "acetowhite" premalignant and malignant lesions. Recently, this form of tissue reflectance-based examination has been adapted for use in the oral cavity and is currently marketed under the names ViziLite Plus and MicroLux DL. These products are intended to enhance the identification of oral mucosal abnormalities. With both systems, the patient must first

rinse with a 1% acetic acid solution followed by direct visual examination of the oral cavity using a blue-white light source. ViziLite Plus uses a disposable light packet, while the MicroLux unit offers a reusable, battery-powered light source. The 1% acetic acid wash is used to help remove surface debris and may increase the visibility of epithelial cell nuclei, possibly as a result of mild cellular dehydration. Under blue-white illumination, normal epithelium appears lightly bluish while abnormal epithelium appears distinctly white (acetowhite). ViziLite Plus also provides a tolonium chloride solution (TBlue), which is intended to aid in the marking of an acetowhite lesion for subsequent biopsy once the light source is removed. ViziLite has also been used to examine a variety of oral lesions, including linea alba, leukoedema, hairy tongue, leukoplakia, traumatic ulcer, fibroma, amalgam tattoo, tori, and frictional keratosis. [13]

Narrow-emission tissue fluorescence (VELscope): Fluorescence spectroscopy involves the exposure of tissues to various excitation wavelengths so that subtle differences between normal and abnormal tissues can be identified. Conversely, fluorescence imaging involves the exposure of tissue to a rather specific wavelength of light, which results in the autofluorescence of cellular fluorophores after excitation. The presence of cellular alterations will change the concentrations of fluorophores, which will affect the scattering and absorption of light in the tissue, thus resulting in changes in color that can be observed visually. The use of VEL scope Vx is a safe and simple technique and the entire examination can be done in about two minutes. However, it is a relatively new device and so far only a limited number of studies have been done on its effectiveness as a diagnostic adjunct for oral cancer [14]. Using this device, Lane et al., investigated the ability of the VELscope to identify precancerous or cancer lesions. The study consisted of 44 patients who had a history of oral dysplasia or HNSCC. Following a COE, the oral cavity was screened using the VELscope to identify areas that demonstrated loss of autofluorescence. In addition, biopsies of the lesions were also obtained. Using histology as the gold standard, the device demonstrated a 98% sensitivity and a 100% specificity for discriminating dysplasia and cancers from normal oral mucosa. [15]

In Vivo Confocal Microscopy: Confocal microscopy is an imaging technique for various researches in cell biology with an advantage of optical sectioning and high resolution imaging. In vivo confocal images from the oral cavity show the characteristic features such as nuclear irregularity which is used to differentiate OSCC from normal oral mucosa. However, further optimization of the instrument is still needed to rate it a promising non-invasive tool for the early detection of oral cancer.

SALIVA-BASED ORAL CANCER DIAGNOSTICS:

Saliva may be used as a diagnostic tool for molecular biomarkers for oral cancer detection. Saliva is a mirror of the body and reflects normal and disease states and its use as a diagnostic fluid meets the demands of an economic, easy to collect and non-invasive diagnostic tool.

Saliva, as a diagnostic tool, has many merits over serum-

• Saliva collection is a non-invasive procedure.

• Non costly

• Large populations can be screened.

Measurement of specific salivary macromolecules and examination of proteomic or genomic targets such as enzymes, cytokines, growth factors, metalloproteinase, endothelin, telomerase, cytokeratins, mRNAs, and DNA transcripts can be done by the saliva [16]. Cyfra 21-1, TPS, carcino-embryonic antigen (CEA), SCC, CA125, and CA19- 9 are the most studied epithelial serum circulatory tumor markers in the saliva of carcinoma patients.

PCR-BASED DIAGNOSTIC AIDS:

The polymerase chain reaction (PCR) is a scientific technique in molecular biology which can be used in the diagnosis and study of infectious diseases and malignancies associated with micro organisms. PCR helps in the study of cancer and provide clearer understanding of the pathogenesis of neoplasia. PCR can be used to detect mutations in cancer-associated oncogenes (e.g., K-ras, Nras), tumor suppressor genes (e.g., p53, p16) etc. and aids as an important detection tool [17]

CONCLUSION:

Potentially malignant disorders pose an important threat to the overall survival of an individual. Oral health professionals play a major role in early detection and treatment of these disorders, thus combating these dreadful lesions and improving the prognosis. A wide variety of diagnostic aids are currently available which are used for early detection of these disorders. There has been a dramatic increase in the development of many potential oral cancer screening techniques in last few years and still many researchers are on the look for any better and faster aids of diagnosing these life threatening cancers.

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