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DIAGNOSTIC METHODS FOR EARLY DETECTION OF ORAL CANCER: AN OVERVIEW

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Abstract

Oral cancer is one of the most mutilating diseases affecting mankind. It is the sixth most common malignancy in the world. Early detection and prompt treatment offer the best chance of cure. The signs and symptoms of oral cancer often resemble less serious conditions more commonly found and similarly usually presenting as a lump, red or white patch or ulcer. Historically the screening of oral cancer and precancerous lesions has relied upon the conventional oral examination. Differentiation between early stage cancers, precancers and benign lesions are often difficult because of the appearance of these lesions. A variety of diagnostic aids and adjunctive techniques are available to assist in the screening of healthy patients for evidence of otherwise occult cancerous change or to assess the biologic potential of clinically abnormal mucosal lesions. As patient awareness regarding the danger of oral cancer increases, the demand for "screening" is expected to increase.

Key Words: Oral cancer, Screening, Early detection of cancer.

INTRODUCTION

Oral cancer is traditionally defined as squamous cell carcinoma of the lip, oral cavity and oro- pharynx. It is the sixth most common malignancy in the world[1, 2]. Despite numerous advances in treatment, the 5-year survival has remained approximately 50% for the last 50 years[3]. This poor prognosis is likely due to several factors such as the development of multiple primary tumors, the advanced extent of the disease at the time of diagnosis etc. The disease primarily arises in the surface epithelium that is readily accessible to direct visual and tactile examination. But some lesions are ignored or missed by patients, health care workers or both. It may be due to an incomplete understanding or awareness that even small asymptomatic lesions can have significant malignant potential. It is expected that early diagnosis of potentially malignant lesions can reduce mortality. One approach to this problem would be to improve the ability of oral health care professionals to detect relevant potentially malignant lesions or cancerous lesions at their earliest or most incipient stage. This may be the best way to ensure patient survival and improved quality of life.[4,5]Oral precancerous lesions may also occasionally regress if the healthcare professional motivates the patient to reduce the risk factors including elimination of carcinogens including tobacco and alcohol.

Oral examination

Conventional oral examination (COE) using normal (incandescent) light, has long been the standard method for oral cancer screening. Conventional visual cancer screening for some anatomic location can be highly successful. For example, visual inspection of skin lesion can be an effective screening method for melanoma, with sensitivity and specificity rate as high as 98%[6,7]. However, while COE has traditionally been the mainstay of oral cancer screening for decades, its utility remain controversial.Although COE may be effective as a screening test; there are still many problem with this approach. First, approximately 5-15% of the general population has oral mucosal abnormalities[8,9]. Without question the vast majority of these lesions are clinically/ biologically benign. Second, the classical clinical presentation of an oral malignancy or premalignant lesion: a red patch or persistent ulcer that cannot be diagnosed as any other condition is well recognized. In reality, most lesions are white patches or plaques, also known as true leukoplakia. The problem, however, is that only a small percentage of leukoplakia are progressive or become malignant and a COE cannot discriminate between these lesions and their non-progressive counterpart. Furthermore, while COE may detect a number of clinical lesions and a small percentage of

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those may exhibit histological features of premalignancy. Therefore, while COE may be useful in the discovery of some oral lesions, it does not identify all potentially malignant lesions, nor does it accurately detect the small proportion of biologically relevant lesions that are likely to progress to cancer. COE may be useful as a method of screening for oral cancer only in high risk groups like chronic smokers or alcoholics .[10]

Early diagnosis and treatment are the goals. Since the COE has undetermined sensitivity and specificity, there is a need for more accurate diagnostic tools that can detect early lesions. The need is great considering the larger number of oral lesions encountered by health care workers performing oral cancer screening, which amount to 5-15% of screened patients.

Vital staining

In vivo vital staining has been used extensively in gynecology for the detection of malignant change via colposcopy. Toludine blue stain areas of cervical carcinoma in situ in delineating abnormal from normal epithelium. In contrast, Lugol's iodine is retained in normal squamous epithelial cells, but not in dysplastic or malignant cells of squamous epithelium of the cervix. Oral carcinoma in situ and early invasive oral carcinoma demonstrate affinity for Toludine blue dye. Lugol's iodine and Toludine blue have been used together in the detection of early carcinoma and the diagnosis of oral lesions.

Toludine blue (also known as tolonium chloride) is an acidophilic metachromatic nuclear stain that may stain nucleic acids and abnormal tissues. Toluidine blue (TB) staining is claimed to be a simple, inexpensive and sensitive adjunct tool for identifying early OSCC and high-grade dysplasias.It has been used as a means of identifying clinically occult lesions in patients whose oral mucosa may otherwise be normal –that is as a screening test or adjunct. Toludine blue has also been demonstrated to help assess the status of margins around oral cancer at the time of resection.[11]Toluidine blue appears to be good at detecting carcinomas but is positive only ~50% of lesions with dysplasia[12,13] In addition, it also frequently stains common benign conditions such as non-specific ulcers.

Methylene blue is a heterocyclic aromatic chemical compound. At room temperature appears as a solid, odorless, dark-green powder, which yields a blue solution when dissolved in water .Considering its low toxicity and the fact that it is cheaper than TB, it may be convenient to substitute it for TB in large-scale oral screening in high-risk patients. [14]

Light-based detection systems

Chemiluminescence (reflective tissue fluorescence) has been used as an adjunct in the examination of the cervical mucosa for premalignant and malignant lesions. Recently this technology has been adapted for use in the oral cavity and is currently marketed under the names Vizilite Plus and MicroLux DL.The patient must first rinse with a1% acetic acid solution followed by direct visual examination of the oral cavity using a blue-white light source.

The normal epithelium appears lightly bluish while abnormal epithelium appears distinctively white.ViziLite Plus uses a disposable chemiluminescent light packet, while the MicroLux unit offers a reusable, battery-powered light source. This technique may help identify lesions that cannot be seen with incandescent light[15]. Well controlled clinical trials are needed that specifically investigate the ability of these devices to detect precancerous lesions that are invisible by COE alone. If such discrimination can be confirmed, it would support the use of this technology as a true screening device.

VELscope (narrow emission tissue fluorescence)

Fluorescence spectroscopy involves the exposure of the tissues to various excitation wavelenghths so that subtle differences between normal and abnormal tissues can be identified.Fluorescence imaging involves the exposure of the tissue to a rather specific wavelength of light, which results in the autoflourescence 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 changes in colour that can be observed visually.Based upon available data,it is found that both imaging and spectroscopy were excellent at distinguishing between normal and malignant tissue[16] .Imaging was found to be more useful for screening of new lesions than spectroscopy because it was not feasible to scan the entire oral cavity using the small optical fibers required for spectroscopy.

The VELscope is a portable device that allows for direct visualization of the oral cavity and is being marketed for use in the oral cancer screening. Under the blue excitation light (400-460 nm) provided by the unit, normal mucosa emits a pale green autofluorescence when viewed through the selective

(narrow band) filter incorporated within the instrument hand piece. In contrast, abnormal or suspicious tissue exhibits decreased levels of normal autofluorescence and appears dark by comparison to the surrounding healthy tissue.

Brush cytology

The Brush Biopsy 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[17,18].The brush biopsy uses a small nylon brush to gather cytology samples then sent for computer scanning and analysis (Oral CDx) to identify and display individual cells.When an abnormal result is reported (atypical or positive),the clinician must follow-up with a scalpel biopsy of the lesion, as the use of brush cytology does not provide a definitive diagnosis.

Liquid Based Cytology

Liquid-based cytology is one of the recent trends in screening technology. Samples are collected using a brush-like device. The obscuring materials like mucus and blood are removed with clearing solution and centrifuged. Supernatant is discarded and pellicle obtained is admixed with cellular base solution which is then transferred to clean slide. It produces a more representative sample of the specimen, with reduced obscuring background material[19].Studies on liquid-based methods have shown an overall improvement on sample preservation, specimen adequacy, better visualization of cell morphology, reproducibility and reduction in cell overlapping[20,21].

Histopathology

The American Academy of Oral and Maxillofacial Pathology recommends that "all abnormal tissue be submitted promptly for microscopic evaluation and analysis". It provides diagnosis as well as information on the clinical behavior of the lesions which helps in treatment.[22]

Even though all the above mentioned clinical as well as cytological methods can be considered as diagnostic adjuncts; the gold standard in diagnosis is still considered to be the histopathology. The diagnostic adjuncts may be used as a guide in selecting cases for biopsy as well as in marking the more representative area within a lesions.

Biomarkers

Application of molecular biology in the diagnostic work - up of potentially malignant lesions are of paramount importance in predicting the biologic behavior of such lesions. Biomarkers associated with higher cancer risk in premalignant lesions include high chromosomal polysomy, high p53 protein accumulation in the parabasal layer and loss of heterozygosity at chromosome3p or 9p. The collective score of these markers is more predictive of cancer risk than the independent score of any single marker.[23]

CONCLUSION

Screening and early detection in populations at risk have been proposed to decrease both the morbidity and mortality associated with oral cancer. However the visual detection of premalignant oral lesions has been problematic because early lesions of oral cancer and precancer are often subtle and rarely demonstrate the clinical characteristics observed in advanced cases such as ulceration, induration, pain, or associated cervical lymphadenopathy. Besides their clinical subtlety, premalignant lesions are highly heterogenous in their presentation and may mimic a variety of common benign or reactive conditions .Combined with an increased public awareness of oral cancer in general; robust diagnostic aids that allow clinicians to detect lesions unseen by conventional examination technique should help more affected patients become long-term survivers of this challenging disease.

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