Advancement in Diagnostic Aids for Oral Premalignant Lesions: A Review

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ABSTRACT: Early diagnosis and treatment remains the key to improved patient survival. Because the scalpel biopsy for diagnosis is invasive and has potential morbidity, it is reserved for evaluating highly suspicious lesions and not for the majority of oral lesions which are clinically not suspicious. Simple visual examination, however, is well known to be limited by subjective interpretation and by the potential, albeit rare, occurrence of dysplasia and early OSCC within areas of normal-looking oral mucosa. As a consequence, adjunctive techniques have been suggested to increase our ability to differentiate between benign abnormalities and dysplastic/malignant changes as well as to identify areas of dysplasia/early OSCC that are not visible to naked eye. Diagnostic tests for early detection include toluidine blue, brush biopsy, Imprint biopsy, chemiluminescence, tissue Auto fluorescence, biomarkers and spectroscopy. The present paper reviews advance techniques used to improve premalignant and malignant lesion diagnosis.

KEYWORDS: Squamous cell carcinoma, Toluidine blue staining, Auto fluorescence, Brush Biopsy, Chemiluminescence, Spectroscopy

INTRODUCTION:

Cancer of the oral cavity is the sixth most common malignancy reported worldwide and one with the highest mortality rate among all malignancies. In India, oral cancer represents a major health problem accounting for up to 40% of all cancers, and is the most prevalent cancer in males and the third most prevalent cancer in females. It often arises from premalignant lesions such as Leukoplakia, Erythroplakia and Oral Lichen Planus (OLP). Detecting oral malignant and potentially malignant lesions in early stages dramatically affects survival rates. Unfortunately, 50% of patients have regional or distant metastases at the time of diagnosis, which reflects a significant diagnostic delay. Diagnosis of oral cancer at an early stage or at the pre-neoplastic level is critical to improve survival in oral squamous cell carcinoma patients. One major problem inherent in current oral cancer screening is that visual inspection often cannot differentiate between lesions harboring dysplasia and/or early cancer from those that do not. This is especially true for innocuous looking lesions which are subjected to “watchful waiting” and close follow-up despite the fact that some precancerous and cancerous cells within them remain undetected and are allowed to progress to a more advanced stage. The practice of not properly evaluating all suspicious lesions, that is, lesions without a specific etiology such as trauma or infection, invariably results in delay of the correct diagnosis, limiting treatment options.

By far clinical examination and histopathological studies have been used for detection of precancerous and cancerous lesions. As with other fields of medicine, in oral cavity diagnostic approaches are going toward noninvasive, simple, inexpensive, painless and accessible methods such as cytology, brush biopsy, toluidine rinses, chemiluminescent devices, and auto fluorescence, spectroscopy. This paper reviews recent advances in techniques for detecting lesions early and predicting their progression or recurrence.

VITAL STAINING:

Toluidine blue, also known as tolonium chloride, is a vital dye, more commonly referred to as TB. It has been used for more than 40 years to aid in detection of mucosal abnormalities of the cervix and the oral cavity. It binds preferentially to tissues undergoing rapid cell division (such as inflammatory, regenerative and neoplastic tissue), that is believed to stain nucleic acids, DNA change associated with Oral premalignant lesions or both. The binding results in the staining of abnormal tissue in contrast to adjacent normal mucosa. Hence, it has been used for many years as an aid to the identification of clinically occult mucosal abnormalities and as a useful way of demarcating the extent of a potentially malignant lesion prior to excision. Analysis of current evidence suggests that TB is good at detecting carcinomas, but its sensitivity in detecting dysplasias is significantly lower. Furthermore, there remain a high percentage of false positive stains which impairs its use in primary care settings also as a valid screening mean.
In addition, controversy exists regarding the subjective interpretation. At present, TB is best used by experienced clinicians as an adjunct to clinical examination in the evaluation of the biologic potential of potentially malignant oral lesions.10-17

CHEMILUMINISCENT DEVICES: (reflective tissue fluorescence)

The chemiluminescence technique serves the purpose of improving the identification, visualization, and monitoring of oral precancerous lesions, and consists of the emission of light from a chemical reaction between hydrogen peroxide and acetylsalicylic acid inside a capsule light stick. This reaction emits a blue/white light (430–580 nm) whose principle is based on the reflective properties of tissues that present cellular alterations such as a higher nuclear/cytoplasmatic rate. The “acetowhite” lesion is more defined and sharper, whereas the normal tissue is dark (Fig-1).18-23

This seems to be an easy, safe and noninvasive system capable of helping the dentist to better visualize lesions, as well as its edges. One disadvantage is that this system is expensive. Furthermore, chemiluminescence light seems to be nonspecific as it does not identify the lesion etiology—whether inflammatory, neoplastic benign, or neoplastic malignant—and this could lead to unnecessary biopsies. The adjunctive use of T-Blue630 is a feature specific to the ViziLite-Plus system. T-Blue630 is the brand name for pharmaceutical-grade toluidine chloride, a toluidineblue dye. After using the ViziLite to identify abnormal “aceto-white” areas, T-Blue630 can be used to mark suspicious areas for further evaluation, e.g. biopsy.18-25

VELSCOPE: (narrow-emission tissue fluorescence)

Tissue autofluorescence has been used in the screening and diagnosis of precancers and early cancer of the lung, uterine cervix, skin and, more recently, of the oral cavity. The concept behind is that changes in the structure and metabolism of the epithelium, as well as changes of the subepithelial stroma, alter their interaction with light. Specifically, these epithelial and stromal changes can alter the distribution of tissue fluorophores and as a consequence the way they emit fluorescence after stimulation with intense blue excitation (400 to 460 nm) light. The autofluorescence signal is finally visualized directly by a human observer. Normal oral mucosa emits a pale green autofluorescence when viewed through the instrument handpiece whilst abnormal tissue exhibits decreased autofluorescence.10, 26, 27 This method uses a small optic fiber and consequently does not cover the entire mouth, so it is employed only for isolated lesions, lesion edge, and cancerization field determination.

Several studies have investigated the effectiveness of the VELscope system as an adjunct to visual examination for (i) improving the distinction between normal and abnormal tissues (both benign and malignant malignant changes), (ii) differentiating between benign and dysplastic/malignant changes, (iii) and identifying dysplastic/malignant lesions (or lesion's margins) that are not visible to the naked eye under white light.10, 18, 25, 28

OPTICAL SPECTROMETRY:

A technique called autofluorescence spectroscopy has been recently tested in oral oncology research. The autofluorescence spectroscopy system consists of a small fiber that produces various excitation wavelengths and a spectrograph that receives and records on a computer and analyzes, via a dedicated software, the spectra of reflected fluorescence from the tissue. This can evaluate physical and biochemical properties of a specific oral site by analyzing the emitted fluorescence light, providing automated, noninvasive discrimination between benign and neoplastic epithelial lesions in many anatomic sites. Several small clinical series demonstrated that the fluorescence intensity from normal mucosa is generally greater than that from abnormal mucosa. Studies suggest that fluorescence spectroscopy can provide a simple, objective tool to improve in vivo identification of oral neoplasia. This technique has the clear advantage of eliminating the subjective interpretation of tissue fluorescence changes. However, the downside is that more variables (e.g. combination of wavelengths, methodology of fluorescence analysis etc). Overall, autofluorescence spectroscopy seems to be very accurate for distinguishing lesions from healthy oral mucosa, with high sensitivity and specificity, especially when malignant tumors are compared to healthy mucosa. However, the ability of the technique to distinguish and classify different types of lesion has been reported to be low. Moreover autofluorescence spectroscopy is for practical reasons not suitable to detect new lesions or to demarcate large lesions as the optical fiber can sample only a small mucosal area. This limits the use of spectroscopy to the evaluation of a well defined small mucosal lesion that has been already identified through visual inspection, with the attempt to clarify its benign or (pre)malignant nature. Further research is needed to support this clinical application of autofluorescence.10, 28

BRUSH BIOPSY:

The Brush Biopsy (CDx Laboratories, Suffren, NY) was introduced as a potential oral cancer case-finding device in 1999, it is one of these new techniques emerging in the recent decade. 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. The oral brush biopsy, also known as OralCDx Brush Test system uses a specially designed brush that is used to obtain a transepithelial specimen, (sample of cells) from a mucosal lesion with representation of the superficial, intermediate and
parabasal/basal layers of the epithelium. This test was specifically designed to investigate mucosal abnormalities that would otherwise not be subjected to biopsy because of low-risk clinical features. A specially designed brush is thenon-lacerational device used for epithelial cell collection and samples are eventually fixed onto a glass slide, stained with a modified Papanicolaou test and analyzed microscopically via a computer-based imaging system. Results are reported as "positive" or "atypical" when cellular morphology is highly suspicious for epithelial dysplasia or carcinoma or when abnormal epithelial changes are of uncertain diagnostic significance respectively.

REFERENCES:


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LIST OF PHOTOGRAPHS

Figure- 1 showing "Acetowhite appearance of the lesion

Figure-2a shows lesion prior to use of T blue

Figure- 2b shows lesion after the use of T blue

Figure-3a showing lesion prior to use of velscope

Figure-3b Appearance following autofluorescence

Figure-4 The system probe was designed to be used in (gentle) optical contact with tissues, and incorporates two optical fibres, one to transmit the light into the tissue and the other one for collecting the scattered light from tissue; the two probes are built-in one bigger probe so the viewer can see only the latter. Placement of the probe in direct contact with the tissue avoids interference with specularly reflected light.

Figure- 5 Use of oral Cdx brush