Progression In Diagnosis Of Oral Cancer

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ABSTRACT- scalpel biopsy can be used since it is invasive and has potential morbidity. Critical diagnostic tools are devised for early detection of oral dysplasia and malignancy since they are practical, non-invasive and can be easily done in an out-patient set-up. Diagnostic tests are brush biopsy, toluidine blue staining, salivary proteomics, DNA analysis, biomarkers and spectroscopy. This review explains the diagnostic aids and their value in detecting oral squamous cell carcinoma and its premalignant lesions.

Keywords: Oral Cancer, Diagnostic tools, Brush Biopsy, Saliva.

INTRODUCTION

In developed countries like United States,survival rates of oral cancer were given 53% between 1975-77and 63% between 1999-2005 [1]. The improved survival rates might be explained by the use of newer diagnostic tools which detect the disease in its primary stage or use of newer chemotherapeutic options.

DIFFERENT METHODS FOR DETECTING ORAL CANCER AND DYSPLASIA

- Visual examination
- Excision biopsy and Histopathology
- Oral brush biopsy
- Toluidine blue
- Light-based detection systems
- Chemiluminescence (ViziLite Plus; Microlux/DL, Orascoptic-DK)
- Tissue fluorescence imaging (VELscope)
- Tissue fluorescence spectroscopy
- Biomarkers
- DNA-analysis
- Laser capture microdissection

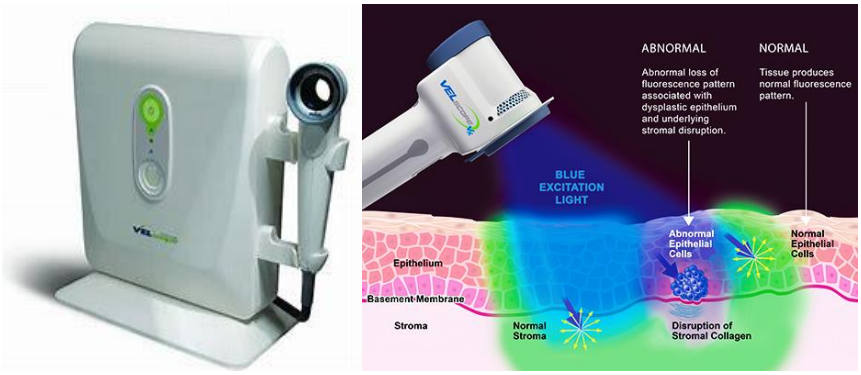
ORAL CANCER SCREENING

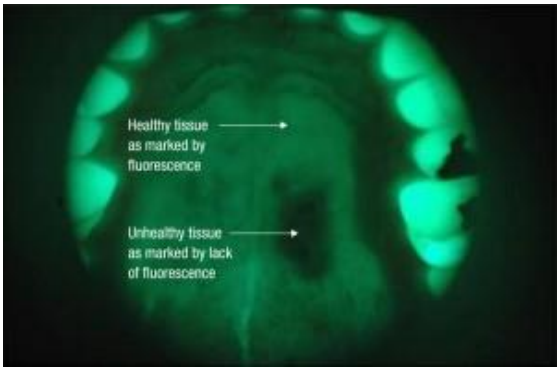
Oral cancer screening means detecting oral precancerous and cancerous lesions. Certain number of cancer screening programs for malignant lesions have shown to significantly decrease patient morbidity and mortality. In India, randomized controlled oral cancer screening trial was conducted with 130,000 individuals, it was concluded that visual examination was anessential method of oral cancer screening for chronic smokers or alcoholics [2]. Since majority of the oral lesions are benign, clinical inspection alone cannot distinguishpotentially precancerous lesions and cancerous lesions. Early diagnosis of oral cancer reduces high mortality rate. Early detection decreases the morbidity of the disease and hence it is necessary for raising awareness among public and developing access to oral health services. For instance: Oral squamous cell carcinoma (OSCC) is often preceded by dysplastic features. If early detection of this disease is done, malignant transformation of dysplasia can be prevented and treated accordingly. Oral precancerous lesions can also be reduced if dental clinician encourages the patient to reduce alcohol and tobacco habits.

LIGHT-BASED DETECTION AIDS

- Light-based oral cancer diagnostic aids have been developed to predict precancerous and cancerous lesions at their earliest stage.
- This method is used additionally to visual examination thus helping in observing the lesions.
- Commercially available light-based systems: Vizilite Plus with TBlue system (Zila Pharmaceuticals, Phoenix, Arizona, U.S.), VELscope (LED Dental, White Rock, British Columbia, Canada) Microlux/DL (AdDent Inc, Danbury, Connecticut) and Orascoptic DK (Orascoptic, Middleton, WI). These are based on the presumption that abnormal metabolic or structural alteration have different absorbance and reflectance properties.
- VEL scope is a device which uses visible light in the 430 nm wavelength for causing fluorescent excitation of some tissue compounds

FIGURE1: VELSCOPE





Using Vizilite, patientfirst rinses with acetic acid, after which oral cavity is examined with an illuminated chemiluminescent light stick

FIGURE 2: ViZilite

Microlux and Vizilite are similar where it needs the patient to first rinse with acetic acid and then the oral cavity is examined with a battery-powered fibre optic visible light instead of a chemiluminescent visible light source.

FIGURE 3: MICROLUX

Orascoptic DK also needs an acetic acid rinse and three-in-one device with a battery-powered handheld light source is used.

- Since none of these devices is a diagnostic test, the manufacturer does not make any claim that these devicesareneither sensitive nor specific to an abnormal oral lesion identification.
  - It has been suggested in a study that the potential benefits of several of these lights, the sensitivity of Vizilite was 0% and the sensitivity of VELscope was 50%.
  - It was concluded that the use of ViziLite or VELscope along with a conventional screening examination was not useful in identifying dysplasia or cancer.Dentists and patients would have a negative ViziLite or VELscope examination result because precancerous and cancerous lesions would be unidentified by both.
- Additional studies are required because these screening aids helps in identifying lesions that may have been overlooked with a conventional oral examination but it cannot be used for detectinga precancerous or cancerous lesion.
- Hence,only a confirmed test examining cells or tissue can define the biologic behaviour of a lesion [3].

DIAGNOSTIC TOOLS

Brush Biopsy

- Oral brush biopsy was used to collect samples from 5% of clinically appearing benignoral mucosal lesions and it is confirmed by using scalpel biopsy technique to detect dysplastic epithelial changes or invasive cancer [4].
- OralCDx® (OraCDx Laboratories, Inc. Suffern, NY), is an oral brush biopsy combined with computer assisted analysis test. It is used as a diagnostic test to detect dysplasia in oral mucosal area where they have no suspicious clinical appearance.
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FIGURE 4: ORAL CDx

- In brush biopsy technique, cells from the oral epithelium are collected. Advantage of this technique is it is a chair-side procedure, easy to perform, painless test. It also helps in evaluating any suspicious lesions such as red and white lesion to detect dysplasia.
- Approximately 10% of all cases appears to be normal. Depending on the clinical findings, the laboratory sometimes recommends scalpel biopsy, retesting or observation.
- Results will be controversial if 2 biopsy samples are collected from the different spot of dysplastic lesion since dysplasia is multicentric.
- Biologic nature of a lesion alters over time as benign lesions may develop dysplastic features and dysplasia can also regress.
- Usually there may be a confusion among oral pathologists about the histologic diagnosis of dysplasia as the brush biopsy and scalpel biopsy results arenot definite to arrive a proper diagnosis.
- Hence comparisons were made between any 2 biopsy methods (i.e. brush biopsy vs. scalpel biopsy or scalpel biopsy vs. scalpel biopsy). Studies should be conducted to compare the results of both biopsies carried out at the same time, same site of the suspicious lesion[5].

Scalpel Biopsy

Sampling by scalpel biopsy and histological diagnosis have been a keystone for detecting premalignant and malignant oral lesions. But scalpel biopsy has certain limitations where the clinicians should be clear about it. An oral biopsy is invasiveand includes psychological implications for the patient and technical difficulties for the clinician. If the lesions are wide spread, then the most representative areas must be sampled to prevent diagnostic errors[6]. Due to some artefacts oral biopsy specimens results in crushing, fulguration or incorrect fixation and freezing[7]. To avoid artifacts there is a controversy about the selection of both technique (incisional versus excisional); punch biopsy may also have some advantages[8].

Toluidine Blue (TB) Staining

It is a simple, inexpensive and sensitive adjunct tool for diagnosing early OSCC and high-grade dysplasia [9]. Procedure is 1% aqueous TB solution is applied to a suspicious lesion for 30 seconds, this acidophilic metachromatic nuclear stain differentiates areas of carcinoma in situ or invasive carcinoma from control groups. This technique is used to assess the marginal status around oral cancer at the time of resection [10]. Though toluidine blue test is useful in detecting oral cancers, it must not be taken as aa alternative for biopsy.

Laser Capture Microdissection

Laser capture microdissection (LCM) defines the molecular basis of malignancy[11]. It acts as an ideal method for the extraction of cells from specimens in which the definite morphology of the captured cells and

surrounding tissue are preserved. It detects the biomarkers and provides protein fingerprint models for early diagnosis of OSCC. LCM combined with SELDITOF-MS technology and bioinformatics appears to be a good diagnostic tool for molecular diagnosis [12].

DNA-Analysis

- DNA image cytometry measures ploidy status to establish the potential of malignant cells.
- After staining with Feulgen dye, the cytological samples are compared with a reference group of cells. A computer-assisted analysis has been designed to detect cellular DNA deviations.
- Various studies have confirmed the advantages of DNA ploidy analysis because it acts as an adjunct to conventional cytology assessment of cytobrush samples for oral cancer diagnosis[13].
- Multimodal cell analysis (MMCA) and mechanical phenotyping detects oral malignancies earlier [14].

Saliva-Based Oral Cancer Diagnosis

Saliva testing is an alternative to serum testing. It is an effective modality for diagnosis, prognosis and monitoring post-therapy status of oral cancer. Advantages of saliva- based diagnosis is it is less expensive, non- invasive and easily approachable for large scale screening. It is also used to measure salivary macromolecules, proteomic or genomic targets such as enzymes, cytokines, growth factors, metalloproteinases, endothelin, telomerase, cytokeratins, mRNAs and DNA transcripts [15].

Lab-on-a-Chip

Microfluidics technology is also referred as lab-on-a-chip or micro-total-analysis systems (TAS). It is used in adaptation, miniaturization, integration, and automation of analytical laboratory procedures in a single device or "chip." Microfluidics is observed as the chemistry or biotechnology equivalent of silicon integrated circuit chip that has transformed into electronics, computers, and communications. Diagnosis of oral dysplasia and malignancy within the chip uses membrane-associated cell proteins which are uniquelyexpressed on dysplastic and cancer cells cell membranealong with their exclusive gene transcription profiles [16].

Microscope

Multispectral digital microscope (MDM) has been used as a tool to detect oral malignancy. It acquires in-vivo images in aunique mode i.e. fluorescence, narrow-band (NB) reflectance, and orthogonal polarized reflectance (OPR) diagnosing oral lesions [17].

Spectroscopy

- Autofluorescence and chemiluminescence are non-invasive in-vivo tools for diagnosing premalignant tissue alterations. It has been suggested that autofluorescence spectroscopy produce valuable information for diagnosis and therapeutic response in oral submucous fibrosis[18].
- Diffuse reflectance spectroscopy (DRS) is also a non-invasive in-vivo tool for detecting premalignant tissue changes [19].
- Pavlovaet al had reported that oral lesion examination with optical tools results in loss of fluorescence intensity and it might fail to differentiate benign from precancerous lesions[20].

Tomography

Optical coherence tomography (OCT)is a non-invasive tomographic imaging modality to identify inflammatory areas, dysplasia and cancer. It records subsurface reflections to develop a cross-sectional architectural tissue image. Multimodal delivery of antibody-conjugated Polyethylene glycol linked gold nanoparticles improves the contrast in in-vivo OCT images of oral dysplasia in a hamster model [21].

CONCLUSION

Diagnosing oral cancer earlier is a first and foremost health objective, where the dentist plays an important role.Diagnostic techniques should not cause any damage from cancer therapy. There are many novel techniques for diagnosis of oral malignancy. Brush biopsy and scalpel biopsy are efficient diagnostic tests for detecting suspicious oral lesions whether it is precancerous or cancerous. Light based screening aids should

only be used as an adjunct to visual examination for evaluating oral lesions which may have been overlooked with a conventional oral examination but not for identifying the biologic nature of a lesion. Nevertheless, controlled trials in high and low risk populations with histologic outcomes and critical appraisal from the medical practitioners are required before they come to regular practice.

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