Review Article

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RECENT ADVANCES IN DIAGNOSIS OF ORAL PRECANCERS AND CANCER: A MINI REVIEW

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ABSTRACT:

Oral cancer is among the 10 most common cancers worldwide. Oral cancer has a tendency to be detected at late stage which is detrimental to the patients because of its high mortality and morbidity rates. Oral cancer is a disease of increasing age, approximately 95 % of cases occurs in people older than 40 years with an average age at diagnosis of approximately 60 years .Early detection of oral cancer is therefore important to reduce the burden of this devastating disease. Therefore, there is an urgent need to devise critical diagnostic tools for early detection of oral dysplasia and malignancy that are practical, noninvasive and can be easily performed in an out-patient set-up.

Hence the purpose of this review is to discuss recent diagnostic modalities in precancer & cancer, which will help in early diagnosis & treatment thereby reducing the mortality & morbidity associated with same.

Keywords: Oral cancer, early diagnosis, diagnostic aids.

INTRODUCTION:

Oral cancer is one of the most fatal disease affecting mankind, annually accounting for more than 3,00,000 cases worldwide & more than 1,30,000 cases in India .Oral cancer is often preceded by oral precancer. Occurrence of oral cancer is most frequently after the age of 40 years, with a peak at 60 years of age. It also affects males twice as often as females. The most common risk factors in this group are tobacco and alcohol use. Recently, several studies suggest that head and neck cancer particularly tongue cancer is increasing in young adults both nationally and internationally. Factors that contribute to this rise are still unknown, suspected etiologic agents include tobacco related habits, various forms of drug abuse, environmental factors and viral such as HPV etc. Prognosis of oral cancer is very discouraging because it is generally diagnosed at a very advanced stage. However, if the oral precancer and cancer are

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detected at an early stage, the 5 year survival rate can increase to as high as 60% and will also help to improve the quality of life. 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 oral cancer.[1-10]

Table 1- **Advanced Diagnostic Aids for Oral Pre cancers and Oral Cancer**

Toluidine Blue: The use of Toluidine blue (tolonium chloride) dye as a mouthwash or topical application as an aid to the diagnosis of oral cancer & precancer. Toluidine blue is an acidophilic meta chromatic dye which selectively stains acidic tissue components, thus staining DNA and RNA. As it binds to nucleic acids (DNA or RNA), it helps in better visualization of high risk areas especially with rapid cell proliferation of oral squamous cell carcinoma (OSCC) and premalignant lesions .[11] Fig-1.

Vizilite: It involves the use of a hand-held, single-use, disposable chemiluminescent light stick that emits light at 430, 540 and 580 nm wavelengths. The use of the light stick is intended to improve the visual distinction between normal mucosa and oral white lesions. Normal epithelium will absorb light and appear dark whereas hyperkeratinized or dysplastic lesions appear white. The difference in color could be related to altered epithelial thickness, or to the higher density of nuclear content and mitochondrial matrix that preferentially reflect light in the pathological tissues.[6]

Oral CDx system: Oral CDx brush biopsy uses the concept of exfoliative cytology to provide a cytological evaluation of a cellular dysplastic changes. The oral CDx provides a complete transepithelial sample as the brush extends deep in the epithelial layers. The oral cytological epithelial samples are fixed onto a glass slide, stained with a modified Papanicolaou test and analyzed microscopically via a computer-based imaging system. However, although exfoliative cytology and brush biopsy techniques are helpful in establishing a more definitive diagnosis of already visible lesions, they are of no value in detecting mucosal changes that are not readily visible to the naked eye. Advances in the development of automated cytomorphometric methods combined with genetic and proteomic profiling may provide the required tool store fine screening strategies in the future.[12,17] Fig-2.

VELscope: VEL scope is a hand-held device which was approved by Federation Dentaire Association for

direct visualization of autofluorescence in the oral cavity. The VEL scope Vx is one of the most powerful tools available today for assisting in oral abnormalities especially oral cancer. The distinctive blue-spectrum light causes the soft tissues of the mouth to naturally fluoresce. 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 [21] Fig – 3.

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 .[21]

Saliva-based oral cancer diagnostics: Saliva from patients has been used in a novel way to provide molecular biomarkers for oral cancer detection. Saliva is a mirror of the body, reflecting virtually the entire spectrum of normal and disease states and its use as a diagnostic fluid meets the demands for an inexpensive, non-invasive and accessible diagnostic tool. Discovery of analytes in saliva of normal and diseased subjects suggests a very promising function of saliva as a local and systematic diagnostic tool. The ability to analyze saliva to monitor health and disease is a highly desirable goal for oral health promotion and research. So far, saliva has been used to detect caries risk, periodontitis, oral cancer, breast cancer, salivary gland diseases and systemic disorders such as human immunodeficiency virus and hepatitis C virus. However, due to lack of knowledge of disease markers and an overall low concentration of these markers in saliva when compared to serum, the diagnostic value of saliva has not been fully realized. However, nowadays, highly sensitive and high-throughput assays such as DNA microarray, mass spectrometry and nanoscale sensors can measure protein and RNA markers at low concentrations in saliva, thus expanding the utility of saliva as a diagnostic tool.[20]

MOLECULAR METHODS:

DNA Ploidy & Quantification of nuclear DNA content: DNA content of nucleus is dependent upon the number of chromosomes. In case of epithelial dysplasia & malignancy

there can be polyploidy or aneuploidy. So the quqntative analysis of DNA content reflects the total chromosomal content. It is done by flow cytometer analysis. Flow cytometer is automated, precise, reproducible, precise. [2,9]

Tumor markers & biomarkers: 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. They are used in identification of a cancerous growth.[15] Tumor 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 .[19]

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., Kras, Nras), tumor suppressor genes (e.g., p53, p16) etc. and aids as an important detection tool.[11] PCR technique has increased the range and sensitivity of diagnostic procedures but still with a major drawback, as contamination and amplification artifacts may give rise to difficulties in the interpretation of the desired results. With the introduction of polymerase chain reaction (PCR), reverse transcriptase PCR (RT-PCR) and other molecular techniques, the diagnosis and prognosis of other lesions such as chronic myelogenous leukemia has also been useful .[5]

PHOTO DIAGNOSIS

Auto fluorescence Spectroscopy: Auto fluorescence spectroscopy has emerged as a promising tool for oral cancer detection. The system consists of a small optical fiber which produces various excitation wavelengths and a spectrograph which receives and records on a computer and analyzes it with the help of software, the spectra of reflected fluorescence from the tissue. However, the technique is controversial and often found with unclear results. Overall, it seems to be very accurate for distinguishing lesions especially malignant tumors from healthy oral mucosa, with a high sensitivity and specificity.[16] It is a non-invasive aid in the detection of various alterations in the structural and chemical

compositions of cells indicating the presence of a diseased tissue. It can be useful in guiding the clinician in identifying the optimal location for biopsy.[15] According to a study, on using violet excitation light, camera-based autofluorescence photodetection technique has presented as a highly promising tool for the diagnosis of oral malignancies.[16]

Fluorescence Photography: Fluorescence photography is non-invasive, rapid, simple and reproducible method in detection of oral cancer. Fluorescence positivity can show enlargement of carcinomas and progression of the disease. The system is usually used in the diagnosis of squamous cell carcinoma. However, biopsies are still necessary. According to a study, fluorescence photography has shown as a useful tool for the diagnosis of oral cancer, especially in patients with OSCC.[15]

Table-2 Studies On Diagnostic Techniques

CONCLUSION:

Early diagnosis of oral cancer is a priority health objective, in which oral health professionals may play a pivotal role. Detection should lead to less damage from cancer therapy and to a better prognosis. There are also a number of novel techniques that may variously help in the diagnosis of oral malignancy. Lately, light-based detection systems have been claimed to improve sensitivity and specificity, but so far, controlled studies have failed to justify their application. Brush biopsy is an effective diagnostic test for evaluating suspicious oral lesions which may be precancerous or cancerous. Light based screening aids should only be employed as an adjunct to the clinical examination for identifying oral lesions that may have been overlooked with a conventional oral examination and not for determining the biologic nature of a lesion. However, controlled trials in both high and low risk populations with histologic outcomes and critical appraisal from the medical community are required before they can be integrated into practice.

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TABLES:

Table 1 Advanced Diagnostic Aids for Oral Pre cancers and Oral Cancer
• Clinical Methods Vital staining – Toluidine Blue Vizilite
• Histopathological method- Oral CDx system
• Visualization Adjuncts Tissue Auto fluorescence VELscope In Vivo Confocal Microscopy
• Saliva-based oral cancer diagnostics
• Molecular Methods DNA Ploidy & Quantification of nuclear DNA content Tumor Markers & Bio Markers PCR-Based diagnostic aids
• Photo diagnosis Auto fluorescence Spectroscopy Fluorescence Photography

Table -2 Studies On Diagnostic Techniques

Year	Author	Type Of Diagnostic Tools	No Of Cases	Comments
1993	Barrellier P,et al	Toluidine blue	235	Detect lesions that had not been detected by visual examination
2002	Svirskye et al	Brush biopsy	243(298 lesions)	93 had dysplasia (79) or carcinoma (14). 150 were negative for either dysplasia or carcinoma. 82% (243/298) of scalpel biopsy-positives had abnormal brush biopsies
2006	Lane PM,et al	VEL scope	44	98% sensitivity & 100% specificity
2006	Kerr AR,et al	Chemiluminescent light	501	Only sharpness was significantly improved

FIGURES:

Fig 1

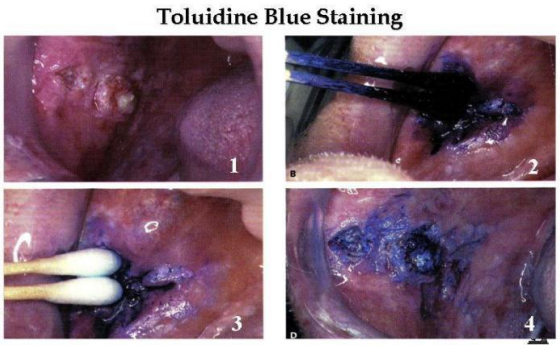

Fig 2 Oral CDx

Fig 3 veloscope