Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 10, pp.59973-59976, October, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

REVIEW ARTICLE

ORAL CANCER- A REVIEW OF RECENT NON-INVASIVE DIAGNOSTIC METHODS

[1]Dr. Rao Naman Rajeshkumar, *[,2]Dr. Abhishek Parikh, [2]Dr. Amit Patel, [3]Dr. Hirenkumar N. and [4]Parsana Mrunal Dave

[1]Former Intern K. M. Shah Dental College and Hospital, Sumandeep Vidyapeeth University, Pipariya
[2]Private Dental Practitioner, Vadodara, Gujarat
[3]Private Dental Practitioner, Surat, Gujarat
[4]Intern at College of Dental Sciences, Amargadh

ARTICLE INFO

Article History:
Received 23rd July, 2017
Received in revised form
26th August, 2017
Accepted 13th September, 2017
Published online 31st October, 2017

Key words:
DNA-Analysis, Microscopy,
Non- invasive diagnostics,
Oral cancer, Screening, Saliva-Based
Oral Cancer Diagnosis.

ABSTRACT

When searched on data bases regarding oral cancers- a lot of articles pops up showcasing different epidemiology in different countries. The real numbers of incidence are always not achievable due to serious lack of precise diagnostic tools. Thus, prognosis for patients with oral cancer remains poor in spite of advanced therapy- the reason being the same due to which a lot of patient suffering is observed Biopsy is one of the favorite diagnostic method used for diagnosis- but it should be only used for evaluating highly suspicious lesions and not for the majority of oral lesions which are clinically not suspicious. There is an urgent need to formulate critical diagnostic tools for early diagnosis of oral dysplasia and malignancy which are practical, noninvasive and can be easily performed in an out-patient setting. The early detection diagnostic tests include brush biopsy, toluidine blue staining, auto fluorescence, salivary proteomics, DNA analysis, biomarkers and spectroscopy. This review describes and examines these new methods which are the best early diagnostic tools for detection of oral cancer.

Citation: Dr. Rao Naman Rajeshkumar, Dr. Abhishek Parikh, Dr. Amit Patel, Dr. Hirenkumar N. and Parsana Mrunal Dave, 2017. "Oral cancer- A review of recent non-invasive diagnostic methods", *International Journal of Current Research*, 9, (10), 59973-59976.

INTRODUCTION

Back ground and epidemiology: According to the cataloguing of the National Cancer Institute of the United States of America, oral cancer involves the following anatomical structures: lip, two thirds of the anterior part of the tongue, buccal mucosa, floor of the mouth, lower gingiva, retromolar trigone, upper gum and hard palate (http://www.cancer.gov/espanol/tipos/cabeza-cuello/pro/tratamiento-labio-boca-pdq).Oral cancer is a public health problem. Out of all cancers, approximately 90% of this type of cancer corresponds to squamous or squamous cell carcinoma (Milián, 1995). The incidence noted in 2012 was 4.0 new cases per 100,000 population: 5.5 new cases per 100,000 men and 2.5 new cases per 100,000 women. The mortality rates are different in males and females- males to 2.7 per 100,000 men and females to 1.2 per 100,000 women (GLOBOCAN, 2015). This pathology has an unequaland scattered distribution where the highest risk countries showing high number of cases are Sri Lanka, India, Pakistan and Bangladesh (Warnakulasuriya, 2009). The lowest being United Kingdom, where this condition is considered as a rare disease (World Cancer Factsheet, 2012).

Corresponding author: **Dr. Abhishek Parikh,**
Private Dental Practitioner, Vadodara, Gujarat.

In United States of America, approximately 45,780 new cases of oral cancer are estimated- roughly 2.8% of all cancers (http://seer.cancer.gov/statfacts/html/oralcav.html). In Latin America, the situation is same- highest incidences are reported in Argentina, southern Brazil and Uruguay. In males, oral cancer is the fifth in frequency in Brazil where approximately-60% of oral cancer is detected in late stages of cancer (III-IV). The 5-year survival rate is 50% (Camelo, 2014 and Peña González, 2006). The annual cases reported in Colombia is 100 to 120 new cases of oral cancer. The risk factors that are observed so far for oral cancer are tobacco, alcohol, genetics, nutrition, viruses, radiation and occupational risks (Rocha, 2009). The data described till now might be less accurate due to the lacking diagnostic tools for oral cancer. This article will focus more towards the new diagnostics for oral cancer which will help getting accurate figures incidence and will ultimately improve patient's quality of life.

Approaches for Early Detection of Oral Cancer

Two approaches- 1. Screening of Oral cancer by conducting programs that identify asymptomatic patients with suspicious lesions and 2. Employing specific and accurate diagnostic tools to identify dysplasia and early oral cancers in asymptomatic

patients. This review will discuss the benefits and limitations of these two approaches.

Screening Oral Cancer

This simply means preliminary assessment and searching for oral precancerous lesions and pre-cancerous conditions, typically before full blown cancerous symptoms. There are number of cancer screening protocols for a variety of malignancies have been proven to reduce the mortality- like the one for breast cancer and cervical cancer. However, there is restriction for detecting oral precancerous or early cancerous lesions- describes the current literature. The only huge randomized controlled trial by Shankar Narayana *et al*. in 2005 concluded the importance of visual examination being useful for high-risk groups (Sankaranarayanan, 2005). Most of the precancerous lesions are benign lesions, clinical inspections do not conclude any sort of differentiation, more commonly the initial features are nearly same showing no difference.

Primitive diagnosis

Early identification of oral cancer is one of the most effective way to reduce the mortality rates from cancers and hence minimizes a severe loss of function, disfigurement, depression and poor quality of life. However, the National Cancer Institute's SEER program, concluded that only small amount or no change in last 20 years in the detection of oral cancers at early stages (http://seer.cancer.gov/csr/1975_2005). Unfortunately, most patients are diagnosed with late or full-blown phase of cancer. Hence early detection is necessary for raising the awareness by conducting free camps and disease discussions with public to improve the current scenario. Although, there has been some delays in awareness, lately a lot of new non-invasive methods have been introduced and worked upon to improve the current scenario.

New non- invasive diagnostics

Laser Capture Microdissection (LCM)

The LCM is one of the latest technology which has changed the current scenario of cancer biology- bringing more precision at molecular caner biology (Mehrotra, 2006). LCM provides an ideal method for the extraction of cells that provides the exact morphology of both the captured cells and the surrounding tissue are preserved- to assess the extent of spread. LCM proves to be more accurate with immune-histochemical (IHC) staining techniques providing more minute microdissection of cellular subsets can be obtained (Fend, 1999). LCM may be useful in detecting the biomarkers and establish protein fingerprint models for early detection of oral cancers.

Light-based oral cancer screening aids

Several light-based oral cancer screening aids have been developed and aimed at assisting in the identification of precancerous and cancerous lesions at their earliest stage. Explicitly, these aids are envisioned to be used as aides-de-camp to the conventional oral cavity examination to help identification of the lesions. 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) are commercially existing light-based systems that are based upon the assumption that abnormal metabolic or structural changes have different absorbance and reflectance properties.

Saliva-Based Oral Cancer Diagnosis

Saliva testing is one of the most non-invasive alternative to blood serum testing, it may be an effective modality for diagnosing/determining the prognosis of oral cancer and for monitoring as well. Saliva also provides a cost-effective and practical approach for the screening of large populations. It may be used to measure specific salivary macromolecules as well as examining proteomic or genomic targets such as enzymes, cytokines, growth factors, metalloproteinases, endothelin, telomerase, cytokeratins, mRNAs and DNA transcripts (Nagler, 2009 and Li, 2004). The most considered epithelial serum circulatory tumor markers in the saliva of cancer patients are Cyfra 21-1, TPS, carcinoembryonic antigen (CEA), SCC, CA125, and CA19-9. Noteworthy increase in salivary concentrations of Cyfra 21-1, TPS and CA125 were shown with sensitivity, specificity, and negative and positive predictive values of 71%, 75%, 71%, and 75%, respectively. CD44 is a multi-structural and multifunctional cell surface transmembrane glycoprotein molecule- which is also detected in saliva (Screaton, 1992).

DNA-Analysis

DNA image cytometry calculates dubious status to check the malignant potential of cells. Staining with Feulgen dye, the cytological samples are compared with a reference group of cells. A computer-assisted analysis- recently designed helps in identification of deviations of cellular DNA content. The genomic instability adds on towards cancer development, and abnormal DNA content may distinguish the dysplastic lesions that might progress to cancer. A lot of literature suggests confirmed the usefulness and effectiveness of DNA ploidy analysis as an adjunct to conventional cytology assessment of cytobrush samples for detection of oral cancer (Bradley, 2010; Maraki, 2006; Maraki, 2006 and Handschel, 2007). The multimodal cell analysis (MMCA) and mechanical phenotyping have been also used for early detection of oral malignancies these days (Remmerbach, 2004; Remmerbach, 2009).

Lab-on-a-Chip

The lab-on-a-chip are also referred as micro-total-analysis systems (TAS) and microfluidics technology- the adaptation, miniaturization, integration, and automation of analytical laboratory procedures into a chip. This method is often regard as the chemistry or biotechnology comparable of the silicon integrated circuit chip that has revolutionized electronics, computers, and communications. The identification of oral dysplastic and cancer cells within the chip utilizes membrane-associated cell proteins that are singularly articulated on the cell membranes of dysplastic cells (Ziober, 2008).

Microscopy

The most recent develop- Spectral cytopathology (SCP) is a technique for diagnostic differentiation of disease in exfoliated individual's cells. SCP collects the information on each cell's biochemical composition via infrared micro-spectral measurement, which then multivariate data analysis.

Aberrations from a cell's natural structure produced specific spectral patterns that were only to the cause of the disease. [25] Multispectraldigital microscope (MDM- also a utilized tool to improve identification of oral neoplasia. This takes and produces in-vivo images in different modes i.e. fluorescence, narrow-band (NB) reflectance, and orthogonal polarized reflectance (OPR) to enable estimation of lesions (Roblyer, 2008).

Conclusion

In conclusion to this review early diagnosis of oral cancer is a primary and priority health objective for which oral health professionals should take extra steps in brining awareness by conducting camps and free public speech to avoid the mortality. Although a lot of new diagnostic aids are developed, a lot of rich and supportive evidences are needed for its applicability from bench side to bed side.

REFERENCES

Bahar, G., Feinmesser, R., Popovtzer, A., Nagler, R.M. 2007. Salivary analysis in oral cancer patients: DNA and protein oxidation, reactive nitrogen species, and antioxidant profile. Cancer. 109(1):54–9. doi: 10.1002/ cncr. 22386. [PubMed] [Cross Ref]

Bradley G, Odell EW, Raphael S, Ho J, Le LW, Benchimol S, Kamel-Reid S. Abnormal DNA content in oral epithelial dysplasia is associated with increased risk of progression to carcinoma. *Br J Cancer*. 2010; 103(9):1432–42. doi: 10.1038/sj.bjc.6605905. [PMC free article] [PubMed] [Cross Ref]

Camelo T, De Almeida M, Soares L, Falcao C, Rabbit F, Clementino T. Oral cancer knowledge and awareness among dental students. Braz J Oral Sci 2014; 13 (1): 28-33. [Links]

Fend, F., Emmert-Buck, M.R., Chuaqui, R., Cole, K., Lee, J., Liotta, L.A., Raffeld, M. 1999. Immuno-LCM: Laser capture micro dissection of immunostained frozen sections for mRNA analysis. *Am J Pathol.* 154:61–6. doi: 10.1016/S0002-9440(10)65251-0. [PMC free article] [PubMed] [Cross Ref]

GLOBOCAN 2012. Estimated Cancer Incidence, Mortality and Prevalence in Worlwide in 2012. Available at: http://globocan.iarc.fr/Pages/fact_sheets_population.asp x . (Retrieved August 18, 2015). [Links]

Handschel, J., Oz, D., Pomjanski, N., Depprich, R., Ommerborn, M.A., Braunstein, S., Kübler, NR, Meyer U, Böcking A. Additional use of DNA-image cytometry improves the assessment of resection margins. J Oral Pathol Med. 2007;36(8):472–5. doi: 10.1111/j.1600-0714.2007.00564.x. [PubMed][Cross Ref]

International Agency for Research on Cancer and Cancer Research UK. World Cancer Factsheet. Cancer Research UK, London, 2012. [Links]

Li Y, St John MA, Zhou X, Kim Y, Sinha U, Jordan RC, Eisele D, Abemayor E, Elashoff D, Park NH, Wong DT. Salivary transcriptome diagnostics for oral cancer detection. Clin Cancer Res. 2004;10:8442–50. doi: 10.1158/1078-0432.CCR-04-1167. [PubMed] [Cross Ref]

Maraki D, Becker J, Boecking A. 2004. Cytologic and DNA cytometric very early diagnosis of oral cancer. *J Oral Pathol Med.* 33:398–404. doi: 10.1111/j.1600-0714.2004.0235.x. [PubMed] [Cross Ref]

Maraki, D., Yalcinkaya, S., Pomjanski, N., Megahed, M., Boecking, A., Becker, J. 2006. Cytologic and DNA-cytometric examination of oral lesions in lichen planus. *J Oral Pathol Med.*, 35(4):227–32. doi: 10.1111/j.1600-0714.2006.00401.x. [PubMed] [Cross Ref]

Mehrotra, R., Gupta, A., Singh, M., Ibrahim, R. 2006. Application of cytology and molecular biology in diagnosing premalignant or malignant oral lesions. *Mol Cancer.* 5:1–11. [PMC free article][PubMed] Retracted

Milián A, González M. Malignant tumors of the oral mucosa. In Bagán (Ed.) Oral Medicine. Barcelona Spain, Masson editorial, 1995; 187-99. [Links]

Nagler, R.M. 2009. Saliva as a tool for oral cancer diagnosis and prognosis. Oral Oncol., 45:1006–10. doi: 10.1016/ j.oraloncology.2009.07.005. [PubMed] [Cross Ref]

National Cancer Institute (NIH). Lip and oral cavity cancer: Treatment for health professionals (PDQ®). Available at: http://www.cancer.gov/espanol/tipos/cabeza-cuello/ pro/ tratamiento-labio-boca-pdq . (Accessed November 17, 2015). [Links]

Papamarkakis K, Bird B, Bedrossian M, Laver N, Wein R Diem M. Cytopathology by optical methods: spectral cytopathology of the oral mucosa. Lab Invest. 2010; 90(4):589–98. doi: 10.1038/labinvest.2010.1. [PMC free article] [PubMed] [Cross Ref]

Peña González A, Arredondo López M, Vila Martínez L. Clinical and epidemiological behavior of oral cavity cancer. Rev CubanaEstomatol [magazine on the Internet]. 2006 Mar [quoted 2015 Nov 17]; 43 (1): Available at: http://scielo.sld.cu/scielo.php?script=sci_ arttext&pid=S0034-75072006000100003&lng=en . [Links]

Remmerbach TW, Mathes SN, Weidenbach H, Hemprich A, Böcking A. Noninvasive brush biopsy as an innovative tool for early detection of oral carcinomas. Mund Kiefer Gesichtschir. 2004;8(4):229–36. [PubMed]

Remmerbach TW, Wottawah F, Dietrich J, Lincoln B, Wittekind C, Guck J. Oral cancer diagnosis by mechanical phenotyping. Cancer Res. 2009;69(5):1728–32. doi: 10.1158/0008-5472.CAN-08-4073.[PubMed] [Cross Ref]

Roblyer D, Richards-Kortum R, Sokolov K, El-Naggar AK, Williams MD, Kurachi C, Gillenwater AM. Multispectral optical imaging device for in vivo detection of oral neoplasia. J Biomed Opt. 2008;13(2):024019. doi: 10.1117/1.2904658. [PMC free article] [PubMed] [Cross Ref]

Rocha, A. Oral Cancer: The role of the dentist in early detection and control. Rev Fac de Odontol Univ Antioquia 2009: 21 (1): 112-21. [Links]

Sankaranarayanan, R., Ramadas, K., Thomas, G., Muwonge, R., Thara, S., Mathew, B., Rajan, B. 2005. Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet.* 365(9475):1927–33. doi: 10.1016/S0140-6736(05)66658-5. [PubMed] [Cross Ref]

Screaton GR, Bell MV, Jackson DG, Cornelis FB, Gerth V, Bell JI. Genomic structure of DNA encoding the lymphocyte homing receptor CD44 reveals at least 12 alternatively spliced exons. Proc Natl Acad Sci USA. 1992; 89:12160–4. doi: 10.1073/pnas.89.24.12160. [PMC free article] [PubMed][Cross Ref]

SEER Cancer Statistics Factsheets: Oral Cavity and Pharynx Cancer. National Cancer Institute. Bethesda, MD, Available at: http://seer.cancer.gov/statfacts/html/oralcav. html . (Accessed November 17, 2015). [Links]

SEER Cancer Statistics Review, 1975-2005, National Cancer Institute. 2008. http://seer.cancer.gov/csr/1975_2005/ based on November 2007 SEER data submission, posted to the SEER web site.

Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncology. 2009; 45: 309-16. [Links]

Ziober BL, Mauk MG, Falls EM, Chen Z, Ziober AF, Bau HH. Lab-on-a-chip for oral cancer screening and diagnosis. Head Neck. 2008; 30(1):111–21. doi: 10.1002/hed.20680. [PubMed][Cross Ref]

****