Review Article

Open Access

Journal of Dental Research and Oral Health

jdro@scientificeminence.com

An Update on Standard Diagnostic Aids for Evaluation of Oral Potentially Malignant and Malignant Lesions

Himanshi Tomar, Vijeev Vasudevan, Trishna Saikia, Devaraju D and Shrihari TG

Department of oral medicine and radiology, Krishnadevaraya College of dental sciences, Rajiv Gandhi University of Health sciences, Karnataka, India

*** Corresponding Author**

Himanshi Tomar, Department of oral medicine and radiology, Krishnadevaraya college of dental sciences, Rajiv Gandhi University of Health sciences, India, Tel: 91-8861928260, E-mail: tomarhimanshi89@gmail.com

Citation

Himanshi Tomar (2021) An Update on Standard Diagnostic Aids for Evaluation of Oral Potentially Malignant and Malignant Lesions. J Dent Res Oral Health 1:1-6

Publication Datess

Received date: August 01, 2021

Accepted date: September 01, 2021

Published date: September 03, 2021

Abstract

Oral squamous cell carcinoma is the sixth most common cancer worldwide. The high mortality rate in cancer is commonly attributed to the difficulties in detecting the lesion at an early and treatable stage. Most common risk factors for oral cancer are tobacco consumption, alcohol and Human Papilloma Virus. It may occur due to poor oral hygiene and poor diet. Early diagnosis and complete treatment of oral cancer is the challenging point of the cancer prevention and control strategy. Due to the potential limitations of the conventional visual oral examination, adjunctive aids to assist in chairside detection of lesions that are suspected of oral cancer or potentially malignant disorders have been developed and are commercially available. This review explains the clinical application of various diagnostic aids in early detection of oral cancer when the tumor is small so that it significantly improves survival and contributes to less morbidity following therapy.

Keywords: Oral Potentially Malignant; Malignant Lesions; Diagnostic Aids

List of abbreviations: OPMD: Oral potentially malignant disorder; NICE: National institute for Health and Care Excellence; VELscope: Visually Enhanced lesion scope; FAD: Flavin adenine dinucleotide; NADH: Nicotinamide adenine dinucleotide; HRME: High Resolution Micro endoscopy; FVL: Loss of Fluorescence; MMIS: Multimodal optical imaging system; TB: Toluidine blue

Introduction

Oral squamous cell carcinoma is the sixth most common cancer for both sexes worldwide. Out of which more than 50 percent of patients report to the specialists when the oral cancer is in advanced stage. At that time it's difficult to treat the oral cancer as it has poor prognosis, expensive and complex treatment and their 5 year survival rate is close to 50 percent in most countries. Even after the treatment, most of the patients faces difficulty in speech, swallowing and mastication, thereby affecting the overall quality of life. So if oral cancer is diagnosed in early stage it will enhance the survival rate by decreasing the morbidity and mortality rate. As fractions of oral cancer are led by premalignant changes which are also known as oral potentially malignant disorders (OPMD), their detection and treatment before the occurrence of oral cancer can be useful in reducing the risk of developing oral cancer. However, the management of OPMDs is not easy to perform due to its varying rates of transformation, inexperienced clinicians and its complicated risk assessment.

Most oral cancers in early stages shows red and white patch on oral mucosa, and later as new lumps and persistent ulcerations, which can be detected by clinicovisual examination and systemic palpation of affected site and neck. Primary health care clinicians face difficulties in detecting these lesions as the above mentioned signs are not specific and can be seen in many benign conditions too [1]. The National institute for Health and Care Excellence (NICE) guidelines revised in the year 2016 is a functional resort for early detection of oral cancer, but it lacks specificity and has low predictive value that is 7.9 percent for the referral of suspected symptomatic oral cancer cases [2]. Till now tissue biopsy is the gold standard for final diagnosis of oral cancer.

Due to possible limitations of conventional visual oral examinations, diagnostic aids that will help in chairside detection of suspected potentially malignant and oral cancer lesions are developed and commercially available [3].

Discussion

Diagnostic aids

Now a days many techniques and devices are available to visualize the changes clinically present in oral cavity and thus helps in chairside detection of lesions as many of the techniques used gives real time result. These diagnostic aids can be divided into

1. Optical imaging devices
2. Vital staining techniques

The optical imaging devices uses high resolution microscopic technique which detects alterations in optical properties of surface epithelium and submucosa. This technique is based on the principal of light absorption, scattering and fluorescence of tissue.

In vivo microscopy provides real time imaging by using specific probes and shows morphometric features at gross level and provides an insight of nuclear and cellular features of lining mucosa. Examples of in vivo microscopy are high resolution endoscopy and confocal microscopy. Optical devices used in imaging are Vizilite, VELscope, Microlux and Orascoptic. Vital staining techniques use either Lugol's iodine or Toluidine Blue to visualize the abnormal tissues.

Propound uses of adjunctive aids includes –

They serve as a diagnostic aids in chair side diagnosis of oral potentially malignant and malignant disorders.

- To confirm the presence of visually detected lesion.
- To visualize the high risk areas when surface change is observed clinically.
- To evaluate the risk of oral potentially malignant disorders.
- To assess the site of biopsy
- For follow up inspection of potentially malignant lesions.

These diagnostic aids helps primary care professionals to refer the patients to secondary health care where again the adjuncts will assist in selecting the biopsy site, when lesion is suspected thereby helping in early detection and treatment.

Visually Enhanced lesion scope (VELscope)

Developed by LED Dental Inc. (White Rock, British Columbia, and Canada) jointly with experts at British Columbia Cancer Agency [4], Visually Enhanced lesion scope is a hand held equipment that emits blue light whose wavelength is 400-460nm. The principle behind VELscope is that at wavelength of 400-460 nm, disease free oral tissue shows auto fluorescence as these tissues contain collagens and fluorophores such as Flavin adenine dinucleotide (FAD) and Nicotinamide adenine dinucleotide (NADH) that acts as an endogenous auto fluorescent substances [5].

In malignancy there is reduced emission of auto fluorescence that results in a dark patch also known as Loss of Fluorescence (FVL) is often seen extending beyond the clinically visible lesion. The published studies on the role of VELscope in detecting OPMDs and malignant disorders till now showed its use in secondary health care centers. The sensitivity and specificity of VELscope in detecting OPMDs is 0.91 (0.73- 0.97) and 0.58 (0.22- 0.87) respectively [6].

Vizilite

Vizilite system depends on chemiluminiscence which is the most widely used technique for examining the cervical mucosa for OPMDs and malignant lesions since many years. The patient is asked to rinse the mouth with an oral rinse solution of 1 percent acetic acid for 1 minute so that the surface debris is removed and oral mucosa is slightly desiccated. Oral cavity is then directly visualized under Blue – White chemiluminescent light stick [7]. The wavelength of blue- white light is 490- 510 nm [8]. Healthy tissues after absorbing this wavelength of light illuminates and appear light blue in color whereas affected cells appears 'aceto- white' showing brighter, sharper and more distinct margins as these cells contain higher nuclear- cytoplasmic ratio that has ability to reflect the illumination [9]. All the studies published till now reported an enhancement in brightness and sharpness of Leukoplakia lesions using Vizilite as compared to conventional visual examination. The major drawback of chemiluminiscence is that the red lesions are not detected over white lesions preferentially. So the OPMDs which are exclusively showing red patches will be missed by mere use of this technique [10, 11].

Microlux

Developed by Ad Dent, Inc., Danbury, CT in USA, Microlux is a hand held instrument that emits blue- white LED light of wavelength ranging between 410- 710 nm, with peaks at wavelength of 460 nm and 560 nm. The principle on which this device works is similar to the above mentioned chemiluminiscence optical instruments [12].

Studies conducted in a secondary health care setup reported the sensitivity of Microlux to be 77.8 percent, with an enhancement in margin detection. The reported disadvantage till now is that the Microlux failed to detect two dysplastic lesions [13].

High Resolution Microendoscopy (HRME)

High Resolution Microendoscopy helps in visualizing morphometric features of keratinocytes that is epithelial cells as seen through a microscope, in vivo. HRME pictures shows dark background with cell nuclei presented as discrete bright dots. Pictures seen by using endoscopy probes are observed for morphological features used by Oral Pathologist to examine atypical cellular and nuclear features observed in dysplasia and carcinoma. The function of acetic acid and Proflavin used as topical contrast agents is as follows

1. Amplify the appearance of cell nuclei for grading as enlarged or crowded.
2. Helps in counting the nuclei.
3. Visualize nuclear pleomorphism
4. Quantification of nuclear to cytoplasmic ratio in real time.

Published compulsive data on application of Microendoscopy for early detection of OPMDs shows promising results by development of multimodal optical imaging system (MMIS) to visualize tissues in situ [14].

Vital staining techniques

Toluidine Blue (TB)

TB is an acidophilic metachromatic dye which in solution take on a blue- violet color. This is the most commonly used adjunctive test to visualize oral mucosal abnormalities. TB can be used as mouth rinse or direct staining with swab. Dye imparts blue color to the mucosa and primarily stains acidic tissue components. Malignant or dysplastic cells will retain their blue color on de-staining with acetic acid which shows positive result and normal tissues will not show any color. Due to the presence of more nucleic acid in abnormal tissues quantitatively and loss of cohesion, the dye is able to penetrate the dysplastic epithelium. So the dysplastic tissues are able to retain the dye and presents a dark blue coloration and is considered as positive result. If the area is representing light blue color then it is considered as equivocal staining. Equivocal staining is seen because of nuclei with chromosomal abnormalities but till date no literature has confirmed to consider equivocal staining as positive result or not [15].

Application of TB dye gives false positive results when there is uptake of dye by any inflammatory or benign ulcerative lesion

which have regenerative potential or retention of dye in natural anatomical crevices. To lower the level of false positive results manufacturers advocates re- application of TB after 2-3 weeks to allow healing of benign ulcerations. But re- application is not a practical approach as patient may become apprehensive after knowing about the positive result and may ask for further investigations that can lead to unwanted biopsy [16].

Similar to false positive results, false negative results occur due to thickening of keratinized mucosa which will not allow the dye to penetrate as seen in the case of Verrucous Leukoplakia. The published reports till date shows sensitivity of TB staining technique to detect OPMDs and malignant disorders as 0.84 (0.74- 0.90) and specificity of 0.70 (0.59- 0.79). Higher sensitivity is seen in cases of carcinomas and high grade dysplastic lesions. Lower sensitivity is seen due to low grade dysplastic changes and inclusion of equivocal test results, as biopsies of equivocal; area represent normal tissue architecture [17].

Limitations

Many adjuncts that may help or assist in detection of OPMDs and malignant lesions are currently under development [19]. The first objective of this technology is to upgrade the detection stage I and stage II malignant disorders and dysplastic changes of oral epithelium and thus anticipating the high risk patient for developing malignancy [20]. But till date no studies or publication confirms or support these adjuncts as major or solely used diagnostic device for early detection of cancer. These studies only discuss about the sensitivity and specificity of these adjuncts and results showed high sensitivity level but poor specificity level. The false positive results produced by these devices will lead to high anxiety level in patients and will lead to unnecessary biopsy of the lesion which is not required. Only few studies have shown the detection of occult lesions using any of these adjuncts but still the specificity level remains poor.

The second objective of this technology is to perceive the convenience of these devices in the visualization of high risk groups that have a remarkably higher risk of cancer because of the presence of high grade OPMDs. The outcome of Vizilite testing have showed low sensitivity for the detection of high risk lesions while TB staining detected high risk oral premalignant lesions [21]. But further studies on TB showed that number of individuals detected in high risk categories were less with poor outcomes and it is arduous to produce a significant conclusion due to absence of long term follow up studies [22-24].

Future Perspective and Conclusion

Based on recent systematic review on adjunctive light- based diagnostic aids there is a narrow documentation for their application in primary care as diagnostic tools [23]. They may help a clinician to refer the case to secondary health care professional to undertake further investigations that is biopsy. The translational value of the studies published till date has been limited as these techniques have not been adapted for routine use [24]. Further research and development is needed to impel these adjunctive aids if they are to be used as diagnostic tools for cancer detection or for risk stratification of OPMDs.

Conflict of Interest

Nil

References

1. Rashid A, Warnakulasuriya S (2003) The use of light-based (optical) detection systems as adjuncts in the detection of oral cancer and oral potentially malignant disorders: a systematic review. J Oral Pathol Med 44: 307–28.

2. NICE (2017) Improving outcomes in head and neck cancers.

3. Singh P, Warnakulasuriya S (2006) The two-week wait cancer initiative on oral cancer; the predictive value of urgent referrals to an oral medicine unit. Br Dent J 201: 717–20.

4. Lane PM, Gilhuly T, Whitehead P (2006) Simple device for the direct visualization of oral-cavity tissue fluorescence. J Biomed Opt.

5. Awan KH, Morgan PR, Warnakulasuriya S (2011) Evaluation of an autofluorescence based imaging system (VELscope) in the detection of oral potentially malignant disorders and benign keratoses. Oral Oncol 47: 274–77.

6. Macey R, Walsh T, Brocklehurst P (2015) Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. Cochrane Database Syst Rev 5: Cd010276.

7. Huber MA, Bsoul SA, Terezhalmy GT (2004) Acetic acid wash and chemiluminescent illumination as an adjunct to conventional oral soft tissue examination for the detection of dysplasia: a pilot study. Quintessence Int 35: 378–84.

8. Epstein JB, Gorsky M, Lonky S (2006) The efficacy of oral lumenoscopy (ViziLite) in visualizing oral mucosal lesions. Spec Care Dent 26: 171–4.

9. Kerr AR, Sirois DA, Epstein JB (2006) Clinical evaluation of chemiluminescent lighting: an adjunct for oral mucosal examinations. J Clin Dent 17: 59–63.

10. Farah CS, McCullough MJ (2007) A pilot case control study on the efficacy of acetic acid wash and chemiluminescent illumination (ViziLite) in the visualisation of oral mucosal white lesions. Oral Oncol 43: 820–4.

11. Awan KH, Morgan PR, Warnakulasuriya S (2011) Utility of chemiluminescence (ViziLite™) in the detection of oral potentially malignant disorders and benign keratoses. J Oral Pathol Med 40: 541-4.

12. McIntosh L, McCullough MJ, Farah CS (2009) The assessment of diffused light illumination and acetic acid rinse (Microlux/DL) in the visualisation of oral mucosal lesions. Oral Oncol 45: 223–7.

13. Muldoon TJ, Roblyer D, Williams MD (2012) Noninvasive imaging of oral neoplasia with a high-resolution fibre-optic microendoscope. Head Neck 34**:** 305–12.

14. Pierce MC, Schwarz RA, Bhattar VS (2012) Accuracy of in vivo multimodal optical imaging for detection of oral neoplasia. Cancer Prev Res (Phila) 5: 801–9.

15. Zhang L, Williams M, Poh CF (2005) Toluidine blue staining identifies high-risk primary oral premalignant lesions with poor outcome. Cancer Res 65: 8017-21.

16. Epstein JB, Silverman S Jr, Epstein JD (2008) Analysis of oral lesion biopsies identified and evaluated by visual examination, chemiluminescence and toluidine blue. Oral Oncol 44: 538-44.

17. Awan KH, Yang Y, Morgan P, Warnakulasuriya S (2012) Utility of toluidine blue as a diagnostic adjunct in the detection of potentially malignant disorders of the oral cavity – a clinical and histological assessment. Oral Dis18: 728-33.

18. Cancela-Rodríguez P, Cerero-Lapiedra R, Esparza-Gómez G (2011) The use of toluidine blue in the detection of pre-malignant and malignant oral lesions. J Oral Pathol Med 40: 300–4.

19. Gillenwater A, Papadimitrakopoulou V, Richards-Kortum R (2006) Oral premalignancy: new methods of detection and treatment. Curr Oncol Rep 8: 146-54.

20. Kerr AR, Shah SS (2013) Standard examination and adjunctive techniques for detection of oral premalignant and malignant lesions. J Calif Dent Assoc 41: 329–41.

21. Chainani-Wu N, Madden E, Cox D (2015) Toluidine blue aids in detection of dysplasia and carcinoma in suspicious oral lesions. Oral Dis 21: 879–85.

22. Awan KH, Morgan PR, Warnakulasuriya S (2015) Assessing the accuracy of autofluorescence, chemiluminescence and toluidine blue as diagnostic tools for oral potentially malignant disorders – a clinicopathological evaluation. Clin Oral Investig 19: 267–72.

23. Rashid A, Warnakulasuriya S (2015) The use of light-based (optical) detection systems as adjuncts in the detection of oral cancer and oral potentially malignant disorders: a systematic review. J Oral Pathol 44: 307-28.

24. Warnakulasuriya S (2016) Translational research in oral oncology – A bridge between basic science and clinical application. Transl Res Oral Oncol 1: 1–2.