ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 6, Issue – 3, May - 2023, Page No. : 120 – 127

Diagnostic accuracy of recent advancements for oral potentially malignant disorders

[1]Tanvi Sahnan, BDS, Goregaon Dental Centre

[2]Naval Ghule, BDS, Goregaon Dental Centre

[3]Amar Shaw, MDS Public Health Dentistry, Goregaon Dental Centre

Corresponding Author: Tanvi Sahnan, BDS, Goregaon Dental Centre

Citation of this Article: Tanvi Sahnan, Naval Ghule, Amar Shaw, "Diagnostic accuracy of recent advancements for oral potentially malignant disorders", IJDSIR- May - 2023, Volume – 6, Issue - 3, P. No. 120 – 127.

Type of Publication: Review Article

Conflicts of Interest: Nil

Introduction

Oral premalignant lesions are usually the precursors of oral carcinomas which is their most feared complication. In 1978, the WHO proposed the terms "precancerous conditions" and "precancerous lesion" and defined precancerous lesions as "a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart." In 2005, the WHO recommended abandoning this terminology and instead proposed to use the term "oral potentially malignant disorders" (OPMDs), which is defined as "the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date."

Most common OPMDs present among Indian population these days are Leukoplakia, erythroplakia , smoker's palate, Oral Submucous Fibrosis (OSMF), Oral Lichen Planus (OLP), actinic keratosis and discoid lupus erythematosus. In India, overall prevalence of OPMD is 13.2-13.9%, while that of leukoplakia alone is 0.2-5.2%, OSMF is 8.06% and erythroplakia is 0.24%.[1] A study conducted by Rahul Srivastava et. al. Among the Indian population reveals that the prevalence of different OPDMs shows a variation among male and female population. Out of 57.56% subjects with OSF, 65.445% were males and 32.20% were females. Out of 23.70% subjects with leukoplakia, 24.21% were males and 22.03% were females. Out of 13.12% subjects with Lichen planus, 4.56% were males and 40.68% were females. Out of 5.62% subjects with oral cancer, 5.79% were males and 5.08% were females ($P < 0.001$)[2]. However, Irrespective of gender, it was very common to observe oral premalignant lesions getting transformed into oral cancer. According to another research, conducted by Caijiao Wang et. al., the overall malignant transformation rate (MTR) of OPMDs is approximately 7.9% and is different among different diseases. The MTR of Lichen Planus was 1.4%, while that of Leukoplakia with Oral epithelial dysplasia could be up to 10.5%. Additionally, the higher the degree of dysplasia, the higher the possibility of oral cancer.[3] However, some early malignant lesions are clinically indistinguishable from benign lesions, and some patients

develop carcinomas in the absence of clinically identifiable OPLs. Furthermore, it can be difficult even for experts to determine which OPLs are at significant risk to progress to invasive carcinoma. Therefore, an accurate, objective, and noninvasive method to help identify premalignant lesions and to distinguish those at risk of malignant conversion is needed.[4] Techniques that have been used to improve earlier detection and diagnosis of oral malignancy include exfoliative cytology, vital tissue staining (toluidine blue), visualization adjuncts(ViziLite Plus with TBlue, ViziLite, Microlux DL, Orascoptic DK, VELscope), and OralCDx brush biopsy in addition to histological examination of tissue.[5] Out of all the diagnostic methods, Biopsy is considered as a fundamental diagnostic tool. However it comes with various drawbacks like it is time-consuming, may cause patient discomfort, and is associated with patient morbidity. Also, the prospect of a biopsy may cause substantial emotional distress in many patients. In addition, it is a diagnostic method with limited sensitivity where one of the most important features is the subjective interpretation of the examining pathologist. These issues underline the importance of discovering and developing new diagnostic methods, improving the existing ones and discovering new therapeutics targets for oral neoplastic diseases.[6,7] These issues lead to the use of new diagnostic methods such as autofluorescence , chemiluminescence and VELscope, that helps in early detection of OPMDs and thereby reducing the chances of malignant transformation and decreasing patient death rate. Autofluorescence imaging is a light based technique that facilitates visualization of oral cancers and detection of OPMDs. It has been performed on the premise that cancer and precancerous tissues, which have undergone abnormal metabolic or structural changes, differ in absorbance and reflective characteristics when exposed to specific wavelengths of light.[6] Chemiluminescence refers to emission of light during a chemical reaction. Blue, green, yellow-green, yellow, orange and red are various colors produced from the reaction. It helps oral physicians to detect lesions at much earlier stages as it is a painless, effective, and fast procedure. Its diagnostic system detects the mucosal tissues undergoing abnormal metabolic or structural changes leading to different absorbance and reflectance profiles when exposed to various forms of light sources.[1] VELscope utilizes blue light excitation between 400 and 460 nm wavelengths to enhance oral mucosal abnormalities by direct tissue autofluorescence. At these excitation wavelengths, normal oral mucosa is associated with a pale green fluorescence when viewed through a filter, whereas abnormal tissue is associated with a loss of autofluorescence and appears dark.[8] Understanding the diagnostic accuracy of these recent advancements would help clinicians to choose the most effective treatment by reaching a correct diagnosis at early stage. Diagnostic accuracy includes specificity, sensitivity, and Receiver Operating Characteristics (ROC) analysis.[1] Sensitivity refers to a test's ability to designate an individual with disease as positive. A highly sensitive test means that there are a few false negative results and thus fewer cases of disease are missed. The specificity of a test is its ability to designate an individual who does not have a disease as negative. A highly specific test means that there are few false positive results. Since no study has previously discussed in detail about efficiency of advanced diagnostic methods in the detection of OPMDs , hence it is necessary to identify diagnostic tests which are both highly specific and sensitive and can be easily performed without any patient discomfort thereby helping in

detection of disease at the earliest stages, preventing its malignant transformation and finally reducing patient mortality or morbidity from disease. Hence, the aim of this paper is to review the accuracy of recent advancements that have been made for diagnosis of potentially malignant disorders of the oral cavity.

Eligibility Criteria

Inclusion Criteria: The inclusion criteria is as follows:

1. In-vivo studies- Observational studies or Clinical trials comparing the diagnostic accuracy of autofluorescence, chemiluminescence, VEL scope
2. prospective or retrospective study,
3. Participant characteristics: Patients with presumptive diagnosis of OPMD
4. Outcome measurements: Diagnostic accuracy including sensitivity, specificity, accuracy, determined using different methods irrespective of the methods of quantifying the outcomes
5. Articles written in English language
6. Articles published from 2000-2022 and available as free full text

Exclusion Criteria: The exclusion criteria were as follows:

1. Non-clinical studies, in-vitro studies, and animal studies
2. Studies done on individuals less than 18 years of age
3. Studies not fully available in the database
4. Article reporting only abstracts were also excluded
5. Studies not reporting primary outcomes of accuracy, sensitivity, and specificity as well as where primary outcomes are not possible to calculate from the given raw data

Search Protocol

A comprehensive electronic search was performed till September 2022 for the studies published within the last 22 years (from 2000 to 2022) using the following databases: PubMed, google scholar, SCOPUS to retrieve articles in the English language. The searches in the clinical trials database, cross-referencing and grey literature were conducted using Google Scholar, Greylist, and OpenGrey. In addition to the electronic search, a hand search was also made, and reference lists of the selected articles were screened

Search Strategy

Appropriate key words and Medical Subject Heading (MeSH) terms like “Autofluorescence,” “Velscope,” “chemiluminescence”, “dysplasia,” “oral precancer,” “oral cancer,” “oral carcinoma,” were selected and combined with Boolean operators like AND,OR. The examples of search strategy used was as follows: (chemiluminescence AND sensitivity AND specificity AND premalignant lesion), (chemiluminescence AND auto fluorescence AND VELscope) (Autofluorescence AND leukoplakia OR lichen planus AND sensitivity AND specificity), (VELscope OR auto fluorescence OR chemiluminescence AND OPMD AND sensitivity AND specificity). The search and screening was then conducted according to the previously established protocol.

Author / Year of study	Country	Sample size	Mean Age of participants (years)	M/F	Type of OPMD	Method of diagnosis	Diagnostic Sensitivity (%)	Diagnostic Specificity (%)
Wei Zheng et.al. /2002	Singapore	28	58	15/13	OPMD	AF	95	97
S. Ram et.al ./2004	University of Malaysia	40	56.75	17/23	SCC, Epithelial dysplasia (Mild,Moderate, Severe) Lichen planus, Benign	Vizilite	100	14.2

					keratosis			
Ram S et.al. /2005	Malaysia	Not Mentioned	35-80	17/23	OPMD	Vizilite	100	14
Farah C et. al /2007	Australia	Not Mentioned	F: 58.7 M:56.8	26/9	OPMD	Vizilite	100	0
Ravi Mehrotra et.al /2008	India	102 156	39 41	Not Mentioned	OPMD	Vizilite Velscope	0 50	75.5 38.9
K. H. Awan et.al/2011	England	70 44	Not Mentioned	Not Mentioned	Leukoplakia or erythroplakia Epithelial dysplasia	AF CL AF CL	87.1 77.1 84.1 77.3	21.4 26.8 15.3 27.8
Scheer et.al. /2011	Germany	Not Mentioned	59.8	39/25	OPMD	Velscope	100	81
Mojsa i et.al. /2012	poland	Not Mentioned	Not Mentioned	21/9	OPMD	CL	57	37
Vashisht N et.al. /2014	India	60	Not Mentioned	Not Mentioned	OPMD	Vizilite	95	84
Enric Jané-Salas et.al. /2015	Spain	60	Not Mentioned	Not Mentioned	OPMD	Velscope	40	80
Kaur J et.al. /2015	Belgium	Not Mentioned	54-76	41/39	SCC OL OLP	Velscope	67 63 60	62 53 61
Moro et.al. /2015	Italy	66/>	14	Not Mentioned	OPMD	AF	99	95
Chaudhry et.al. /2016	Australia	Not Mentioned	>18Y	74/26	OPMD	Vizilite	41	41
Lalla Y et.al. /2016	Australia	Not Mentioned	M:58.6 F:62	39/49	OPMD	Vizilite AF	13 88	85 63
Scheer et.al. /2016	Germany	Not Mentioned	Not Mentioned	22/19	OPMD	Velscope	40	89
Xiaobo Luo et.al. /2016	China	2761	Not Mentioned	Not Mentioned	SCC OPMD	AF	89	80
Do Hyun Kim et.al. /2020	South Korea	2812	Not Mentioned	Not Mentioned	OPMD	AF	82.4	62.4
Do Hyun Kim et.al. /2020	Korea	998	Not Mentioned	Not Mentioned	OPMD	CL	84.9	42.9
Jayanta Saikia et.al. /2020	India	Not Mentioned	Not Mentioned	Not Mentioned	OPMD	ViziLite Velscope	71-100 30-100	0-84.6 15-100
María Rosa Buenahora et.al. /2020	Colombia	Not Mentioned	Not Mentioned	Not Mentioned	OPMD	AF CL	86 67	72 48
Amar kumar shaw et.al.	India	1833	50.2	(56/44)%	Leukoplakia Lichen Planus	CL	75 78	98 60

/2022					OSMF		89	76
Antonio Moffa et. al. /2021	Italy	Not Mentioned	Not Mentioned	Not Mentioned	OPMD	AF CL	81.3 84.9	52.1 51.8
Swathi KV, et.al /2022	India	84	44	Not Mentioned	OPMD	CL with Lugol's iodine CL with toluidine blue	91.7 100	66.7 60

AF- Autofluorescence

CL- Chemiluminescence

F- Female

M- Male

OL- Oral Leukoplakia

OLP- Oral Lichen Planus

OPMD- Oral Potentially Malignant Disorder

SCC- Squamous Cell Carcinoma

Discussion

Oral cancer is the eighth most common form of cancer in the world. It represents more than 90% of all malignant neoplasms of the mouth. Oral cancer occurs at a different rate in different areas of the world, ranging from 2 to 10 per 100,000 people each year. Oral cancer is prevalent in South Asian nations such as Sri Lanka, India, Pakistan, and Bangladesh. In India, the frequency is 7-17 per 100,000 people each year, with 75,000 - 80,000 new cases per year.It is necessary to identify oral cancer in the earliest stage possible so that mortality and morbidity due to oral cancer can be reduced. Various cancer screening programmes can help to achieve this goal. Along with-it patients should be made aware to take their oral health seriously and visit for routine dental checkups to eliminate any kind of potential risk at the beginning stage. It will be basically Secondary Prevention of the disease. Secondary prevention emphasizes early disease detection, and its target is healthy-appearing individuals with subclinical forms of the disease. The subclinical disease consists of pathologic changes, but no overt symptoms that are diagnosable in a doctor's visit. Secondary prevention often occurs in the form of screenings Unfortunately, early detection of oral precancerous and cancerous lesions has proved difficult due to the lesions' asymptomatic nature, doctors' casual approach to benign lesions, and the fact that 50 % of patients had regional or distant metastases at the time of diagnosis. But keeping the progression of oral premalignant lesion to oral cancer in mind, early diagnosis and intervention is necessary. Various conventional methods can be used for this purpose. Surgical biopsy is a gold standard diagnostic procedure, and several diagnostic procedures have been attempted to replace it. However, it is used as an adjuvant to surgical biopsy rather than as a replacement. New developments like auto fluorescence and chemiluminescence can play a bigger role in early intervention with less impairment and a higher chance of cure.

The aim of this systematic review and meta-analysis was to summarize existing evidence on diagnostic accuracy of chemiluminescence and auto fluorescence To the best of the authors' knowledge, this systematic review and meta-analysis provides a comprehensive quantitative analysis of chemiluminescence and auto fluorescence for various OPMDs on which diagnostic reasoning can be established. Number of articles using CF and AF as diagnostic tools were 13 and 15 respectively. The average sample size selected (based on the articles which fits into the inclusion criteria) for CF was 403.8 and for AF it was 749.6. For

chemiluminescence, among the included studies, sensitivity ranged from 0-100% while specificity ranged from 0-98%. Likewise for autofluorescence, sensitivity ranged from 40-100% and specificity from 15.3-97%. Based on the articles selected, the average sensitivity for AF is 75.7% and for CL it is 73.9%, and average specificity for AF is 50.48% and for CL it is 62.9%. HIghest sensitivity of 100% using CL was recorded by S.Ram et.al., Farah et.al, Swathi et. al. and using AF, it was recorded by Scheer et.al. Highest specificity of 98%using CL was recorded by Amar kumar shaw et.al. and 97% using AF by Wei zheng et.al.

Conclusion

Both CL and AF overall had good sensitivity, however specificity values are very mediocre. The study findings provide evidence and this strongly supports the fact that CL and AF can be used as an alternative diagnostic adjunct to biopsy for early screening and diagnosis of various OPMDs. Thus, it can be concluded that CL and AF can be useful for a secondary level of prevention for early oral squamous cell carcinoma under early diagnosis and prompt treatment. Future research must focus on improving the accuracy of CL and AF in detection of OPMDs with clear and robust methodology.

References

1. SHAW AK, MAHAJAN M, RSHNEY S, JENA M, ROHATGI L, BASHIR S, TEWARI S, ROY J. Diagnostic Accuracy of Chemiluminescence for Oral Potentially Malignant Disorders: A Systematic Review and Meta-analysis. Journal of Clinical & Diagnostic Research. 2022 Jul 1;16(7).
2. Srivastava R, Sharma L, Pradhan D, Jyoti B, Singh O. Prevalence of oral premalignant lesions and conditions among the population of Kanpur City, India: A cross-sectional study. Journal of family medicine and primary care. 2020 Feb;9(2):1080.
3. Wang C, Qi X, Zhou X, Liu H, Li M. Diagnostic value of objective VELscope fluorescence methods in distinguishing oral cancer from oral potentially malignant disorders (OPMDs). Translational Cancer Research. 2022 Jun;11(6):1603.
4. Gillenwater A, Papadimitrakopoulou V, Richards-Kortum R. Oral premalignancy: new methods of detection and treatment. Current oncology reports. 2006 Apr;8:146-54.
5. Gupta S, Shah JS, Parikh S, Limbdiwala P, Goel S. Clinical correlative study on early detection of oral cancer and precancerous lesions by modified oral brush biopsy and cytology followed by histopathology. Journal of cancer research and therapeutics. 2014 Apr 1;10(2):232-8.
6. Kim DH, Kim SW, Hwang SH. Autofluorescence imaging to identify oral malignant or premalignant lesions: Systematic review and meta-analysis. Head & Neck. 2020 Dec;42(12):3735-43.
7. Mehrotra R, Gupta A, Singh M, Ibrahim R. Application of cytology and molecular biology in diagnosing premalignant or malignant oral lesions. Molecular cancer. 2006 Dec;5(1):1-9.
8. Bhatia N, Lalla Y, Vu AN, Farah CS. Advances in optical adjunctive AIDS for visualisation and detection of oral malignant and potentially malignant lesions. International journal of dentistry. 2013 Oct;2013.
9. Mehrotra R, Singh M, Thomas S, Nair P, Pandya S, Nigam NS, Shukla P. A cross-sectional study evaluating chemiluminescence and autofluorescence in the detection of clinically innocuous precancerous and cancerous oral lesions. The Journal of the American Dental Association. 2010 Feb 1;141(2):151-6.

10. Swathi KV, Maragathavalli G, Maheswari TU. Comparing the efficacy of chemiluminescence with lugol's iodine versus toluidine blue in the diagnosis of dysplasia in tobacco associated oral lesions-A diagnostic study. Indian Journal of Dental Research. 2021 Oct 1;32(4):459.
11. Awan KH, Morgan PR, Warnakulasuriya S. Assessing the accuracy of autofluorescence, chemiluminescence and toluidine blue as diagnostic tools for oral potentially malignant disorders—a clinicopathological evaluation. Clinical oral investigations. 2015 Dec;19:2267-72.
12. Ram S, Siar CH. Chemiluminescence as a diagnostic aid in the detection of oral cancer and potentially malignant epithelial lesions. International journal of oral and maxillofacial surgery. 2005 Jul 1;34(5):521-7.
13. Moffa A, Giorgi L, Costantino A, De Benedetto L, Cassano M, Spriano G, Mercante G, De Virgilio A, Casale M. Accuracy of autofluorescence and chemiluminescence in the diagnosis of oral Dysplasia and Carcinoma: A systematic review and Meta-analysis. Oral Oncology. 2021 Oct 1;121:105482.
14. Kim DH, Lee J, Lee MH, Kim SW, Hwang SH. Efficacy of chemiluminescence in the diagnosis and screening of oral cancer and precancer: a systematic review and meta-analysis. Brazilian Journal of Otorhinolaryngology. 2022 Jun 27;88:358-64.
15. Saikia J. Advanced Diagnostic Aids in Detection of Potentially Premalignant Oral Epithelial Lesions-A Review. Acta Scientific Dental Sciences. 2020;4:11-8.
16. Yang EC, Tan MT, Schwarz RA, Richards-Kortum RR, Gillenwater AM, Vigneswaran N. Noninvasive diagnostic adjuncts for the evaluation of potentially premalignant oral epithelial lesions: current limitations and future directions. Oral surgery, oral medicine, oral pathology and oral radiology. 2018 Jun 1;125(6):670-81.
17. Kim DH, Lee J, Lee MH, Kim SW, Hwang SH. Efficacy of chemiluminescence in the diagnosis and screening of oral cancer and precancer: a systematic review and meta-analysis. Brazilian Journal of Otorhinolaryngology. 2022 Jun 27;88:358-64.
18. Buenahora MR, Peraza-L A, Díaz-Báez D, Bustillo J, Santacruz I, Trujillo TG, Lafaurie GI, Chambrone L. Diagnostic accuracy of clinical visualization and light-based tests in precancerous and cancerous lesions of the oral cavity and oropharynx: a systematic review and meta-analysis. Clinical Oral Investigations. 2021 Jun;25:4145-59.
19. 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(8):820–824.
20. Scheer M, Neugebauer J, Derman A, Fuss J, Drebber U, Zoeller JE (2011) Autofluorescence imaging of potentially malignant mucosa lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2:10– 577.
21. Awan KH, Morgan PR, Warnakulasuriya S (2011) Evaluation of an autofluorescence based imaging system (VELscopeTM) in the de[1]tection of oral potentially malignant disorders and benign keratoses. Oral Oncol 47(4):274–277.
22. Mojsa I, Kaczmarzyk T, Zaleska M, Stypulkowska J, Zapala[1]Pospiech A, Sadecki D (2012) Value of the ViziLite Plus System as a diagnostic aid in the early detection of oral cancer/premalignant epithelial lesions. J Craniofac Surg 23:e162–e164.

23. Kaur J, Jacobs R (2015) Combination of autofluorescence imaging and salivary protoporphyrin in oral precancerous and cancerous lesions: Non-invasive tools. J Clin Exp Dent 7(2):e187–e191.
24. Moro A, De Waure C, Di Nardo F et al (2015) The GOCCLES® medical device is effective in detecting oral cancer and dysplasia in dental clinical setting. Results from a multicentre clinical trial. Acta Otorhinolaryngol Ital 35(6):449–454.
25. Scheer M, Fuss J, Derman MA, Kreppel M, Neugebauer J, Rothamel D, Drebber U, Zoeller JE (2016) Autofluorescence im[1]aging in recurrent oral squamous cell carcinoma. Oral Maxillofac Surg 20(1):27–33.
26. Chaudhry A, Manjunath M, Ashwatappa D, Krishna S, Krishna AG (2016) Comparison of chemiluminescence and toluidine blue in the diagnosis of dysplasia in leukoplakia: a cross-sectional study. J Investig Clin Dent 7(2):132–140.
27. Lalla Y, Matias MAT, Farah CS (2016) Assessment of oral muco[1]sal lesions with autofluorescence imaging and reflectance spectros[1]copy. J Am Dent Assoc 147(8):650–660.
28. Vashisht N, Ravikiran A, Samatha Y, Chandra Rao P, Naik R, Vashisht D (2014) Chemiluminescence and toluidine blue as diag[1]nostic tools for detecting early stages of oral cancer: an invivo study. J Clin Diagn Res 8(4):ZC35–ZC38.
29. Luo X, Xu H, He M, Han Q, Wang H, Sun C, Li J, Jiang L, Zhou Y, Dan H, Feng X. Accuracy of autofluorescence in diagnosing oral squamous cell carcinoma and oral potentially malignant disorders: a comparative study with aero-digestive lesions. Scientific reports. 2016 Jul 15;6(1):29943.
30. Jané-Salas E, Blanco-Carrión A, Jover-Armengol L, López-López J. Autofluorescence and diagnostic accuracy of lesions of oral mucosa: a pilot study. Brazilian Dental Journal. 2015 Nov;26:580-6.