Original Article

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VELSCOPE-FOR EARLY DETECTION OF PREMALIGNANT/MALIGNANT LESIONS IN THE ORAL CAVITY

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ABSTRACT:

Aim: To check the efficacy of VELscope in identifying early soft tissue abnormalities (premalignant/malignant,etc) in the oral cavity which is not visible to the naked eye on clinical examination.

Materials &Methods: It is a prospective, cross-sectional study performed by conducting oral cancer screening camps in the community over a period of 6 to 9 months in the Indian population (esp-mumbai suburbs) Around 700 males and females between 18 – 90 years of age ,with habits chewing and/or smoking tobacco.

Results: In our study out of the 740 patients selected for the screening for early detection, 669 patients had no abnormality detected on clinical examination and thus were included in this study. Out of the 669, 8 patients (6 male and 2 females) showed changes loss of florescence on velscope examination with nothing detected clinically, biopsy of these sites was done and evaluated using histopathological examination out of which none were reported malignant/ premalignant.

Conclusion: With our study we conclude that velscope did not help in early detection of oral lesions before it is visible to naked eye examination, its efficacy is flawed in terms of sensitivity and needs improvement.

Key words: early lesions, efficacy of velsope, malignant and premalignant lesions.

INTRODUCTION:

Oral cancer ranks in the top three of all cancers in India, which accounts for over thirty per cent of all cases reported. Its prevalence is high amongst the Indian population. Most important factors in late detection of the lesion is unawareness amongst patients, fewer diagnostic aids and low affordability. Secondly, rural areas in middle and low-income countries also have inadequate access to trained providers and limited health services. This delay has also been largely associated with advanced stages of oral cancer. Patients with early lesions have better chances of cure and lesser treatment associated morbidities.

One of the difficulties associated with clinical detection of oral cancer, until recently, is that the only diagnostic tool available is visual and tactile examination of oral mucosa. While those diagnostic procedures are reasonable but cannot detect changes at the cellular

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level that has not evolved for the naked eye to see. The advent of adjunct tool for use as a part of the conventional oral examination has been helpful to improve the early detection of oral cancer. In this study, we evaluate a simple, low cost, portable optical imaging system for early detection of oral cancer as an adjunct to clinical evaluation following a conventional examination.

MATERIALS & METHODS

- Study: Prospective, cross-sectional

- Place of study: BSES MG HOSPITAL, Oral Cancer screening camps in the community.

Study Period: 6 to 9 month

Study Population: Indian population, male and female living in the city of Mumbai , 18 -90 years of age

- Study Design: Screen 700-800 patients amongst the Indian population (especially residing in Mumbai suburban areas).

To be screened and evaluated using VELSCOPE

Inclusion Criteria:

1)-All Patients with tobacco habits chewing and/or smoking and nothing significant detected on clinical examination.

2)-Patients willing to participate in the study.

Exclusion criteria:

1) Patients unwilling to participate in the study

2) Patients with grade 3 and 4 trismus

3) Patient with lesion visible on clinical examination.

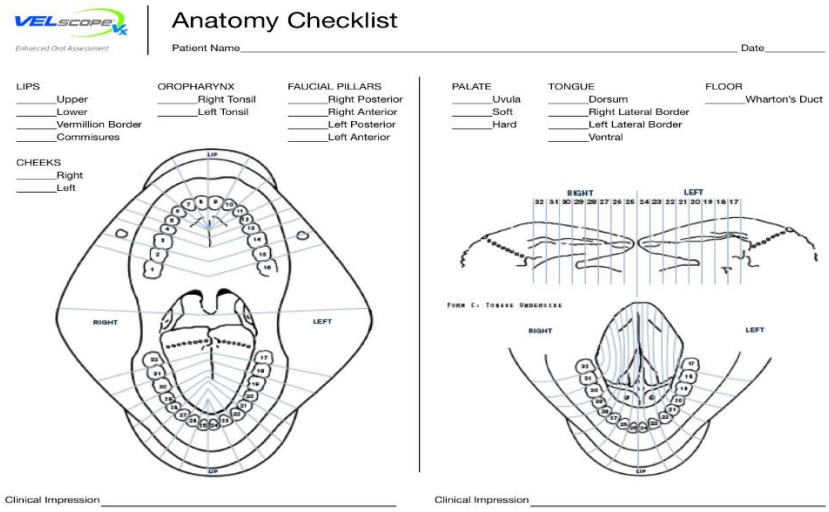
METHOD:

- Select an appropriate subject according to the inclusion criteria of the study
- Make the subject sit on a chair
- Take a brief history
- perform a clinical examination using tongue depressor and light source (3-4.5 volts)
- Examination of the following areas in the oral cavity was performed

- lower and upper lip and vermillion border of lip
- commisures of mouth
- lower labial mucosa and sulcus
- buccal mucosa and buccal sulcus
- upper labial mucosa and sulcus
- gingiva
- tongue-dorsal,ventral,lateral borders
- floor of the mouth
- hard palate, soft palate, uvula

- anterior and posterior faucial pillars- right and left
- tonsils- right and left

➢ If loss of fluorescence seen – take a biopsy from the site of maximum loss of fluorescence



RESULTS:

TABLE 1:
Age

Sr. No		Number	Percent
1	20-39	186	26.1
2	40-59	438	57.8
3	60-79	114	15.9
4	80-99	2	0.2
	TOTAL	740	

TABLE 2:
Sex

Sr. No		Number	Percent
1	Female	83	11.2
2	Male	657	88.8
	TOTAL	740	

TABLE 3:
Habits- Tobacco

Sr. No		Number	Percent
1	Smoked	30	4.1
2	Smokeless	663	89.5
3	Both	47	6.4
	TOTAL	740	

TABLE 4:

Provisional Diagnosis

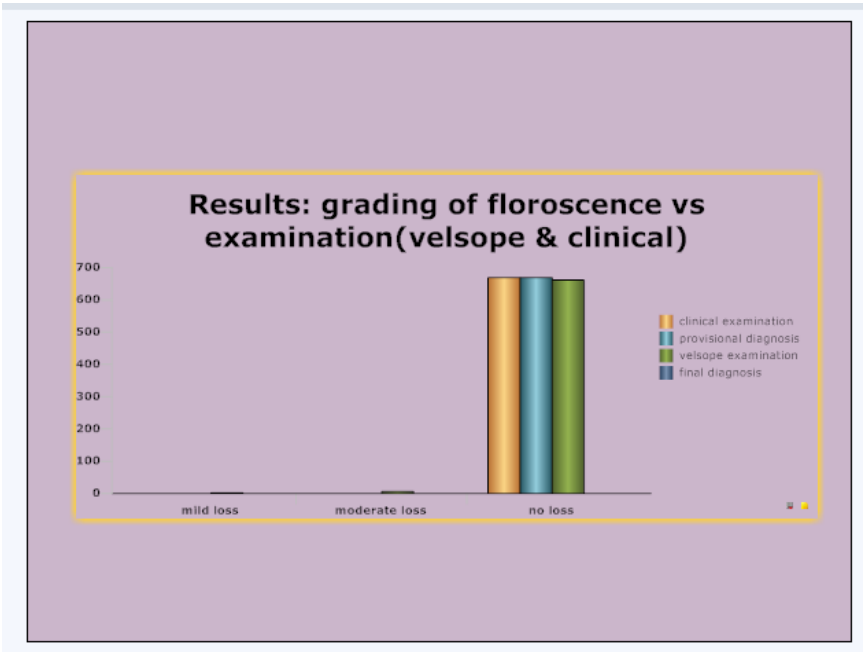
Sr. No		Number	Percent
1	Apthous ulcer	2	0.2
2	Cheek bite	8	1.0
3	Denture stomatitis	1	0.1
4	Denture trauma	2	0.2
5	Depapillation of tongue	1	0.1
6	Erythroleukoplakia	4	0.5
7	Fibroma	3	0.4
8	Fordyces spots	1	0.1
9	Food burn	1	0.1
10	Frictional keratosis	1	0.1
11	Leukoplakia	11	1.4
12	Lichen Planus	2	0.2
13	Linea Alba	2	0.2
14	Maxillary tori	1	0.1
15	Mucosal changes	6	0.8
17	Oral submucous fibrosis	11	1.4
18	Preleukoplakia	9	1.2
19	Tobacco pouch keratosis	2	0.2
20	Traumatic ulcer due to denture	1	0.1
21	Ulcer	2	0.2
22	**NAD**	**669**	**90.4**

669 patients had no abnormality detected on clinical examination and thus were included in this study.

TABLE 5: MASTER CHART

Grading of Fluoresce	Clinical examination	Provisional diagnosis	VELscope examination-patient no.	Biopsy site	Final diagnosis
Mild Loss	NAD	NAD	32	left corner at angle of mouth	hyperkeratotic and parakeratotic benign squamous mucosa
	NAD	NAD	56	Left buccal mucosa	Benign Inflamed hyperplastic squamous mucosa
Moderate Loss	NAD	NAD	129	Mandibular left buccal vestibule	benign hyperplastic squamous mucosa and congested blood vessels seen beneath
	NAD	NAD	176	left buccal mucosa	mildly inflammed hyperplastic mucosa
	NAD	NAD	177	Mandibular right buccal	inflammed hyperplastic

				vestibule	squamous mucosa
	NAD	NAD	310	right buccal mucosa	Benign Inflamed hyperplastic squamous mucosa
	NAD	NAD	311	Mandibular left buccal vestibule	mildly inflammed hyperplastic mucosa
	NAD	NAD	418	left corner at angle of mouth	hyperkeratotic and parakeratotic benign squamous mucosa
No loss	NAD	NAD	Rest of all (740)	No Biopsy Taken	NAD



Bar diagram

Only 8 patients out of 669 showed loss of florescence on velscope(2=mild{n=0.2989%},6=moderate{n=0.896%) with no abnormality detected clinically.

On H/P examination the biopsies from these 8 patients showed only inflammatory changes.

Fig 1.1:Patient 176- No lesion seen on clinical examination.On velscope moderate loss of fluorescence seen on left buccal mucosa.

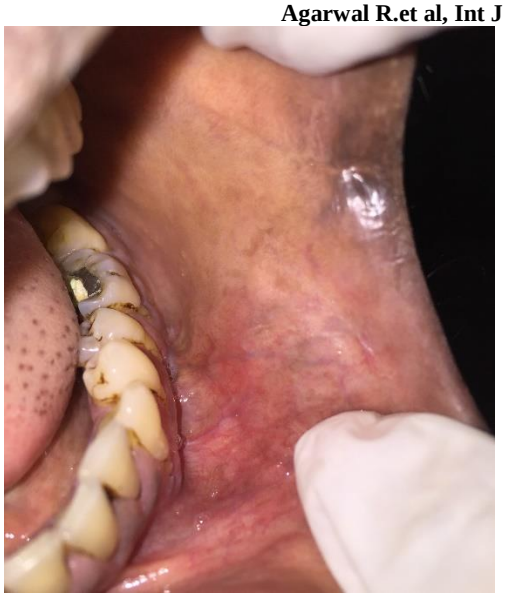



Fig 1.2:Patient 177- No lesion seen on clinical examination.On velscope moderate loss of fluorescence seen on Mandibular right buccal vestibule

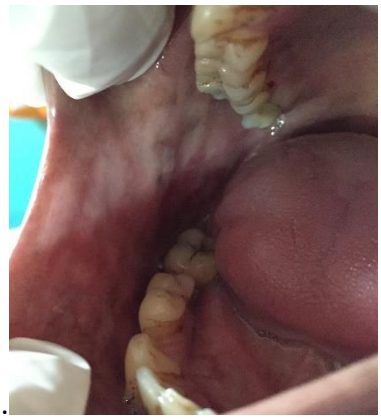
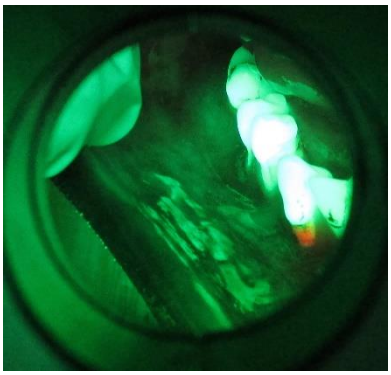



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Fig 1.3:Patient 310- No lesion seen on clinical examination.On velscope a patch of moderate to severe/complete loss of fluorescence seen on right buccal mucosa.

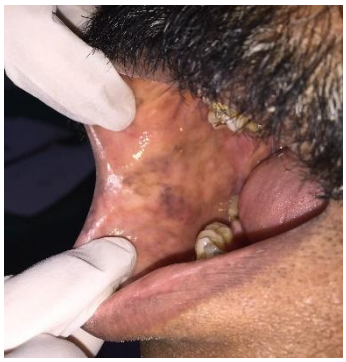
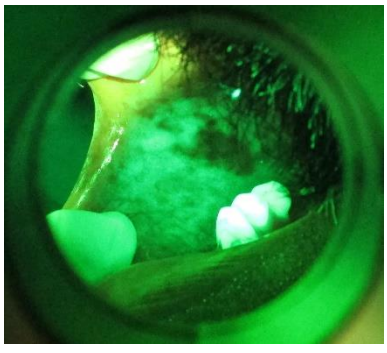
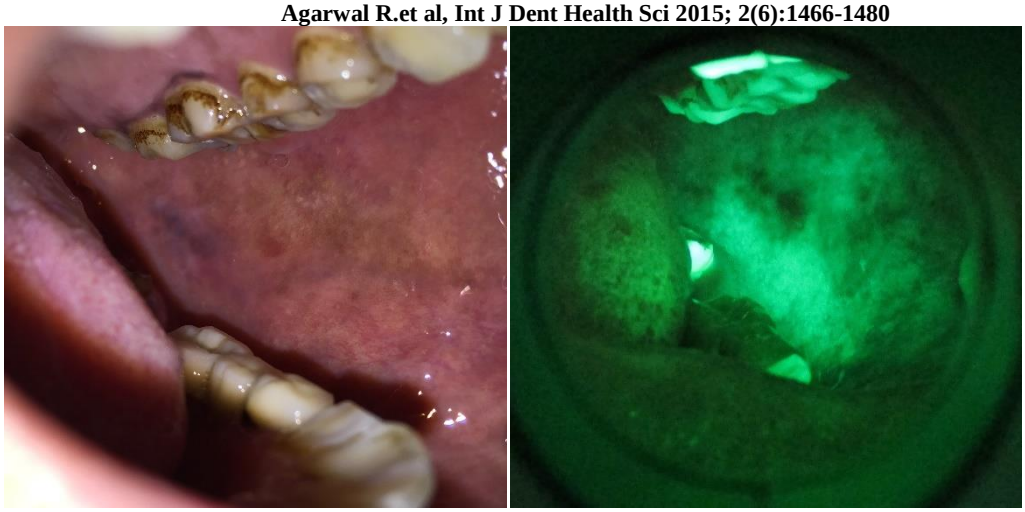



Fig 1.4:Patient 129- No lesion seen on clinical examination.
On velscope mild to moderate loss of fluorescence seen on Mandibular left buccal vestibule.



Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value

	DISEASE NUMBER	NON DISEASE NUMBER	TOTAL NUMBER
POSITIVE NUMBER	0-A(TRUE POSITIVE CASES)	8-B (FALSE POSITIVE CASES)	0
NEGITIVE NUMBER	0–C(FALSE NEGITIVES)	661 -D (TRUE NEGITIVE)	100

- **Positive Predictive Value: A/(A+B) × 100**
- **Negative Predictive Value: D/(D+C) × 100**
- Cell A contains true positives, subjects with the disease and positive test results. Cell D subjects do not have the disease and the test agrees.
- Cell B identifies individuals without disease but for whom the test indicates 'disease'. These are false positives. Cell C has the false negatives.
- To determine cell C is not applicable to our test as there is no other tool to check except clinical examination which is exclusion criteria so for the calculation purpose it stands 0.

Prevalence of Disease= $T_{disease}$/ Total × 100

= 0/669x100

=0

- **Sensitivity(**Sensitivity is the probability that a test will indicate 'disease' among those with the disease)**= A/(A+C) × 100**

  =0/0+0

  =0
- **Specificity(**Specificity is the fraction of those without disease who will have a negative test result)**= D/(D+B) × 100**

  =661/661+8 x 100

  =98.804%

Prevelance is influenced by the population used for study but specificity and sensitivity are characteristics of the test.

REVIEW OF LITERATURE:

1)Efficacy of tissue autofluorescence imaging (velscope) in the visualization of oral mucosal lesions
Camile S. Farah PhD1,*, Lidija McIntosh BDSc1, Anastasia Georgiou MDSc2 andMichael J. McCullough PhD3

Technology that highlights potentially malignant oral lesions in a highly sensitive and specific manner will aid clinicians in early diagnosis of these conditions.[This study assessed the efficacy of direct tissue autofluorescence imaging Visually Enhanced Lesion Scope (VELScope) in the detection of oral mucosal lesions.
One hundred twelve patients referred with a potentially malignant oral mucosal lesion were examined under routine incandescent light, and then with VELScope, noting loss of autofluorescence and presence of blanching. Incisional biopsies were performed to provide definitive histopathological diagnoses. VELScope enhanced the visibility of 41 lesions and helped uncover 5 clinically undetected lesions. VELScope examination alone showed a sensitivity of 30% and a specificity of 63%. Its accuracy at identifying dysplasia was 55%.
VELScope examination cannot provide a definitive diagnosis regarding the presence of epithelial dysplasia. Loss of autofluorescence is not useful in diagnosing epithelial dysplasia in its own right without relevant clinical interpretation.

2)Evaluation of an autofluorescence based imaging system (VELscope™) in the detection of oral potentially malignant disorders and benign keratoses
K.H. AwanP.R. MorganS. Warnakulasuriya

Early detection of oral cancer is crucial in improving survival rate. Identification and detection of oral potentially malignant disorders (OPMD) allow delivery of interventions to reduce the evolution of these disorders to malignancy. A variety of new and emerging diagnostic aids and adjunctive techniques are currently available to potentially assist in the detection of OPMD. The objective of the present study was to evaluate the accuracy of autofluorescence against conventional oral examination and surgical biopsy. A total of 126 patients, 70 males and 56 females (mean age 58.5 ± 11.9 years) who presented to the Oral Medicine Clinics at King's and Guy's Hospitals, London with oral white and red patches suspicious of OPMD were enrolled. Following a complete visual and autofluorescence examination, all underwent an incisional biopsy for histopathological assessment. Seventy patients had oral leukoplakia/erythroplakia, 32 had oral lichen planus, 9 chronic hyperplastic candidiasis and rest frictional keratosis

or oral submucous fibrosis . Of 126 lesions, 105 (83%) showed loss of fluorescence. Following biopsy 44 had oral epithelial dysplasia (29 mild, 8 moderate and 7 severe). The sensitivity (se) and specificity (sp) of autofluorescence for the detection of a dysplastic lesion was 84.1% and 15.3% respectively.

While VELscope was useful in confirming the presence of oral leukoplakia and erythroplakia and other oral mucosal disorders, the device was unable to discriminate high-risk from low-risk lesions.

3)Incidental detection of an occult oral malignancy with autofluorescence imaging: a case report Nadarajah Vigneswaran*1, Sheila Koh2 and Ann Gillenwater3

Autofluorescence imaging is used widely for diagnostic evaluation of various epithelial malignancies.[1] Cancerous lesions display loss of autofluorescence due to malignant changes in epithelium and subepithelial stroma. Carcinoma of unknown primary site presents with lymphnode or distant metastasis, for which the site of primary tumour is not detectable.[2,3] We describe here the use of autofluorescence imaging for detecting a clinically innocuous appearing occult malignancy of the palate which upon pathological examination was consistent with a metastatic squamous cell carcinoma. Case Description: A submucosal nodule was noted on the right posterior hard palate of a 59-year-old white female during clinical examination. Examination of this lesion using a multispectral oral cancer screening device revealed loss of autofluorescence at 405 nm illumination. An excisional biopsy of this nodule, confirmed the presence of a metastatic squamous cell carcinoma. Four years ago, this patient was diagnosed with metastatic squamous cell carcinoma of the right mid-jugular lymph node of unknown primary. She was treated with external beam irradiation and remained disease free until current presentation. This case illustrates the important role played by autofluorescence tissue imaging in diagnosing a metastatic palatal tumour that appeared clinically innocuous and otherwise would not have been biopsied.[4,5]

4)Evaluation of a low-cost, portable imaging system for early detection of oral cancer

Mohammed S Rahman†1,2, Nilesh Ingole2, Darren Roblyer1,3, Vanda Stepanek1,3, Rebecca Richards-Kortum*†1,3,

Ann Gillenwater†1,3, Surendra Shastri2 and Pankaj Chaturvedi

There is an important global need to improve early detection of oral cancer. [6] Recent reports suggest that optical imaging technologies can aid in the identification of neoplastic lesions in the oral cavity; however, there is little data evaluating the use of optical imaging modalities in resource limited settings

where oral cancer impacts patients disproportionately.[7] In this article, we evaluate a simple, low-cost optical imaging system that is designed for early

detection of oral cancer in resource limited settings. We report results of a clinical study conducted at Tata Memorial Hospital (TMH) in Mumbai, India using this system as a tool to improve detection of oral cancer and its precursors.[8]

Methods: Reflectance images with white light illumination and fluorescence images with 455 nm excitation were obtained from 261 sites in the oral cavity from 76 patients and 90 sites in the oral cavity from 33 normal volunteers.

Quantitative image features were used to develop classification algorithms to identify neoplastic tissue, using clinical diagnosis of expert observers as the gold standard. [9]

Using the ratio of red to green autofluorescence, the algorithm identified tissues judged clinically to be cancer or clinically suspicious for neoplasia with a sensitivity of 90% and a specificity of 87%.[10]

Results suggest that the performance of this simple, objective low-cost system has potential to improve oral screening efforts, especially in low-resource settings.[11]

Clinical evaluation of an autofluorescence diagnostic device for oral cancer detection: a prospective randomized diagnostic study

5)Rana, Majeed[a]; Zapf, Antonia[b]; Kuehle, Marco[a]; Gellrich, Nils-Claudius[a]; Eckardt, André M.

The prognosis for patients with oral squamous cell carcinoma remains poor despite advances in multimodal treatment concepts. Early diagnosis and treatment is the key to improved patient survival. A device (VELscope) that uses autofluorescence technology, allowing direct fluorescence visualization of the oral cavity, might be a useful tool for oral cancer detection or as an adjunct to standard clinical examination. A total of 289 patients with oral premalignant lesions were randomly divided into two groups for clinical examination of precancerous oral lesions. In group 1, 166 patients were examined conventionally with white light, and in group 2, 123 patients were examined with the autofluorescence visualization device (VELscope) in addition to the white light examination. Biopsies were obtained from all suspicious areas identified in both examination groups (*n*=52). In the first step, baseline characteristics of the two groups (only white light vs. white light and VELscope) were compared to exclude selection bias. In the second step, for the group examined with white light and VELscope (123 patients), the diagnostic strategies were compared with regard to sensitivity and specificity using biopsy as the gold standard. The results showed that using the VELscope leads to higher sensitivity (100% instead of 17%), but to lower specificity (74% instead of 97%). Thus, we can conclude that the VELscope is a

useful new diagnostic device for detection of oral cancer diseases.

6)Oral cancer awareness for the general practitioner: new approaches to patient care

CS Farah and MJ McCullough

Early in 2006 another direct visualization device for examining tissues in the oral cavity by fluorescence was released and examined in a pilot study.[12,13] This device is called a Visually Enhanced Lesion Scope (VELScope). [14]It is a handheld device that facilitates the direct visualization of oral cavity fluorescence for the detection of high-risk, potentially malignant and early malignant lesions. A blue excitation light, between 400 to 460 nm, is employed to excite green-red fluorescence from fluorophores in the oral tissues. Tissue fluorescence is viewed directly along an optical axis collinear with the axis of excitation to reduce inter- and intra-operator variability.[15]This robust field of view device enables the direct visualization of fluorescence in the context of surrounding normal tissues. Because changes in the natural fluorescence of healthy tissue generally reflect light scattering biochemical or structural changes indicative of developing tumour cells, the VELScope allows the practitioner to shine a light onto a suspicious sore in the mouth and look through an attached eye piece to watch directly for changes in colour.[16] Normal oral tissue is said to omit a pale green fluorescence while potentially early tumour or dysplastic cells appear dark green to black. Several studies have shown that human oral cancer tissue manifests different autofluorescence spectra when compared to normal tissue.It is thought that the high concentrations of protoporphyrin IX present in malignant tissue is responsible for this changing and application of 5-aminolaevulinic acid (ALA) to the mucosa amplifies this autofluorescence.

A pilot study of 44 patients examined with the VELScope and using histology of biopsied specimens as the gold standard, found that the device achieved a sensitivity of 98 per cent and a specificity of 100 per cent when discriminating normal oral mucosa from severe dysplasia or invasive carcinoma. From the 50 tissue sites evaluated from 44 subjects which all underwent biopsy and histopathological examination by a trained pathologist, 7 were classified as normal, 11 had severe dysplasia, and 33 biopsies were found to be oral squamous cell carcinoma. Reading the pattern of the 50 sites, the authors, clinicians trained in oral medicine, correctly identified all the normal biopsies, 10 of the 11 severe dysplasias and all of the 33 oral squamous cell carcinomas.

It is this examination that should ultimately determine the need for further diagnostic tests such as cytology or biopsy.

7)Exciting new advances in oral cancer diagnosis: avenues to early detection

Ravi Mehrotra and Dwijendra K Gupta

VELscope is a commercially available light-based system that is based upon the assumption that abnormal metabolic or structural changes have different absorbance and reflectance properties.VELscope is a handheld device that uses visible light in the 430 nm wavelength in order to cause fluorescent excitation of certain compounds in the tissues.[17,18] With Vizilite, patients' first rinse with acetic acid and then the oral cavity is examined with an illuminated chemiluminescent light stick. [19] The sensitivity of Vizilite was 0% and the sensitivity of VELscope was also poor-50%.[20] We concluded that the use of ViziLite or VELscope along with a conventional screening examination was not beneficial in identifying dysplasia or cancer and clinicians/and patients could have a false sense of security after obtaining a negative ViziLite or VELscope examination result because potentially large numbers of precancerous and cancerous lesions would be missed by both. [21] Until additional studies are performed, these screening lights should only be used to help identify lesions that may have been overlooked with a conventional oral examination and not for determining whether a lesion is precancerous or cancerous. Only a definitive test examining cells or tissue can determine the biologic behavior of a lesion.

DISCUSSION:

The oral cavity and mucosa should be examined thoroughly(22) The utility of autofluorescence as a diagnostic test, especially its accuracy in the detection of oral epithelial dysplasia and cancer, has to be assessed. Velscope works on the mechanism of TISSUE AUTOFLUROSCENCE.

Visualising tissue autofluroscence takes place on basis of different wavelengths exhibited.

TISSUE FLUOROPRES: A) Components of cell metabolism- FAD

B) Structural components – collagen, keratin, fibrin. Progressive dyplasia in oral mucosa absorbs light at different wavelengths and shows loss of fluorescence.

Tissue fluoropres are molecules that emit energy in the form of fluorescence when excited by light. Fluorophores may be located within cells or in the extracellular matrix and include structural proteins such as collagen and elastin, the metabolic co-factors nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide (FAD), as well as several aromatic amino acids, and porphyrins.(36-38) The autofluorescent spectrum is thought to be influenced by the concentration of these fluorophores as well as by absorption and scattering properties related to tissue morphology and biochemistry(23,24).

Morphologic alterations associated with epithelial neoplasia, including increased epithelial thickness, nuclear size, and microvascularity, are considered

responsible for the associated decreased autofluorescence seen with malignancy. It has also been suggested that decreased tissue fluorescence may reflect changes in metabolic activity associated with proliferating neoplastic cells,[36-38] however, the specific alterations in tissue architecture and biochemical composition which are responsible for spectral changes associated with epithelial neoplasia are not well understood[25].

For this study, 740 individuals were first clinically examined under incandescent light and then later screened using VELScope for any possible findings. After careful examination, it could be concluded that there was no loss of fluorescence in majority of the patients. If there was either moderate or high loss of fluorescence seen on the palate, buccal mucosa, lower labial vestibule or lateral borders of the tongue on VELScope, a biopsy was taken with the patient's consent.

In our study, about 86.3% of those that were examined used smokeless tobacco, about 4% smoked cigarettes and about 6% used both smoking and smokeless tobacco. On clinical examination, no abnormality was detected in about 86.3% of the patients On VELScope examination, 732 patients out of 740 showed no loss of fluorescence, only 8 showed loss of fluorosecnce in areas where no lesion was visible to the naked eye, these 8 patients were biopsied and sent for histopathological examination , which were non malignant In terms of specificity velscope was 98.804% accurate but in terms of sensitivity velscope was a failure. Koch et al study showed specificity 98% for early detection with similar results to our study[26]. In the study by Farah et al fluorescence was reported resulting in false negative test results[27,28]. On the contrary no false negatives were reported in our study and 8 false positive cases were reported.

It is evident that velsope can be used as a adjunct tool in diagnosis but its utilization and reliability remains questionable.

CONCLUSION:

With our study we conclude that velscope did not help in early detection of oral lesions before it is visible to naked eye examination, its efficacy is flawed in terms of sensitivity and needs improvement.

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