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Significance of chemiluminescence & staining in oral precancers: Our experience

KEYWORDS: Oral precancers, chemiluminescence, toluidine blue, biopsy.

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ABSTRACT *Oral cancer is the most common cancer in India with an incidence of 12.6 per 100,000 populations with a mortality of 50-70 %.This form of cancer is pre eminently treatable if diagnosed early.*
AIM: Our Aim is to study the reliability and effectiveness of chemiluminescence and staining as a non invasive screening tool for oral pre cancers and to compare the results with the gold standard of biopsy.
Materials & Methods: We have studied 100 patients with in the age group of 21 – 70 years with oral precancers in a cross sectional, interventional study, where after clinical examination patients were screened by chemiluminescence and staining with toluidine blue using Vizilite plustm and were then subjected to biopsy. The data was then subjected to statistical analysis.
Results: The sensitivity and specificity of chemiluminescence to that of biopsy is 58.06% & 71.05%. The sensitivity & specificity of toluidine blue staining to that of biopsy is 87% & 81%.
Conclusion: Accuracy of staining by toluidine blue is higher than that of chemiluminescence illumination, but still awaits further proofing to be used as a replacement for biopsy.

Introduction:
Oropharyngeal cancers are the 8th most common cancer worldwide. In India oral cancer is the most common cancer with an age standardized incidence of 12.6 per 100,000 populations. [1] It accounts for 50 -70 % of total cancer mortality.[2]

Though easily accessible for examination, oral cavity cancers are usually first diagnosed when they become symptomatic & approximately two thirds of the patients present with advanced disease, regional metastasis as a consequence of which they have poor prognosis.[3]

This form of cancer is pre-eminently curable if it is diagnosed early. This helps in improving patients life by decreasing the morbidity and mortality associated with this disease. As has been stated by S P Khandekar, PS Bagdey, R R Tiwari, in 2006 in their study that "detecting oral cancer in early stages, when these are amendable to single modality therapies, offers the best chance of long term survival".[2]

The most commonly encountered & accepted precancerous lesions in the oral cavity are leukoplakia and erythroplakia. [4] With 5-25% Leukoplakia being premalignant lesions & 80% of erythroplakia harbouring malignancy. [5,6] The step towards prevention is early detection of malignancy.

Materials & Methods
A total number of one hundred patients spanning in an age group of 21 to 70 years were included in the study. A hospital based cross-sectional & interventional study was carried out after taking approval from the institutional ethical committee. Out of one hundred patients 70 were male & 30 were females. Each patient in the study was enrolled after a proper informed & written consent with inclusion criteria being predisposed patients presenting with pre malignant lesions in the oral cavity diagnosed clinically by the authors. Those excluded were established cases of malignancy, patients with dentures & patients with pigmented lesions. We have used Vizilite plustm as it contains both vizilitetm chemical light source and T-bluetm (toluidine blue dye for staining).

After doing a thorough clinical examination & notifying the lesions, Patients were given 1% acetic acid rinse (vizilitetm rinse) 30ml solution for 1 minute followed by an examination by chemiluminescent illumination (vizilitetm light stick). Vizilitetm rinse is again applied over the lesion & it is stained by T-blue (toluidine blue dye) and results are notified. Again vizilitetm rinse is applied over the stained lesion to remove the toluidine blue dye. Patient is asked to rinse oral cavity by water to remove the excess toluidine blue.[7, 8] Biopsy was taken from the identified lesions and biopsy results were notified. The data was then subjected to statistical analysis.

Results
The age group in our study spanned from 21 to 70 years, with highest incidence in the age group of 41-50 years age group. Tobacco chewing (in any form) was the most common addiction either alone or concomitant with other addictions with 65% patients addicted to it. Buccal mucosa was the commonest site of presentation of these lesions with 62% patients presenting with the lesions over this site.

The overall sensitivity and specificity of chemiluminescence in detecting oral precancers (dysplasia, carcinoma in situ & malignancy) was 58.06% & 71.05% (Table 1).

Chemiluminescence	Biopsy		Total
	Positive	Negative	
Positive	36	11	47
Negative	26	27	53
Total	62	38	100

Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
58.06%	71.05%	76.60%	50.94%

Table 1. Sensitivity & specificity of chemiluminescence

With 27 true negative, 36 true positive, 26 false negative, and 11false positive results and Kappa Coefficient of 0.271.

The results for toluidine blue staining using T-Bluetm (Table 2) are With 31True negative, 54 true positive, 8 false negative, and 7 false positive and Kappa coefficient of 0.680.

T blue	Biopsy		Total
	Positive	Negative	
Positive	54	7	61
Negative	8	31	39
Total	62	38	100

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Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
87.10%	81.58%	88.52%	79.49%

Table 2. Sensitivity and specificity of T-blue

Discussion

It is a well known fact that scalpel biopsy and subsequent histological examination is the cornerstone for diagnosing premalignant & malignant oral lesions, but an oral biopsy is invasive and involves both psychological implications for the patients as well as technical difficulties for the health practioner. Like in cervical cancers where non invasive screening methods predominate the scene nothing much has been done for oral cancer screening using non invasive methods. Though we know the stigmata associated with oral cancers.

It has been stated that low intensity multichromatic light is differently absorbed and reflected from the tissues of varying densities. [9] The vizilite™ uses the same principle as it imparts multichromatic low intensity light with spectral wavelengths in between 430-580 nm which produces a visible blue light. [8] Gynaecologists have long been aware of the ability of acetic acid to enhance regions of thickened surface keratin of uterine cervix. In the oral cavity, likewise, it makes the keratin whiter & more visible.

The vizilite™ light stick takes advantage of this property of acetic acid and adds blue light to even further enhance keratin detection as the lesions appear "aceto white" in a blue background of normal epithelium (Fig 1a,b).[7, 8] This light is obtained by fracturing the two capsule system of vizilite™ light stick and mixing the contents.

Fig 1, a. With out chemiluminescence
Fig 1,b. Positive Chemiluminescence

Staining in our study was done by using toluidine blue (T-Blue ™). It is an acidophilic dye that selectively stains acidic components such as DNA and RNA. In a dysplastic or malignant lesion there is high turnover of cells with high amount of nuclear acids, besides this intercellular canaliculi are much larger in dysplastic and malignant cells resulting in staining and intensive penetration of dye in dysplastic and malignant tissues. A dark blue stain is considered as positive (Fig 2) and if there is no colour absorbed by the lesion it is considered as negative. [10]

Fig 2 Positive Toluidine Blue stain.

In our study, chemiluminescence and staining were compared to the gold standard of biopsy. We found that the sensitivity and specificity of toluidine blue (table2) is high than that of chemiluminescence (table1), with a high diagnostic accuracy than that of chemiluminescence. Moreover toluidine blue has low false positives and false negatives (table 2) than that of chemiluminescence (table1).

There have been studies using the same concept by Ravi Mehrotra; Mamta Singh; Shaji Thomas [11], and by Navneet Sharma, Mubeen [8], but the results of these studies are mixed and every one insists on further evaluation of these methods.

Lauren L. Patton; Joel B. Epstein.[12] and A. Ross Kerr, Lingen MW et al [13] in their independent review of various adjuncts in oral cancer screening have mentioned that "the main problematic issues associated with these studies

are their mixed results which necessitates further studies to establish the role of these adjuncts in oral pre cancer screening."

Further though study by Navneet Sharma, Mubeen [8] have proven the cost effectiveness of toluidine blue when they have used it separately, the same cost effectiveness was not there in our study using Vizilite plus™.

Conclusion

From our study we have concluded that chemiluminescence is not superior to Toluidine blue in detecting oral precancers. Toluidine blue has a higher diagnostic accuracy and can be used as a diagnostic adjunct in detecting oral precancers and has a potential to be used as a screening tool in population at risk for oral cancers.

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