Chemiluminescent Light: Role in Early Detection of Cancer

Sarfaraz Singh Padda, Yashmeet Kaur, Raman Narang, Bhawandeep Kaur, Pinakapani Ramakrishna

ABSTRACT

Aim and objective: This clinical study was undertaken to evaluate the use of chemiluminescent light in detection of dysplastic areas in oral premalignant lesions.

Materials and methods: Thirty-six patients were voluntarily included in the study, having a clinical diagnosis of oral squamous cell carcinoma (OSCC) (7) or having precancerous lesions or conditions like leukoplakia (11), lichen planus (LP) (9) and OSMF (9) were included in the study. All the selected patients having suspected lesions were initially screened with ViziLite followed by TB staining. The findings were respectively recorded in patient's performa. Histopathological presence or absence of dysplasia was taken as gold standard, to calculate and compare sensitivity, specificity, positive predictive value and negative predictive value of ViziLite and toluidine blue (TB).

Results: TB and ViziLite both gave 100% sensitivity, however specificity of TB (88.46%) was much higher than ViziLite (33.33%). Similarly both TB and ViziLite both gave 100% (NPV), and however (PPV) of toluidine blue (75%) was much higher than ViziLite (33.33%).

Conclusion: ViziLite just enhances already existing whitish lesion making its visualization easy and help us to delineate the margins more precisely but doesn't guide us much in selection of the most characteristic site for biopsy within the already existing lesion.

Keywords: Chemiluminescent, ViziLite, Premalignant lesion, Premalignant condition.


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Conflict of interest: None declared

INTRODUCTION

Cancer of the oral cavity is the sixth most common malignancy reported worldwide, and it has one of the highest mortality rates among all the cancers.1 In India oral cancer is the most prevalent cancer in men. It makes 40% of all the cancers in the country.2 The International Agency for Research on Cancer (IARC) and the World Health Organization (WHO) have recently stressed that we can reduce a third of a predicted 15 million cancer cases in the future and more effectively manage another third by planning effective cancer control and screening strategies.3,4

Moreover the literature of comparison of ViziLite with toluidine blue (TB), the oldest, cheapest and most widely inflammatory disorders of the oral mucosa such as lichen planus (LP) and oral submucous fibrosis (OSMF), which have been associated with an increased risk of OSCC development.10-13 It is believed that identification and monitoring of these premalignant lesions and conditions will allow clinicians to detect and treat the early intraepithelial stages of oral carcinogenesis, for example mild, moderate or severe dysplasia and carcinoma in situ, all of which generally precede the development of invasive OSCC.14 The prognostic implications of diagnosis and treatment of these early intraepithelial stages of oral carcinogenesis are highly significant due to high survival rates of early OSCC.

The WHO has clearly identified prevention and early detection as major objectives in the control of the oral cancer burden worldwide. Presently, screening of oral cancer and its preinvasive intraepithelial stages, as well as its early detection, is still largely based on visual examination of the mouth. There is strong available evidence to suggest that visual inspection of the oral mucosa is effective in reducing mortality from oral cancer in individuals exposed to risk factors. Simple visual examination, however, is well known to be limited by subjective interpretation and by the potential, albeit rare, occurrence of dysplasia and early OSCC within areas of normal-looking oral mucosa. As a consequence, adjunctive techniques have been suggested to increase the ability to differentiate between benign abnormalities and dysplastic/malignant changes as well as to identify areas of dysplasia/early OSCC that are not visible to naked eye.

In 2002, ViziLite (Zila Pharmaceuticals, Phoenix, AZ) became the first FDA-approved adjunct technology to conventional head and neck examination for improving visualization of early lesions. In June 2004, ViziLite was given a dental reimbursement code by code revision committee of the ADA. The ViziLite system involves an oral rinse with 1% acetic acid solution for 1 minute which slightly desiccates the oral mucosa. A diffuse chemiluminescent blue/white light with an average wavelength of 490 to 510 nm is then activated and used to examine oral tissues. Normal cells absorb the light and appear blue, whereas abnormal cells having a higher nuclear/cytoplasmic ratio reflect light and appear more acetowhite, with brighter, sharper, more distinct margins.15

The literature reporting the efficacy of ViziLite in early detection of oral premalignant lesions is very limited. Moreover the literature of comparison of ViziLite with toluidine blue (TB), the oldest, cheapest and most widely
used screening method of oral premalignant lesions is even more limited.

This clinical study was undertaken to evaluate the use of chemiluminescent light in detection of dysplastic areas in oral premalignant lesions. To compare the efficacy of two diagnostic tools, i.e. chemiluminescent light and toluidine blue in detection of dysplastic areas in oral premalignant lesions.

**MATERIALS AND METHODS**

Thirty-six patients were voluntarily included in the study, having a clinical diagnosis of OSCC (7) or having precancerous lesions or conditions like leukoplakia (11), LP (9) and OSMF (9) were included in the study. Patients having lesions on the dorsum of the tongue or having erythematous area within the lesion from an evident source of irritation were excluded from the study.

All the selected patients having suspected lesions were initially screened with ViziLite followed by TB staining. The findings were respectively recorded in patient’s performa. Histopathological presence or absence of dysplasia was taken as gold standard, to calculate and compare sensitivity, specificity, positive predictive value and negative predictive value of ViziLite and TB.

- **Screening with ViziLite:** Patients were made to rinse with 1% solution of acetic acid (present in the packing) for one-minute. Capsule of ViziLite was activated by bending and breaking inner glass vial so that chemicals react and produce a bluish-white light. The intensity of ambient light was dimmed and lesion was examined under this diffuse bluish-white chemiluminescent light. Areas appearing acetowhite (white) under this diffuse bluish-white chemiluminescent light were considered ViziLite positive; areas appearing bluish under this chemiluminescent light were considered ViziLite negative.16 All the findings were recorded and photographed.

- **Toluidine blue staining:** Patients were made to rinse with 1% solution of acetic acid having extensive involvement of oral cavity in LP and OSMF while in patients of leukoplakia and OSCC having localized lesions 1% acetic acid was just topically applied on the lesion with the help of applicators for 1 minute. Patients were then made to rinse with 1% solution of TB or 1% solution of acetic acid was just topically applied on the lesion with the help of applicators for 1 minute. Patients were made to rinse with 1% solution of acetic acid or 1% solution of acetic acid was applied locally on the area of the lesion. Areas appearing blue because of retention of dye were considered as toluidine positive. In case multiple areas retained the dye then the area having darkest hue of blue was considered. All the findings were recorded and photographed.

- **Selection of site of biopsy:** Patients in whom ViziLite was positive and TB was negative, biopsy was taken from the ViziLite positive area. Patients in whom ViziLite was negative and TB was positive, biopsy was taken from the TB positive area. Lesions which were positive for both ViziLite and TB, and both the areas coincided, and then single biopsy was taken from that area. In case both the areas did not coincide then biopsies were done from both the areas. In case lesions were negative for ViziLite and TB then biopsy was taken from area which clinically looked like having some dysplastic area, e.g. erythematous, erosive or indurated area. All the biopsied tissues were subjected to histopathological examination to look for features of dysplasia.

**RESULTS**

Thirty-six patients (25 male and 11 female), with age ranging from 27 years to 72 years (mean age 51 years) formed the study group. Of 36 patients, 27 patients where ViziLite positive, while 9 where ViziLite negative (Table 1). While on staining with TB, 13 where TB positive while 23 where TB negative (Table 1). Histopathological examination of tissue taken from site determined by the criteria mentioned above revealed dysplasia in only 9 patients. Lesion wise detail is given in Table 1. All the 9 patients in whom histopathological examination showed dysplasia, TB was also positive, hence 4 patients gave false positive with TB. Of 27 patients who were ViziLite positive, only 9 showed dysplasia in histological examination, hence 18 patients gave false positive with ViziLite (Table 2). All the 13 patients who were TB positive, also showed positive result with ViziLite. False-positive with ViziLite (18) were much higher as compared to TB (4). TB and ViziLite both gave 100% sensitivity, however specificity of TB (88.46%) was much higher than ViziLite (33.33%). Similarly both TB and ViziLite both gave 100% NPV, and however PPV of toluidine blue (75%) was much higher than ViziLite (33.33%) (Table 3).

**DISCUSSION**

In our study the sensitivity and negative predictive value (NPV) of ViziLite is equivalent to that of TB (100%). However, specificity and positive predictive value (PPV) of TB is quite high, i.e. 88 and 75% respectively as compared to specificity and PPV of ViziLite 33%. S Ram et al in 200516 also had reported similar low specificity for ViziLite. Low specificity and PPV of ViziLite can be attributed to high false-positive results given by ViziLite (18) as compared to TB (4). Leukoplakia and lichen planus clinically appear as whitish keratotic areas in oral cavity. Their appearance...
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Table 1: Lesion-wise distribution of viziLite and toluidine blue tests

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No. of cases</th>
<th>ViziLite</th>
<th>Toluidine blue</th>
<th>Biopsy (dysplasia)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Leukoplakia</td>
<td>11</td>
<td>11</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>LP</td>
<td>9</td>
<td>9</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>OSMF</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>OSCC</td>
<td>7</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>27</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 2: Comparative result of ViziLite and toluidine blue tests

<table>
<thead>
<tr>
<th></th>
<th>True positive</th>
<th>True negative</th>
<th>False positive</th>
<th>False negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>ViziLite</td>
<td>9</td>
<td>9</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Toluidine blue</td>
<td>9</td>
<td>23</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3: Sensitivity and specificity of ViziLite and toluidine blue tests

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ViziLite</td>
<td>100</td>
<td>33.33</td>
<td>33.33</td>
<td>100</td>
</tr>
<tr>
<td>Toluidine blue</td>
<td>100</td>
<td>88.46</td>
<td>75.00</td>
<td>100</td>
</tr>
</tbody>
</table>

Fig. 1: Enhancement of LP lesion under ViziLite

Fig. 2: Illustrates difficulty in identifying acetowhite area in a already existing leukoplakia

Fig. 3: Visualization of OSMF under ViziLite

ViziLite produces a distinct and disturbing glare (Fig. 4) which mimics acetowhite area which produces a false-positive result. However, these glares can be differentiated from a true acetowhite area by changing the position/angle of the ViziLite which results in the change of position of glare whereas in a true acetowhite areas position does not alter. Oh and Laskin also reported of similar distracting highlights of oral mucosa which made visualization under ViziLite more difficult.

ViziLite just enhances any whitish patch or lesion in the oral cavity irrespective of the nature of the lesion which is enhanced when visualized under ViziLite (Fig. 1). However, visualization of acetowhite area with in this whitish keratotic patch cannot be detected (Fig. 2), which causes high false-positive results. Similar findings had been reported by Kerr AR in 2006.

This is probably the first clinical study where OSMF has been visualized under this chemiluminescent light. The whitish blanched mucosa of OSMF makes it difficult to identify any acetowhite area under ViziLite (Fig. 3). Thus, visualization of OSMF under ViziLite does not offer any advantage as compared to visualization under the normal incandescent light.

In identification of frank OSCC, the ViziLite was found to be as effective as TB. Visualization of oral cavity under...
might be keratotic, inflammatory, physiological variant, malignant or potentially malignant oral mucosal white lesion. Similar findings have been cited by Farah et al in 2006.19

CONCLUSION

ViziLite just enhances already existing whitish lesion making its visualization easy and help us to delineate the margins more precisely but does not guide us much in selection of the most characteristic site for biopsy within the already existing lesion. On the contrary, the TB gives a more precise localized area which retains the dye and helps us in selecting the most characteristic site for biopsy in a much better way.

REFERENCES


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Fig. 4: Glare produced by ViziLite