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Comparative Evaluation of VEL scope and Methylene blue in the Diagnosis of Oral Potentially Malignant Disorders

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Abstract

Oral potentially malignant disorders (OPMDs) such as leukoplakia, oral lichen planus, and oral submucous fibrosis are important precursors to oral cancer, making early diagnosis essential. Conventional oral examination remains the primary diagnostic method, but adjunctive tools such as VELscope and methylene blue staining have been developed to enhance detection of dysplastic changes. This prospective study included 30 patients aged 18–60 years clinically diagnosed with OPMDs. All patients underwent VELscope examination followed by methylene blue staining, and findings were compared with biopsy results, the gold standard. The study revealed an 83.3% prevalence of dysplastic lesions. VELscope demonstrated 90.90% sensitivity and 37.5% specificity, while methylene blue staining showed 59.09% sensitivity and 12.57% specificity. The positive predictive value was 80% for VELscope and 65% for methylene blue staining, whereas the negative predictive value was 60% and 10% respectively. These findings suggest that VELscope is a simple, chairside, light-based screening tool with higher diagnostic accuracy compared to methylene blue staining. However, biopsy remains the definitive method for confirmation and grading of dysplasia.

Key words : OPMDS, VELscope, Methylene blue, Histopathology.

Oral cancer is the sixth most common cancer globally, accounting for over 90% of all malignant neoplasms of the oral cavity[25]. Oral potentially malignant disorders (OPMDs) such as leukoplakia, erythroplakia, oral lichen planus, and oral submucous fibrosis are well-

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recognized precursors, with malignant transformation rates reported between 1.4% and 36.2% [2,17]. Considering the high morbidity and mortality associated with oral squamous cell carcinoma (OSCC), early detection of OPMDs is critical for improving survival, reducing treatment burden, preserving function, and lowering healthcare costs[22].

Conventional oral examination through inspection and palpation remains the primary screening method, but subtle or subclinical lesions are often missed, and distinguishing between benign, premalignant, and malignant changes may be difficult[5]. Although histopathological biopsy is the gold standard, it is invasive, sometimes unacceptable to patients, and requires careful site selection for diagnostic accuracy[12].

To address these limitations, non-invasive adjunctive diagnostic aids have been introduced. Vital staining methods such as methylene blue have long been used due to their simplicity, affordability, and ability to enhance lesion visibility and guide biopsy. (Figure 1.B) However, disadvantages include possible allergic reactions, staining discomfort, and variable patient acceptance[4,16].

Light-based detection systems such as VELscope, Vizilite, and VELscan have more recently emerged as promising alternatives. VELscope, a handheld autofluorescence device emitting blue light (400–460 nm) (Figure 1.B) excites natural fluorophores in the oral mucosa, with normal tissue appearing pale green and abnormal tissue dark due to loss of fluorescence[6,9]. It enables real-time, chairside evaluation without discomfort, making it a practical adjunct. Despite limitations in specificity and false-positive rates, integration of VELscope into clinical practice may aid early detection of high-risk lesions, thereby improving patient outcomes through timely intervention[19].

Aim :

To compare the reliability of Velscope and vital tissue staining - Methylene blue staining as a screening tool in the detection of dysplasia in Oral leukoplakia, Oral lichen planus, Oral sub mucous fibrosis with histopathological confirmation.

Objectives :

1) To assess the sensitivity and specificity of velscope in the detection of dysplasia in oral leukoplakia, oral lichen planus, Oral Sub Mucous Fibrosis (OPMDs) and to compare with histopathology.

2) To assess the sensitivity and specificity of vital tissue staining like methylene blue staining in the detection of dysplasia in oral leukoplakia, oral lichen planus, Oral Sub Mucous Fibrosis and to compare with histopathology.

3) To compare the efficacy of velscope and (methylene blue in the detection of dysplasia in oral leukoplakia, oral lichen planus, Oral Sub Mucous Fibrosis.

This prospective comparative study was conducted in the Department of Oral Medicine and Radiology for one year after institutional ethics approval. Sample size was calculated using G Power 3.1.9.4 ($\alpha = 0.05$, effect size = 0.67), yielding a study power of 0.88 for 30 subjects. Patients aged 18–60

years, clinically diagnosed with oral leukoplakia, oral lichen planus, or oral submucous fibrosis, were included. Exclusion criteria were malignancy, previous or ongoing treatment, recurrence, and systemic conditions contraindicating biopsy. Informed consent was obtained from all participants.

Each patient underwent clinical photography, followed by VELscope examination. Normal mucosa appeared green, while dark or brownish fluorescence indicated possible dysplasia. Thereafter, 1% methylene blue staining was applied, with dark blue uptake considered positive [Figures 2,3,4]. Biopsy sites were selected based on VELscope or staining findings, or clinical judgment when both were negative. Incisional biopsies were performed under aseptic conditions, and histopathology served as the gold standard for dysplasia detection.

Statistical analysis :

The effectiveness of these chairside diagnostic tests were compared with the histopathology and analysed statistically using IBM SPSS Statistics 26 (IBM, Chicago). Chi-square test and the Receiver Operating Characteristic (ROC) curve were plotted to assess the sensitivity and specificity of the above-mentioned diagnostic tests, allowing for a comprehensive assessment of their performance.

Sensitivity = True Positives / (True Positives + False Negatives)

• Specificity = True Negatives / (True Negatives + False Positives)

• Positive Predictive Value (PPV) = True Positives / (True Positives + False Positives)

• Negative Predictive Value (NPV) = True Negatives / (True Negatives + False Negatives)

This prospective *in vivo* clinical study included 30 subjects aged 18–60 years, comprising 20 males and 10 females clinically diagnosed with oral potentially malignant lesions. Among them, 10 cases each were identified as oral leukoplakia, oral lichen planus, and oral submucous fibrosis. Histopathological evaluation revealed dysplasia in 25 out of 30 cases. The overall prevalence of dysplastic changes was 83.3%. Velscope correctly detected 20 OPMDs as true positive and 3 as true negative with a sensitivity of 90.90% and specificity of 37.5% [Table 1-6].

Five cases in which 3 of Oral leukolplakia, 2 of lichen planus were incorrectly daignosed as dysplastic lesion on Velscope

Thus the sensitivity for VELscope was found to be 90.90% & specificity of 37.5% with a positive predictive value of 80% and a negative predictive vale of 60% [Table 1-6]. Methylene blue stain detected 13 Oral potentially malignant lesions as true positive, and 1 as true negative, 9 lesions were incorrectly diagnosed as non dysplastic and 7 lesions were incorrectly diagnosed as dysplastic on methylene blue staining.

Thus the sensitivity for methylene blue staining was found to be 59.09 % while the specificity was 12.5% with a positive predictive value of 65% and a negative predictive value of 10%.[Table 1-6].

VELscope demonstrated an AUC of 0.871, indicating excellent diagnostic accuracy. Methylene blue had a moderate AUC of 0.700, reflecting lower reliability.[Roc Curve 1,2]

Table-1. Distribution of oral submucous fibrosis cases by methylene blue staining and histopathology results

Oral submucous fibrosis		Histopathology		Total
		Positive	Negative	
Methylene blue stainig	Positive	4	0	4
	Negative	6	0	6

Table-2. Distribution of oral submucous fibrosis cases by VELscope and Histopathology results

Oral submucous fibrosis		Histopathology		Total
		Positive	Negative	
Velscope	Positive	10	0	10
	Negative	0	0	0

Table-3. Distribution of Oral leukoplakia cases by Methylene blue and Histopathology results

Oral leukoplakia		Histopathology		Total
		Positive	Negative	
Methylene blue stainig	Positive	4	4	10
	Negative	1	1	10

Table-4 Distribution of oral leukoplakia cases by VELscope and Histopathology results

Oral leukoplakia		Histopathology		Total
		Positive	Negative	
Vel scope	Positive	4	3	7
	Negative	1	2	3

Table-5 Distribution of oral lichen planus cases by Methylene blue and Histopathology results

Oral lichen Planus		Histopathology		Total
		Positive	Negative	
Methylene blue stainig	Positive	5	3	8
	Negative	2	0	2

Table-6. Distribution of oral lichen planus cases by VELscope and Histopathology results

Oral lichen Planus		Histopathology		Total
		Positive	Negative	
Vel scope	Positive	6	2	8
	Negative	1	1	2

This emphasizes VELscope's clinical utility for early dysplasia detection, consistent with reports by Farah *et al*.[6] and Lane *et al*.[11]

Thus the overall diagnostic accuracy of Methylene blue staining for the early diagnosis of OPMDs was found to be 60% according to our study
The results were statistically significant ($P < 0.001$)

Oral potentially malignant disorders (OPMDs) represent a diverse group of mucosal lesions with a recognized risk of malignant transformation, most often into oral squamous cell carcinoma (OSCC)[24]. Early identification of dysplastic changes is essential for timely intervention and improved prognosis [23]. While conventional oral examination (COE) forms the foundation of clinical assessment, its sensitivity in detecting early or subclinical epithelial changes is limited[15]. To overcome this, adjunctive diagnostic methods have been developed. Vital stains such as methylene blue and toluidine blue have been widely employed because of their ability to bind preferentially to dysplastic tissue[2]. However, their utility is constrained by false positives, particularly in the presence of inflammation or keratinization[18].

Light-based optical devices, such as VELscope, have recently gained attention as non-invasive diagnostic adjuncts that allow real-time visualization of mucosal changes based on tissue autofluorescence[11]. VELscope enhances detection of epithelial alterations that are not evident under white light, thereby improving sensitivity and guiding biopsy site selection[10]. The present study compared the diagnostic accuracy of VELscope and methylene blue staining in detecting dysplasia in OPMDs, with histopathology serving as the gold standard.

In oral submucous fibrosis (OSMF), VELscope achieved 100% sensitivity and specificity, detecting all histopathologically confirmed dysplastic lesions. In contrast, methylene blue yielded only 40% sensitivity, although specificity remained 100%. This suggests that VELscope is superior in identifying subepithelial changes within fibrotic tissues, which are poorly visualized by surface staining methods. These findings are consistent with Hanken *et al.*[8] and Rana *et al*.[21], who also highlighted the higher diagnostic utility of VELscope in high-risk lesions. The poor performance of methylene blue in OSMF corroborates previous reports on its limited uptake in dense, fibrotic, or keratinized mucosa[14].

For oral leukoplakia, VELscope showed 80% sensitivity and 40% specificity, while methylene blue achieved 80% sensitivity and 50% specificity. Both tools identified the majority of dysplastic lesions but generated

false positives, particularly in benign keratotic patches. Mehrotra *et al*.[14] reported similar findings, attributing these false positives to hyperkeratosis and inflammation mimicking dysplasia. Epstein *et al*.[3] also emphasized the tendency of autofluorescence devices to over-detect, given that loss of fluorescence can occur in non-dysplastic inflammatory conditions.

In oral lichen planus (OLP), VELscope demonstrated 85.7% sensitivity but low specificity (33.3%), while methylene blue showed 71.4% sensitivity with 0% specificity. Both modalities tended to over-diagnose due to inflammation-related fluorescence changes or nonspecific dye uptake. Awan *et al*.[1] similarly noted VELscope's misidentification of inflammatory lesions, while Martin *et al*.[13] documented poor staining accuracy of methylene blue in ulcerated tissues.

Receiver operating characteristic (ROC) analysis further reinforced these observations. VELscope demonstrated an area under the curve (AUC) of 0.871, indicating excellent diagnostic performance, whereas methylene blue showed an AUC of 0.700, reflecting only moderate accuracy. These findings align with Farah *et al*.[7], who reported similarly high AUC values for VELscope in detecting epithelial dysplasia, and with other studies noting methylene blue's inconsistent specificity in keratotic or inflamed lesions[20]. Overall, VELscope outperformed methylene blue in sensitivity across all lesion types and also showed higher specificity in leukoplakia and OLP. Positive predictive value (PPV) was greater for VELscope (80%) than methylene blue (65%), while negative predictive value (NPV) was significantly higher for VELscope (60% vs 10%). These results suggest that VELscope is more reliable for both confirming and ruling out disease when compared with methylene blue.

Despite these advantages, VELscope demonstrated relatively low specificity, leading to potential false positives. Hence, while it may serve as an effective adjunctive tool for early detection and biopsy site selection, it cannot replace histopathology, which remains the definitive diagnostic standard.

As the study was conducted with a relatively low sample and short period of follow-up, further studies are needed with a larger sample size and longer duration for more accurate results to reduce the bias, if any exists.

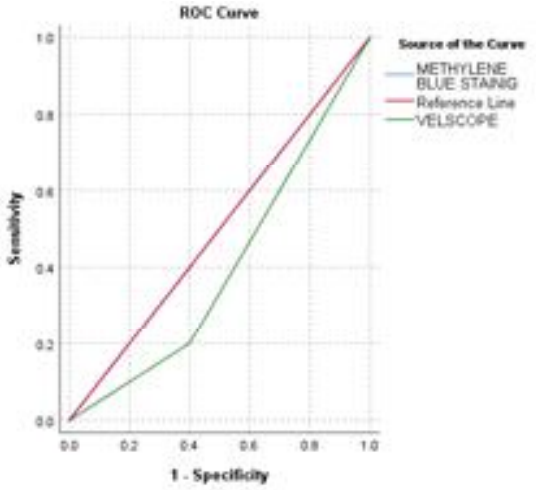
This study found that VELscope showed superior diagnostic performance over methylene blue in detecting dysplastic changes in OPMDs, particularly in leukoplakia and oral submucous fibrosis. It offered higher sensitivity, better accuracy, ease of use, patient acceptance, and digital documentation. However, histopathology and clinical evaluation remain the gold standard for OPMD management.

The ROC (Receiver Operating Characteristic) curve illustrates the diagnostic ability of methylene blue staining (blue line) and VELscope (green line) for detecting oral leukoplakia, with the reference line (red) representing a test with no discriminatory power Area under Curve (AUC = 0.5).

X-axis = 1 - Specificity (False Positive Rate)

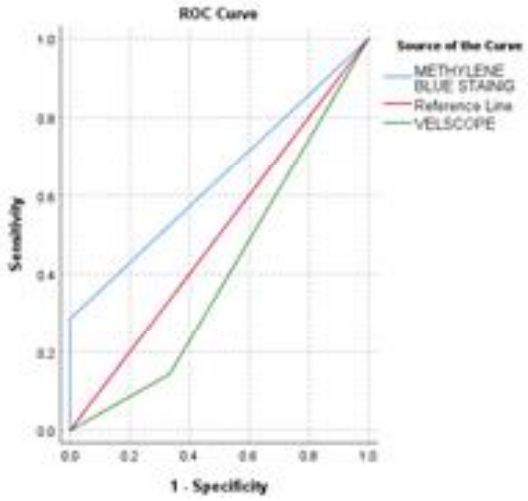
Y-axis = Sensitivity (True Positive Rate)

The red diagonal line is the reference line (a test with no discriminative ability) (Roc Curve 1).



Roc Curve 2 :

The ROC curve 2 illustrates the diagnostic ability of methylene blue staining (blue line) and VELscope (green line) for detecting oral lichen planus (OLP), with the reference line (red) representing a test with no discriminatory power (AUC = 0.5).



Figures :

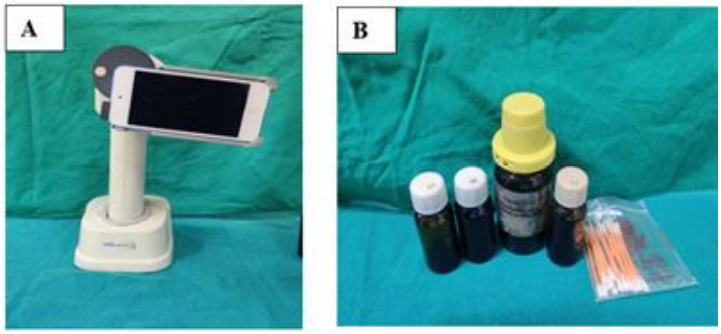
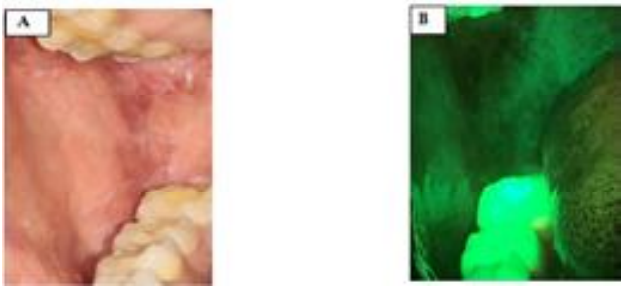


FIGURE-1 - VELscope (1.A) ,Vital stains (1.B)



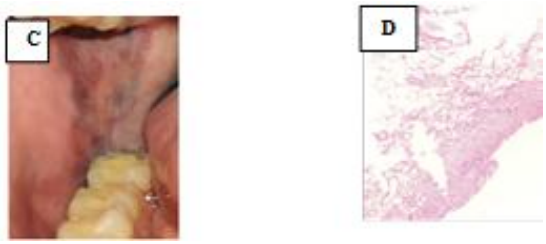


FIGURE-2 – Lichen planus (2.A) under velscope (2.B), stained with vital stains Methylene blue (2.C), Histopathology Image(2.D)

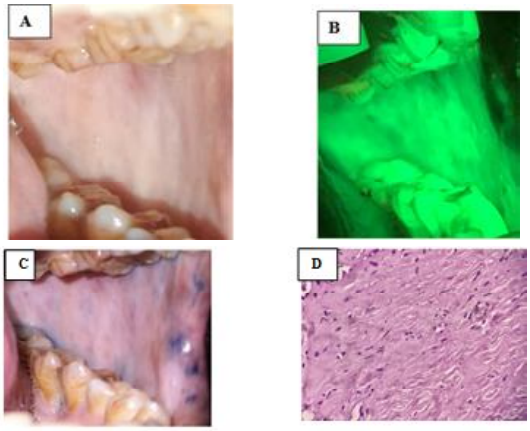


FIGURE-3 - OSMF (3.A) under velscope (3.B), stained with vital stains Methylene blue (4.C), Histopathology Image (4.D)

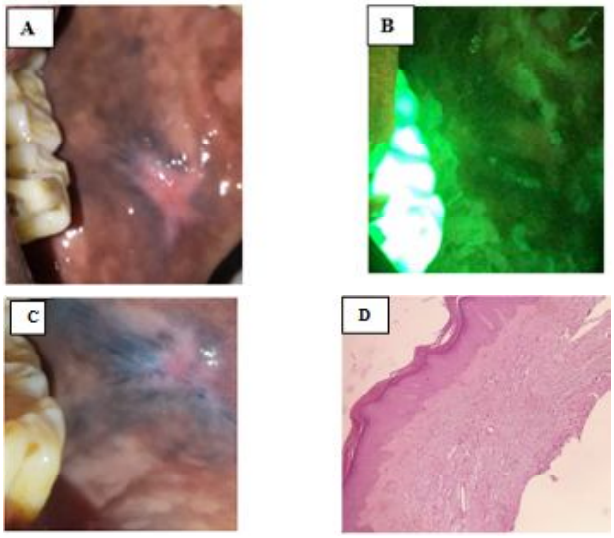


FIGURE-4 – Leukoplakia (4.A) under velscope (4.B), stained with vital stains Methylene blue (4.C), Histopathology Image (4.D)

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