Original Article - Evaluative Study

# Lugol's iodine identifies dysplastic tissue in precancerous lesions: A clinical trial

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## ABSTRACT

**Introduction:** Intraepithelial dysplasia, or "invisible" precancerous lesions, provides a challenge for visualization to the surgical team. The prognostic relevance of dysplasia and carcinoma in situ at surgical margins is well documented. **Materials and Methods:** We evaluated the use of Lugol's iodine in visualizing the surgical margins of dysplastic tissue by an observational study of 100 patients having oral precancerous lesions between June 2013 and March 2016. **Conclusion:** Lugol's iodine is a simple, inexpensive, and apparently effective means of diagnosing and visualizing the surgical margins of the dysplastic tissue in oral precancerous lesions.

**Keywords:** Head and neck cancer, Lugol's iodine, oral dysplasia, oral precancerous lesions

## INTRODUCTION

Intraepithelial dysplasia, or "invisible" precancerous lesions, provides a challenge for visualization to the surgical team. The prognostic relevance of dysplasia is well documented.[1] Distinguishing between normal and dysplastic mucosa is a very difficult job, and often the undetected presence of such a lesion leads to its delayed treatment and exacerbation [Figures 1 and 2]. We describe staining technique to aid the process of diagnosis and visualization by describing its effectiveness in 100 clinical cases. Lugol's iodine was selected as the staining agent of choice because of its availability, ease of use, cost-effectiveness and widespread use by endoscopists in the identification of intraepithelial neoplasia in the esophagus.[2,3] The mucosal surfaces of the oral cavity are histopathologically similar to the esophagus and therefore it is expected that Lugol's iodine would be equally beneficial in the identification of intraepithelial neoplasia of the oral cavity.

## PATIENTS AND METHODS

A total of 100 patients with white patches in different sites of the oral mucosa were included in the clinical trial. All the patients included in the study were with a mean age of 45 ± 10 years. To determine the extent of the precancerous lesion, sites that could possibly show epithelial dysplasia adjacent to the lesion were irrigated with Lugol's iodine solution. The technique for topical application of an aqueous solution of Lugol's iodine is shown in Table 1.

A large area of the oral cavity is covered by parakeratinized stratified squamous epithelium. Cells of the intermediate and superficial layers contain glycogen in their cytoplasm.[4] Whereas, dysplastic and invasive cancer cells contain little or no glycogen. Iodine is glycophilic, and so the application of Lugol's iodine solution results in uptake of iodine in normal glycogen-containing epithelium and stains it mahogany brown



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or black [Figures 2 and 4]. Areas of dysplasia and invasive cancer do not take up iodine (as they lack glycogen) and appear mustard-yellow or saffron-colored [Figures 3 and 4].[5]

The criteria for clinical diagnosis were (1) homogeneous leukoplakia: A predominantly white, uniform, and flat lesion, not able to be scraped, with a smooth, wrinkled, or corrugated surface that may exhibit shallow cracks;[6,7] (2) nonhomogeneous leukoplakia: A predominantly white or red and white lesion with an irregular, nodular, or exophytic surface;[6,7] (3) erythroplakia: A velvety red lesion with imprecise borders that could not be diagnosed as any other lesion;[6,7] (4) reticular lichen planus: A predominantly white lesion with intertwining lines or striae that confer a lacy or annular appearance;[7] (5) erosive/ulcerated lichen planus: A predominantly red, irregular erosion or ulceration associated with a reticular form, especially in the peripheral region of the lesion and with pseudomembranes covering the ulcerated areas;[7] and (6) superficial ulcerations suspicious of malignancy: Localized, superficial lesions without invasion or loss of mobility of neighboring chronic tissues that do not heal after local treatment.

**Table 1: Method of application of the Lugol's iodine staining technique**

| |
|---|
| Oral examination and annotation of location, size, clinical characteristics, and photographing of the lesion |
| Cleaning of the lesion with a cotton tip soaked in 10% $H_2O_2$ (for the elimination of saliva, food, or tissue remains) |
| Cleaning of lesion with water jet |
| Application of Lugol's iodine solution with cotton tip for 30 s |
| Photographing of lesion |

The study has been approved by the appropriate ethical committee of our institution in which it was performed, and subjects gave informed written consent to the work.

## RESULTS

A total of 100 cases clinically diagnosed with oral precancerous lesions were taken up for the study. Lugol's iodine was chosen as the material of choice for staining due to its low cost, wide availability, and ease of use. Lugol's iodine successfully stained the normal nondysplastic tissue around all the 100 precancerous lesions, forming a well-demarcated margin. The demarcated margins in all the 100 lesions were clinically appreciable. This enhanced clinical diagnosis and enabled us to measure the size of the dysplastic area more accurately. The clinical diagnosis of the oral lesions analyzed, and the results of staining are presented in Table 2.

## DISCUSSION

Precancerous (also referred to as "potentially malignant") oral lesions involve the skin lining of the mouth (known as the

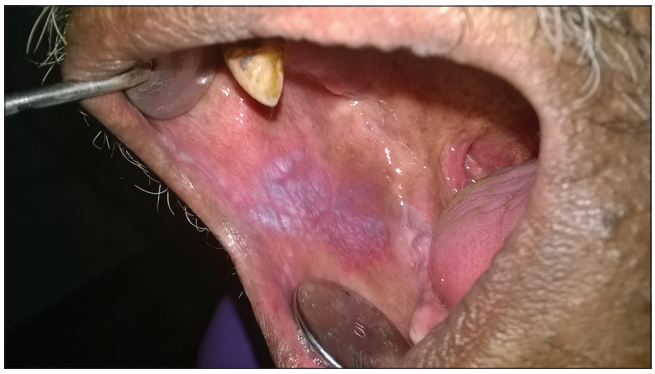

**Figure 1:** A precancerous lesion, histopathologically diagnosed as homogenous leukoplakia with ill-defined margins

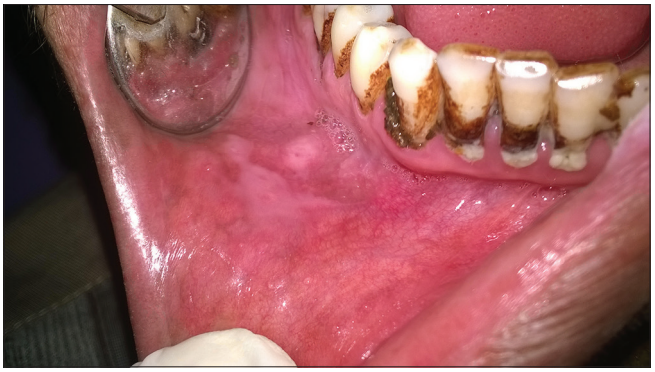

**Figure 2:** A precancerous lesion, histopathologically diagnosed as homogenous leukoplakia with ill-defined margins

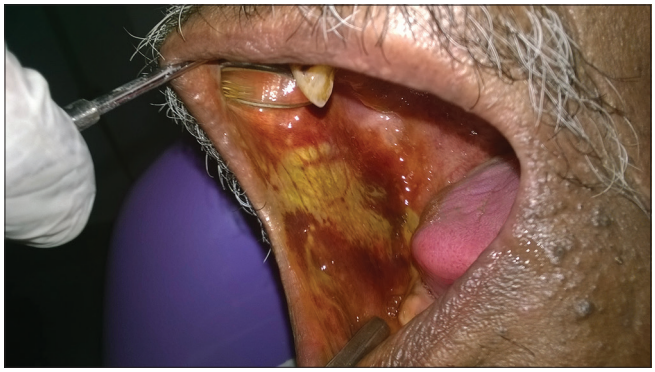

**Figure 3:** The same lesion after being stained with lugol's iodine solution. The margins of the lesion which appeared to be ill-defined become much more prominent after staining and hence assist the clinician to correctly estimate the size and extent of the lesion

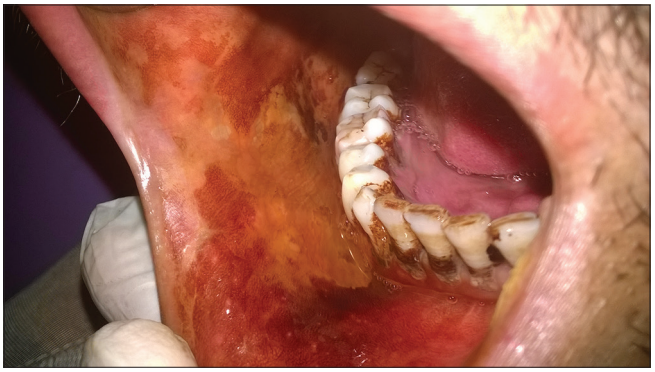

**Figure 4:** The same lesions after being stained with Lugol's iodine solution. The margins of the lesions which appeared to be ill-defined become much more prominent after staining and hence assist the clinician to correctly estimate the size and extent of the lesion

**Table 2: Clinical diagnosis of oral lesions and results of staining**

| Clinical diagnosis | Number of patients | Did Lugol's iodine demarcate the margins? | |
|---|---|---|---|
| | | Yes | No |
| Homogenous leukoplakia | 65 | Y | - |
| Nonhomogeneous leukoplakia | 15 | Y | - |
| Reticular lichen planus | 10 | Y | - |
| Superficial ulcerations | 10 | Y | - |
| Total (100 cases) | Result: Lugol's iodine demarcated the margins for all 100 cases | | |

epithelium) and may be at risk for transforming into oral cancer.[8] There is, however, a varied opinion to predict as to which lesions will transform and how long it will take. The frequency of dysplastic or malignant alterations in oral precancerous lesions has ranged from 15.6% to 39.2% in several studies.[8-12] Most of the earlier studies showed a risk of malignant transformation in the range of 3.6%–6.0%. However, several of the more recent studies have shown more alarming malignant transformation rates ranging from 8.9% to 17.5%.[13-15] Although the reason for these results is unclear, it may be due to a more restrictive definition of what is considered clinically a precancerous lesion and further underscores the seriousness of it.

The location of an oral precancerous lesion has a significant correlation with the frequency of finding dysplastic or malignant changes at biopsy. The same correlation stands true for the size and extent of the lesion. Therefore it becomes of detrimental importance to evaluate correctly the extent of these lesions. As proved in this study, Lugol's iodine can play a major role in demarcating the margins of the lesion thereby enabling the clinician to estimate the correct size and extent of the precancerous lesion leading to early diagnosis and better management of the patient.

Although most oral carcinomas have adjacent areas of epithelial dysplasia, some carcinomas may not evolve from epithelium with top-to-bottom dysplastic changes but rather arise from basilar keratinocytes. Silverman *et al*. monitored 257 patients with oral leukoplakia; 22 had a diagnosis of epithelial dysplasia, the remaining 235 had hyperkeratosis. Eight of the 22 (36.4%) with epithelial dysplasia developed carcinoma. The time from initial diagnosis of either epithelial dysplasia or hyperkeratosis to carcinoma ranged from 6 months to 39 years. In another study, reported by Lumerman *et al*., (15.9%) of 44 patients with oral epithelial dysplasia identified in a histopathological study developed carcinoma.[16,17] Mean time from biopsy to cancer diagnosis was 33.6 months. The estimated median time for this progression depends on the histopathologic severity of the epithelial dysplasia: 58 months for mild, 38 months for moderate, and 12 months for severe.[18]

## CONCLUSION

We can, therefore, conclude that Lugol's iodine can play a major role in demarcating the margins of the precancerous lesions, thereby enabling the clinician to estimate the correct size and extent of the precancerous lesion leading to early diagnosis and better management of the patient.

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### Conflicts of interest
There are no conflicts of interest.

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