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The scope and prospects of Lugol's Iodine vital staining in diagnosis of oral lesions

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Abstract

Lugol's iodine vital staining represents a cost-effective adjunctive diagnostic tool for detecting oral epithelial dysplasia and squamous cell carcinoma. This technique exploits the differential glycogen content between normal and dysplastic epithelium, enabling the visualization of lesion margins that may be clinically unremarkable. Current evidence demonstrates high sensitivity for malignancy detection and significant utility in surgical margin delineation, although the specificity remains moderate. This review examines the mechanistic basis, diagnostic performance, clinical applications, and future directions of Lugol's iodine staining in contemporary oral medicine practice.

Keywords: Lugol's iodine, vital staining, malignancy detection, oral cancer, surgical margin

Introduction

Oral potentially malignant disorders and oral squamous cell carcinoma continue to present diagnostic challenges, particularly in delineating the extent of dysplastic changes adjacent to clinically visible lesions. Early detection and accurate margin assessment are critical determinants of treatment outcomes and local recurrence rates [1]. Vital staining techniques, particularly those using Lugol's iodine solution, have emerged as valuable adjunctive tools that complement conventional clinical examinations. The principle underlying iodine staining relies on the glycophilic nature of iodine, which binds to intracellular glycogen abundant in normal stratified squamous epithelium. Dysplastic and neoplastic cells contain minimal or no glycogen due to altered cellular metabolism and loss of differentiation [2], rendering these areas unstained and readily distinguishable from the surrounding normal mucosa.

Biological Basis of Iodine Vital Staining

The diagnostic efficacy of Lugol's iodine stems from the fundamental differences in cellular metabolism and differentiation between normal and dysplastic oral epithelium. Iodine solution penetrates the normal epithelium to the parabasal layer, and the staining patterns correlate directly with glycogen distribution in the superficial layers [3]. Iodine-negative epithelium demonstrates significantly elevated expression of p53, Ki67, and glucose transporter 1 (GLUT1), which are markers associated with increased cellular proliferation and altered glycolytic metabolism [3]. This molecular foundation explains why dysplastic tissues fail to retain the characteristic mahogany-brown coloration of the normal mucosa. This technique provides a visual representation of metabolic and differentiation abnormalities that precede the morphological changes detectable by routine clinical examinations.

Diagnostic Performance and Clinical Validation

Multiple studies have evaluated the diagnostic accuracy of Lugol's iodine staining for oral lesions. In a prospective hospital-based study of 28 patients with suspicious oral lesions, Lugol's iodine staining achieved a clinical relevance level of 90.9% in detecting oral cancer and dysplasia, with histopathological confirmation of dysplasia or neoplasia in all clinically positive specimens [1]. When applied to floor-of-mouth screening in high-risk patients, iodine staining demonstrated 100% sensitivity and 59.6% specificity for detecting squamous cell carcinoma [4].

Comparative studies have assessed Lugol's iodine in combination with other diagnostic modalities, with chemiluminescence plus Lugol's iodine showing 91.7% sensitivity and 66.7% specificity for dysplasia detection in tobacco-associated lesions [5]. Double-staining protocols combining methylene blue with Lugol's iodine have demonstrated superior diagnostic accuracy compared to single-dye techniques, with sensitivity and specificity approaching 100% for dysplasia detection in oral leukoplakia [6].

Surgical Margin Assessment and Recurrence Prevention

Perhaps the most clinically significant application of Lugol's iodine lies in intraoperative margin assessment during surgical resection of oral malignancies. Studies involving 100 patients with oral precancerous lesions have demonstrated that Lugol's iodine successfully delineates well-defined margins around all lesions, enhancing clinical

diagnosis and enabling more accurate measurement of dysplastic areas [2]. A retrospective analysis comparing conventional surgery to iodine-guided resection revealed no local recurrence in the vital staining group versus seven of 25 patients in the conventional group, with five-year primary control rates of 100% and 75%, respectively [7].

The application of Lugol's staining during glossectomy for early tongue cancer in 93 patients resulted in negative surgical margins in 81 cases, with no local recurrence observed during follow-up [8]. A systematic review of intraoperative margin visualization techniques reported that iodine staining demonstrated negative predictive values ranging from 92% to 99%, with evidence suggesting a particular benefit in identifying mild-to-moderate dysplasia [9].

Comparative Effectiveness and Technical Considerations

Adjunctive diagnostic aids, including vital staining, autofluorescence, and chemiluminescence, serve complementary roles in early detection, with vital staining offering advantages in terms of cost-effectiveness and ease of application [10]. Comparative studies between fluorescence visualization and iodine staining for tongue cancer margins have shown that both techniques effectively delineate oral epithelial dysplasia adjacent to primary tumors, with iodine staining being the more accessible option [11].

The application technique significantly influenced diagnostic accuracy. Lugol’s solution concentrations ranging from 3% to 10% have been employed, with sequential staining protocols demonstrating enhanced margin delineation. The procedure involves topical application for 20-30 seconds followed by gentle rinsing, with unstained or lightly stained areas warranting biopsy or extended surgical margins.

Future Directions and Integration with Emerging Technologies

Future research priorities include large-scale randomized controlled trials comparing the diagnostic accuracy of iodine staining and narrow-band imaging, with an emphasis on discriminating between different grades of dysplasia and invasive carcinoma [9]. The integration of vital staining with advanced imaging modalities, molecular diagnostics, and artificial intelligence-assisted lesion characterization represents a promising avenue for enhancing the early detection of oral cancer. Standardization of staining protocols, concentration optimization, and establishment of evidence-based guidelines for interpretation will strengthen its clinical utility.

Conclusion

Lugol's iodine vital staining represents a valuable, adjunctive tool for oral lesion diagnosis and surgical margin assessment. Its high sensitivity for detecting dysplasia and malignancy, combined with the demonstrated benefits of reducing local recurrence rates, supports broader implementation in clinical practice. Although it does not replace histopathological examination, this technique effectively guides biopsy site selection and surgical margin determination. Continued research on optimal protocols, combination approaches, and integration with emerging technologies will further enhance the role of vital staining in the comprehensive management of oral cancers.

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