Review Article

Advancement in Diagnostic Aids for Oral Premalignant Lesions

ABSTRACT

INTRODUCTION: Precancerous lesions, conditions, and early-stage oral cancer cannot be sufficiently identified solely through visual inspection and may be prone to be inadvertently disregarded. Distinguishing between early-stage cancer, precancerous lesions, and benign tumors can pose a challenge due to the striking resemblance in their visual characteristics. Using surgical biopsy as a diagnostic modality is widely regarded as the gold standard in the medical community. However, it is essential to acknowledge that acquiring professional services for this procedure can prove impractical in certain circumstances. Hence this paper presents a concise review of a wide range of advanced diagnostic aids employed in detection of Oral Premalignant Lesions (OPL).

METHOD: The literature search utilized appropriate keywords to search online databases like PubMed, Medline, Google Scholar, EBSCO, Wiley science library, and Saudi digital library.

RESULTS: Alternative screening methods that are noninvasive, readily executed, and exhibit a high degree of accuracy are the established criteria for considering a test as a viable substitute for histopathology. Early diagnosis is a paramount factor in the effective management of oral cancer. Vital staining, immunocytochemistry, fluorescence imaging, laser confocal microscopy, Raman spectroscopy, and Fourier transform infrared spectroscopy diagnostic modalities are employed for the timely identification of oral premalignant lesions.

CONCLUSION: Recent advances have improved the diagnostic aids in easy and accurate detection of oral premalignant lesions therebyfacilitating effective management and mitigation strategies at an early stage of the lesion.

KEYWORDS: Diagnostic Aids, Oral premalignant lesions,vital staining, immunocytochemistry, fluorescence imaging

1. INTRODUCTION

Oral premalignant lesions (OPLs) are antecedents to oral cavity cancers, exhibiting varying progression rates and advancement toward invasive pathology [1]. These lesions can include white patches, leukoplakia, erythroplakia, tongue lesions, and other types of abnormalities in the mouth[2]. OPLs may be asymptomatic or cause irritation, such as pain, burning sensation, and difficulty swallowing[3]. The timely identification and management of OPLs is crucial in enhancing patient outcomes and mitigating mortality risk [4].

Diagnosis of OPLs typically relies on visual observation by experienced practitioners followed by biopsy and analysis under a microscope. The lesion biopsy remains the "Gold standard" in detecting the OPLs. However, recent developments have introduced new methods for diagnosing OPLs, which can be more accurate and cost-effective than traditional methods. These include immunocytochemistry, vital staining tests, fluorescence imaging, and laser confocal microscopy[5].

Immunocytochemistry is a method used to detect antigens in cells that may indicate OPLs. It is relatively noninvasive and can be done quickly. However, it has its drawbacks, such as a lack of specificity and the need for additional confirmation tests. The vital staining test effectively identifies premalignant lesions with higher sensitivity than the naked eye examination. Fluorescence imaging uses fluorescent light to detect changes in tissue structure, which may indicate OPLs. Laser confocal microscopy allows for high-resolution imaging, providing detailed information about tissue morphology to help identify OPLs[5–7].

Each of the diagnostic methods has advantages and disadvantages. Immunocytochemistry is quick, noninvasive, and cost-effective but may lack specificity. The toluidine blue dye test effectively identifies lesions with high sensitivity but may be time-consuming in larger tissue areas. Fluorescence imaging helps detect changes in tissue structure, which can indicate premalignant lesions.However, it requires expensive equipment. Laser confocal microscopy provides detailed information about tissue morphology that can help identify OPLs. It also requires complex imaging equipment and has a higher cost than other methods[5,7].

In light of the imminent progress in diagnosing OPLs, innovative methodologies are presently being explored. Among these, Raman spectroscopy and Fourier transform infrared spectroscopy are currently undergoing active exploration in the medical field. Both of these methodologies can be utilized to identify changes in tissue structure that may indicate OPLs with enhanced accuracy compared to existing techniques. Moreover, researchers are presently examining the potential utilization of artificial intelligence in detecting OPLs by analyzing images obtained from different imaging techniques[8–10].

2. METHODS

2.1 SEARCH STRATEGY

The literature search carried out using appropriate search strings and keywords such as “advances in diagnostic aids for oral premalignant lesions” current diagnostic aids for early detection of premalignant lesions, updates on diagnostic aids for oral premalignant lesions.

2.2 DATABASES

Electronic databases like PubMed, Medline, Google Scholar, EBSCO, Wiley science library, and Saudi digital library were searched for retrieving published articles.

2.3 ELIGIBILITY CRITERIA

Articles published in English language from 2000-2023 were considered in the review. However, other than English language articles and those published before 2000 were excluded from the review.

3. RESULTS AND DISCUSSION

3. 1 VITAL STAINING

Vital staining is an important technique used in oral pathology to assess the health of oral tissues. It involves special dyes applied to oral tissues and helps detect early signs of oral diseases such as premalignant lesions, oral cancer, and other oral abnormalities. When these dyes interact with oral tissues, they can produce color changes, which help medical professionals identify areas that may require further evaluation or treatment[11,12].

Toluidine Blue (TBO) and Lugol's Iodine solution are the most commonly used vital stains. The former is used to diagnose premalignant lesions, while the latter is used to identify superficial oral lesions. Both effectively detect oral disease compared to conventional oral examination techniques[13]. It has been demonstrated that TBO and Lugol's Iodine solution could detect premalignant lesions with a sensitivity of over 90% and specificity of 60-63% [14].

Other vital staining techniques such as Bromophenol Blue (BPB), Fluorescein, and Acridine Orange Stain (AOS) have also been developed over the years. BPB effectively identifies areas of hyperkeratosis in oral mucosa, while Fluorescein can detect microbial colonization or necrotic tissue changes in mucosal surfaces. AOS effectively detects dysplastic cells in oral mucosa, indicating premalignant conditions[15].

In addition to being a useful diagnostic tool, vital staining can help medical professionals determine the extent of disease involvement or rule out false positive diagnoses. For example, if a suspicious area identified during an oral examination does not stain upon application of dye, then it may not warrant further evaluation since it could represent normal tissue instead of a premalignant lesion or early cancerous growth. Thus, vital staining can be essential in guiding clinical decision-making processes related to oral pathology cases and should always be considered as part of any diagnostic workup for OPLs or other suspicious areas noted on the exam. [16].

3.2 IMMUNOCYTOCHEMISTRY

Immunocytochemistry is a technique used in oral pathology to detect the presence or absence of antigens in oral cells. This technique identifies tissue-specific markers that indicate premalignant oral lesions and is frequently employed in laboratory diagnosis for oral medicine.The procedures associated with immunocytochemistry involve preparing a slide containing a tissue sample from the oral cavity and then applying antibodies that have been previously conjugated to an enzyme or fluorescent dye. Once applied, these antibodies attach themselves to antigen sites on oral cells. The reactive sites are then stained and visualized under high-powered microscopes, allowing clinicians to identify and diagnose oral pathology more accurately[17,18].

In recent years, technological advances have enabled researchers to use immunocytochemistry to study more complex oral diseases at the cellular level. For example, it has been used to detect and measure gene expression related to oral cancer and other premalignant oral lesions. Additionally, this technique can be utilized both diagnostically and prognosticallyproviding clinicians with valuable insight into the progression of oral diseases over time [19].

Besides its diagnostic capabilities, immunocytochemistry plays an essential role in research related to oral health care, enabling scientists to gain deeper insights into diseases such as oral cancer and periodontal disease. Various research studies have employed this technique to uncover molecular differences between healthy and diseased tissues [20]. In addition, immunocytochemistry has been used in many studies seeking new targets for drug development [21].

Overall, immunocytochemistry is a powerful tool for aiding clinicians in diagnosing oral pathology. It also holds promise for advancing our understanding of various oral cavity diseases. As more research studies continue employing this technique in their investigations – both diagnostically and prognostically – we may come one step closer to providing better treatments to those suffering from premalignant conditions within the mouth.

3.3 FLUORESCENCE IMAGING

Fluorescence imaging is another technique employed in oral pathology to detect oral lesions. It utilizes light-activated molecules known as fluorophores that become fluorescent when exposed to light and emit a brightly colored glow [22]. A microscope can then detect this glow, allowing clinicians to visualize areas of tissue associated with oral diseases.

The use of fluorescence imaging makes it possible to detect oral lesions more quickly than traditional methods – such as histology stainingwhich require time-consuming preparation before they can be viewed under a microscope. Additionally, due to its noninvasive nature, it can be used in live samples where other techniques may not be applicable.

Various studies have used Fluorescence imaging to identify oral premalignant lesions, oral squamous cell carcinomas, and oral lichen planus. For example, it was found to be accurate for detecting oral pre-malignancy compared to traditional histology staining [23]. Similarly, fluorescence imaging has also provided an ideal tool for diagnosing oral lichen planus in biopsy samples[24]

In summary, fluorescence imaging is a valuable tool for oral pathology – allowing clinicians to detect oral diseases quickly and accurately. It holds potential as an efficient diagnostic aid that could enable early detection of oral diseases before they progress further, improving patient outcomes.

3.4 LASER CONFOCAL MICROSCOPY

Laser confocal microscopy is another imaging modality used in oral pathology that enables clinicians to visualize oral lesions in greater detail than histology staining. Unlike regular fluorescence microscopy, laser confocal microscopy utilizes a scanning laser beam to scan an area of interest in three dimensions while focusing light onto the sample [25]. This precise imaging technique eliminates most of the background noise caused by out-of-focus light and gives unprecedented image clarity, allowing for identifying oral premalignancies at very early stages.It is highly effective for diagnosing oral premalignant lesions such as leukoplakia and lichen planus [26]. It can also quantify oral carcinomas accurately and monitor their progression over time [25].

In summary, laser confocal microscopy is an invaluable imaging tool for oral pathology, providing clinicians with a powerful diagnostic aid. It has many advantages over traditional methods such as histology staining and fluorescence imaging – allowing for the detection of oral premalignancy at very early stages and accurate quantification of oral carcinomas.

3.5 RAMAN SPECTROSCOPY

Raman spectroscopy is a powerful imaging technique used in oral pathology that enables clinicians to identify oral lesions with very high accuracy. It works by shining a laser beam onto the sample and measuring the scattered light off of it, providing information about its chemical composition. This method does not require any staining or tagging, making it fast and noninvasive compared to traditional methods such as histology staining [27].

It has been found to provide a highly accurate diagnosis of oral premalignancies, such as oral leukoplakia [28]and oral lichen planus [29]. Additionally, recent studies have suggested that Raman spectroscopy could also be used to diagnose oral carcinomas and efficiently monitor their progression over time [27]. In summary, Raman spectroscopy is an invaluable imaging tool for oral pathology. It provides clinicians with a powerful diagnostic aid that can accurately detect oral pre-malignancies and oral carcinomas – allowing for early detection of oral diseases before they progress further, improving patient outcomes.

3.6 FOURIER TRANSFORM INFRARED SPECTROSCOPY

Fourier transform infrared spectroscopy (FTIR) is a powerful analytical tool for oral pathology that can provide consistent and reliable data about the chemical composition of oral tissues. This technique works by shining an infrared beam onto the sample, which then vibrates and causes specific absorption bands in the spectrum. These absorption bands can identify specific molecules within an oral tissue sample [30].FTIR has been proven effective for diagnosing oral premalignancies, such as oral leukoplakia and oral lichen planus (Su and Lee 2020). It has also been shown to accurately diagnose oral carcinomas, allowing for early detection and improved patient outcomes [31].

In summary, both Raman spectroscopy and FTIR are invaluable imaging tools for oral pathology. They provide clinicians with powerful diagnostic aids that can accurately detect oral premalignancies and oral carcinomas – allowing for early detection of oral diseases before they progress further, improving patient outcomes.

3.7ViziLite®

ViziLite® (Zila Pharmaceuticals, Phoenix, Arizona, United States) is a chemiluminescence-based detection device intended to aid in the early detection of Premalignant disorder and oral sqauamous cell carcinoma [32].This capsule is composed of a flexible plastic outer container made up of acetyl salicylic acid and a glass vial containing hydrogen peroxide. To initiate it, the capsule must be bent to shatter the inner glass ampoule, causing the two compartments' compounds to react. Consequently, a bluish-white light (430–580 nm) with a duration of 10 minutes is produced [33]. A variant (ViziLite® PLUS) combines chemiluminescence and toluidine bluelabelling system.

The past research demonstrated that ViziLite®, a diagnostic tool, successfully detected a subclinical lesion. This finding indicates that ViziLite® may be valuable in detecting hidden epithelial abnormalities [34]. ViziLite® demonstrates superior diagnostic efficacy compared to tolidine blue in identifying oral squamous cell carcinoma and potentially malignant disorders within a limited patient group with oral lesions [35]. A recent research has shown the enhanced efficacy of ViziLite® in illuminating lesions with more brightness and improved demarcation compared to the use of incandescent light [36].

3.8. Velscope®

The VELscope® device, developed by LED (Medical Diagnostics in White Rock, BC, Canada), is a portable tool used to observe autofluorescence in the oral mucosa directly. It was introduced to the market in 2006 after clearance from the FDA [37].VELscope® is user-friendly and does not need to implement technical steps, such as dimmed light, pre-rinse procedures, or lesion-marking solutions. The experimental setup has a 120 W arc lamp and a carefully designed arrangement of filters and reflectors, specifically calibrated to generate light within the 400-460 nm wavelength range. It has been shown that the produced light effectively penetrates the oral mucosa and stimulates the activation of endogenous autofluorescence molecules, known as fluorophores [38]. Initial investigations concerning limited cohorts of individuals yielded promising outcomes. In the first trial, 44 patients diagnosed with oral dysplasia or oral squamous cell carcinoma were assessed using conventional oral examination and VELscope®. According to Lane et al., the study's findings indicate that the device can distinguish between potentially malignant disorders and oral squamous cell carcinoma in comparison to normal oral mucosa, demonstrating high levels of sensitivity and specificity [39].

4. CONCLUSION

In conclusion, recent advancements have improved diagnostic aids for detecting oral premalignant lesions. The various types of oral premalignant lesions and their symptoms should be discussed, as well as the different methods used to diagnose them, such as immunocytochemistry, vital staining tests, fluorescence imaging, and laser confocal microscopy. Each method has advantages and disadvantages, which should be considered when choosing the most appropriate method. Potential developments in oral premalignant lesions diagnosis should also be discussed, such as Raman spectroscopy, Fourier transform infrared spectroscopy, and the use of artificial intelligence to detect lesions from images. Advanced diagnostic aids with high sensitivity and specificity should be utilized for early detection oforal premalignant lesions for better treatment outcomes.

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