

Review

Application of Oral CDx Brush Biopsy in Oral Cancer Detection

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ABSTRACT

The incidence of oral cancer worldwide has increased over the years and especially in India. It is very important to detect the oral cancer early in which oral health professionals play a leading role. Various diagnostic aids have been developed as an aid to the routine oral cancer screening examination. The techniques that help in a earlier detection and diagnosis of an oral malignancy include Oral CDx, Velscope, Vizilite, Microlux DL, Toluidine Blue. This article highlights the various applications of Oral CDx brush biopsy in oral cancer.

Keywords: Oral Cancer, Oral CDx, Toluidine Blue, Vizilite.

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INTRODUCTION

There is a high prevalence of oral cancer and of other premalignant and malignant lesions of the oral cavity in developing countries such as India. Prevalence rate of oral cancer worldwide is 300,000 annually and in India it accounts for about 20 per 100,000 populations [1]. Tissue biopsy and histopathological examination remains the gold standard diagnostic method for oral mucosal lesions that are suggestive of a premalignancy and malignancy [1], but it is usually a bloody test that implies undergoing surgery and may result in certain technical limitations for some of the professionals. It may also have psychological implications in patients [2]. The most efficient ways of reducing the mortality associated with the oral cancer is by detecting early the malignant and potentially malignant oral lesions. Oral cancer is one of the most curable cancers if it is diagnosed early with 80% chances of survival [3]. Oral health professionals play an crucial role in early detection of precancerous lesions and conditions and should examine all patients who are at risk [4,5]. Numerous new techniques have been developed to help in clinical examination and to improve the diagnosis of malignant and pre-malignant lesions [1]. Oral exfoliative cytology is the microscopic study and interpretation of the characteristics of oral mucosal cells that are shed naturally or artificially [6]. Cytological study of oral cells is usually well accepted by the patient as it is relatively simple, risk-free, non-invasive and inexpensive technique. Cytobrush is easy to use in the oral cavity and the oral epithelial cells can be easily obtained by this technique [7]. This article explains the role of oral CDx in oral cancer detection, its advantages and disadvantages.

REVIEW

For cervical smears in gynaecological lesions a brush was developed in 1980's which was later modified to be specially used for oral smears too. By using this method a better cell spreading on the glass slide was obtained as compared to smears formed by using wooden spatula and also there was an improvement in the cellular morphology of the smears. The CDx brush test was introduced in 1999 to investigate suspicious oral lesions for dysplasia or cancer that would not otherwise have been biopsied because of low risk [8].

In patients with squamous cell carcinomas (SCC) of head and neck surgical resection of the tumor and regional lymph node dissection still remains the treatment choice. Patients with squamous cell carcinomas have only a fair prognosis with an overall 5 year survival rate of about 45% [9]. It can be difficult to distinguish SCC and other lesions of oral mucosa only on the HandE basis [10]. The resected margins are routinely examined by immunohistology, still the histological diagnoses of oral mucosa lesions may fail at times [11,12]. Apart from squamous cell carcinoma and its precursors (dysplasias), some other neoplasias can also be diagnosed specifically by means of brush biopsy techniques eg. naevus cell naevi, basal cell carcinomas, malignant melanomas, malignant lymphomas. Variety of non-neoplastic diseases can be differentiated using exfoliative cytology like pemphigus vulgaris, HPV infections, Herpes simplex, candida [13,14].

Oral CDx (Oral CDx Laboratories, Inc. Suffern, NY), with computer aided analysis is a specialized oral brush, which has the ability to penetrate the thickness of the mucosa and collect representative sample of the lesion [15]. Basal and

parabasal cells which are the precursor of malignant changes are collected by this specialized brush, which is then analyzed by computer [16]. It identifies dysplasia in common oral spots that usually do not have any suspicious clinical features. The brush biopsy technique collects cells from the entire thickness of the oral epithelium when compared with exfoliative cytology. Oral brush biopsy technique is a painless, easy to perform, chair-side test that can be helpful in identifying even the common small red and white oral lesions which are suspicious to rule out any dysplasia [7]. The biopsy kit consists of a specially designed stiff bristle brush, a form, a fixative (alcohol/polyethylene glycol), a glass slide and a container for sending samples to the CDx laboratory [17]. When performing the test, the brush is placed on the lesion and is rotated in one spot until it produces hemorrhagic spots or any reddening. This allows a sample which is

representative of the whole epithelium, including the basal, intermediate and superficial layers. The sample is then placed on the glass slide, fixed, and is sent to the CDx laboratory where the analysis is done with the help of a computer based imaging system. Results can be reported as “negative” (without epithelial abnormalities), “atypical” (epithelial changes of uncertain diagnostic meaning), “positive” (evidence of dysplasia or carcinoma) or “inadequate” (incomplete transepithelial specimen), with “atypical” or positive results requiring incisional biopsy for definitive diagnosis [3]. Most of the test results are likely to be benign as most oral lesions are benign in nature. Nearly 10% of all cases usually turn out to be abnormal. For the abnormal cases the lab advises certain guidance recommending either scalpel biopsy or retesting [7] (**Table 1**).

Table 1: Indications and contraindications.

Indications	Contraindications [18,19]
Red or white spots, chronic ulcers, mucosal lesions with an abnormal epithelial surface lesions	Lesions with intact normal epithelium
Common benign and small abnormalities that have been routinely seen and not suspicious enough to warrant referral for biopsy	Mucocelles, haemangiomas, Fibromas, submucosal masses, pigmented lesion
Harmless looking lesions	Highly suspicious lesions(immediate scalpel biopsy)
Precancerous lesions	Lesions with obvious etiology Herpes, Aphthous ulcers, Traumatic ulcers

Many studies have been carried out involving the oral CDx brush biopsy and strong evidence exists supporting its accuracy. In all the studies where the same lesion was tested simultaneously by both brush and scalpel biopsy, Oral CDx showed to have sensitivity and specificity exceeding 90% [20]. According to a systemic review by Potter et al., Oral CDx test can help in detecting dysplastic changes in high risk mucosal lesions but its application remains doubtful in low risk populations [21]. The main drawback of this test is the

time delay before the incisional biopsy as it requires an average time of over 100 days before the diagnosis of a malignant lesion [22,23]. Oral CDx may be useful in patients with multiple lesions where patient may not give consent to multiple scalpel biopsies. It may be useful in the non-compliant patient who is unlikely to comeback for a follow-up exam or accept an immediate referral to an oral surgeon [24] (**Table 2**).

Table 2: Advantages and disadvantages of oral CDx in oral cancer detection.

Advantages	Disadvantages[25-27]
Easy to perform chair side test	Requires two procedures(Brush test and Scalpel biopsy)
Less invasive procedure	Detects only cellular atypia
Early detection of oral cancers and precancers can be made.	Cannot give a definitive diagnosis
No bleeding or less bleeding in comparison to scalpel biopsy	Time consuming and costly
Less painful compared to other biopsy procedures	Delayed diagnosis

CONCLUSION

Oral brush biopsy test can act as an adjunct in detecting clinically innocuous lesions as it is less invasive procedure and is readily accepted by the patients and it also gives dentists an initial screening means before performing the incisional biopsy of lesions that had not clinically appeared to be oral cancer. Sensitivity and specificity of brush biopsy needs improvement. Biopsies of different tissue types and sites require specific techniques. Additional methods like

DNA-image cytometry may enhance the result which has to be investigated by further studies.

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