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EXFOLIATIVE CYTOLOGY: AN ADJUVANT IN DIAGNOSING EARLY LESIONS

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ABSTRACT

The cause-effect relationship of tobacco chewing to oral malignancy is well known. Although the clinical signs and symptoms may be absent or unapparent, early changes in the oral mucosal cells can be detected using the simple technique of exfoliative cytology. The review aims at studying the changes observed in the mucosal cells of tobacco chewers. The dysplastic changes of the cells are observed with various parameters. Also the recent advances of exfoliative cytology in the detection of various disease conditions have been emphasized.

KEYWORDS: Exfoliative cytology, tobacco chewers, dysplasia.

INTRODUCTION

Oral cancer due to tobacco use is the most widely prevalent malignancies in the world.[1] The use of tobacco varies within different endemic areas in India.[1] This is significant in stating that environmental factors influence the pathogenesis of cancers of the head and neck.[2] The WHO has estimated the number of deaths from tobacco use to rise from 1.4% in 1990 to 13.3% of all deaths in 2020.[3] 30-80% of the malignancies of the oral cavity arise from pre malignant lesions such as luekoplakia, erythroplakia and oral submucous fibrosis.[4] The effects of tobacco should be studied in detail for the quantitative exfoliative cytology to be of value in the detection of dysplasia like mucosal disorders.[5] The review hence aims to study the cytomorphometric changes in the squames of the buccal mucosa.

Exfoliative cytology is the microscopic examination of shed or desquamated cells from the epithelial surface usually the mucous membrane. It also includes the study of those cells that

have been collected by scraping the tissue surface or collected from body fluids such as sputum, saliva, etc.[6]

Walsh was the first person to describe cancer cells in sputum of patient's as early as in 1843. Later, Lebert in 1851 emphasized the altered size of cells and nuclei as a basis of diagnosing cancer. Then, Bealem[7] in 1960 attempted cytological diagnosis of oropharyngeal cancer. Furthermore, Dudgeon in 1927 devised a direct smear technique of surgical specimen for rapid diagnosis. George N Papanicolaou and Traut[7] in 1941 started using what is today called as "PAP test" as a routine procedure for early detection. In 1943 cytodiagnosis became a routine procedure for diagnosing cervical cancers. Later, Ziskin[7] in the year 1940 was the first person to have reported the use of exfoliative cytology in oral cavity. Montgomery and Von Hamm[7] in 1951 used exfoliative cytology for the diagnosis of oral cancer. In 1963 Sandler [7] devised various methods of obtaining smears from the oral cavity.

Rationale of Exfoliative Cytology

It lies in the epithelial physiology of the cells. The continuous exfoliation of epithelial cells is a part of physiological turnover. Deeper cells are strongly adhered in normal conditions but become loose in case of malignancy. They hence exfoliate along with the superficial cells which are analyzed quantitatively and qualitatively by the clinician.[6]

TECHNIQUES OF EXFOLIATIVE CYTOLOGY

Conventional Technique

A wooden spatula is used to scrape the buccal mucosa, but due to the pressure on the cells, folding and alteration of cytoplasm etc during smearing, a cytobrush is now a preferred device for the same. This technique demonstrates better cell spreading on objective slide and also improves in the cellular adequacy of the smears. A monolayer of cells is desired after a smear preparation which is attained after a minimal experience.[8]

Other techniques reviewed by Sandler include cotton tip applicators, vigorous normal saline rinse, forceful aspiration of cells from the surface and aspiration of resting saliva from the floor etc.

Use of Toluidine blue for site specificity

The smears are collected from the buccal mucosa before and after a toluidine blue rinse. The oral cavity is made to rinse with water and then a smear is taken using a cytobrush. The mouth

is then rinsed with 10ml of 1% acetic acid for 30 seconds, followed by 10ml of toluidine blue rinse and finally repeated with 1% acetic acid. Another smear is taken using a new cytobrush. Both the smears are spread on to a clean microscopic glass slide, fixed and stained using standard PAP staining protocol. The smears are then observed under 40X & 100X magnifications with an eyepiece grid and 100 cells per slide were counted to note the changes in the cells.[9]

Recent advances as adjuvant in cytology[8]

1) OralCDx

The oral brush biopsy with computer assisted analysis is useful in common spot lesions with no suspicious clinical features. The cells are collected cells from the full thickness of the oral epithelium.

2) ViziLite Plus with Toluidine blue

It is a chemiluminescent light detection system commonly used in the detection of cervical neoplasias. Low energy blue-white light is generated in areas of epithelial cell proliferation. This is referred as an 'acetowhite' change.

3) Microluk DL

A low energy blue light is generated from a blue-white light emitting diode and a diffused fiber-optic light guide used for detection of altered cells.

4) Orascoptic DK

It is a three-in-one, battery operated, handheld LED instrument which is available with an oral lesion screening instrument attachment.

5) VELscope

it works on the principle that structural changes and altered metabolic activity of tissues of the oral cavity have variable fluorescence. It is a multiuse device with a handheld scope. The mucosa is scanned visually for changes in tissue fluorescence.

Uses of exfoliative cytology[10, 11]

- Early detection and control of oral cancer, microbial diseases and dermatological lesions.
- Assessment of nutritional iron deficiencies.
- In forensic dentistry for the determination of age and sex.

- For the study of cellular changes in systemic conditions like diabetes mellitus, pregnancy, ageing and alcoholism.
- For predicting the cellular response of a tumor to irradiation.
- For evaluating toxic reactions post cancer in some hereditary diseases.

Advantages of exfoliative cytology[10]

- Non-invasive and painless technique
- Requires minimal skills and is easily done at the chair side
- Excellent patient compliance
- Cost effective
- Can be performed in large numbers with minimal use of instruments
- Helps in early detection of lesions
- It can be used in patients with systemic disorders where biopsy is contraindicated for example, hemangiomas,[12] multiple nuerofibromas,[12] patients receiving bisphosphonates.[12]

Disadvantages of exfoliative cytology[12]

- It may show false negative results
- It is used only as an adjuvant to diagnosis
- Risk of contamination
- Has low sensitivity
- Sampling maybe inadequate
- It cannot be used in non epithelial lesions.

TABLE 1: CLASSIFICATION OF CYTOLOGICAL SMEARS

CLASS I	**NORMAL**	**Only normal cells are observed**
CLASS II	ATYPICAL	Presence of minor atypia due to inflammation. No signs of malignancy.
CLASS III	INTERMEDIATE	Wider atypia suggestive of severe dysplasia, carcinoma-in-situ or cancer
CLASS IV	SUGGESTIVE OF CANCER	Shows few epithelial cells with malignant changes. Biopsy is mandatory.
CLASS V	POSITIVE FOR CANCER	Cells show characteristic malignant changes. Biopsy is mandatory.

[courtesy: shafers textbook of oral pathology- 5th edition**]**

TABLE 2: CYTOLOGICAL ALTERATIONS IN THE SMEARS[9]

Architectural changes	**agglomerations or clumping of squamous cells and altered nuclear cytoplasmic ratio**
Nuclear changes	nuclear pleomorphism and binucleation
Cellular changes	cellular pleomorphism and presence of micronuclei
Other changes	Includes presence of bacterial colony units and keratin flakes.

CONCLUSION

Oral exfoliative cytology is a simple, non-invasive technique in which a smear is analyzed quantitatively and qualitatively for the early detection of potential malignant lesions. With recent advancements in this method, various parameters like the cellular diameter, nuclear diameter, cellular to nuclear cytoplasmic ratio, nuclear shape and discontinuity, optical density and nuclear texture of potentially cancerous cells can be assessed. All major forms of tobacco use cause oral cancer. Detection of high risk oral premalignant lesions and intervention is one of the main ways to reduce the morbidity, mortality and cost of treatment associated with oral cancers. The cellular changes which occur in the buccal mucosa of tobacco chewers could be due to the release of various by-products like nitrosamines and nitrosonornicotine which is infiltrated into the mucosal cells and cause the change in cellular morphometry.

Thus exfoliative cytology is useful as an early indicator is assessing the mucosal cells for dysplastic changes and necessitates for the appropriate early preventive measures to avoid the development of oral malignancies. Although specific markers are essential for the confirmation of malignant conditions, exfoliative cytology is a useful adjuvant in diagnosing certain conditions in the affected individuals.

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