

REVIEW ARTICLE

MICRONUCLEI: A PROGNOSTIC TOOL

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ABSTRACT: Squamous cell carcinoma is one the most common oral mucosal malignant tumor, diagnosis of oral squamous cell carcinoma rarely presents difficulty, it is the cancer staging and histo pathological grading that are more important for prognosis, micronuclei are good prognostic indicator. Micronuclei screening can be done easily by exfoliative cytology, one of the most valuable diagnostic method other than routine histopathology (H and E-stained sections) and immunohistochemistry. It has been used in the detection of oral squamous cell carcinoma and has been shown to have a sensitivity of 94%, specificity of 100%, and an accuracy of 95%. Micronuclei frequencies were also found to be raised with increasing histological grades of squamous cell carcinoma.

KEYWORDS: Micronuclei, Exfoliative cytology, Squamous cell carcinoma.

INTRODUCTION: A micronucleus is the erratic nucleus that is formed during the anaphase of mitosis or meiosis. Micronuclei (the name means 'small nucleus') are cytoplasmic bodies having a portion of acentric chromosome or whole chromosome which was not carried to the opposite poles during the anaphase. Chromosomal damage by carcinogens to dividing basal cells of the epithelium results in the production of micronuclei in the daughter cells which migrate up through the epithelium and are exfoliated.

The micronucleus test on exfoliated cells has been successfully used to: (1) recognize population groups at an elevated risk for cancer of the oral cavity or urinary bladder; (2) estimate synergistic or additive effects of carcinogen exposure (cigarette smokers plus drinkers of alcoholic beverages); (3) pinpoint the site within an organ from which most carcinomas will develop.¹ Micronuclei are induced in oral exfoliated cells by a variety of substances, including genotoxic agents and carcinogenic compound in tobacco, betel nut, and alcohol.

Tobacco-specific nitrosamines have been reported to be potent clastogenic and mutagenic agents which are thought to be responsible for the induction of chromatid/chromosomal aberrations resulting in production of micronuclei.² The genotoxic and carcinogenic chemicals released from betel nut and tobacco and also the calcium hydroxide content of lime present in the betel quid are thought to be responsible for promotion of reactive oxygen species from areca nut extracts. These reactive oxygen species can in turn cause damage to the DNA.⁷

FORMATION OF MICRONUCLEI: Micronuclei are extra nuclear cytoplasmic bodies. They are induced in cells by numerous genotoxic agents that damage the chromosomes. The damaged chromosomes, in the form of acentric chromatids or chromosome fragments, lag behind in anaphase when centric elements move towards the spindle poles. After telophase, the undamaged chromosomes, as well as the centric fragments, give rise to regular daughter nuclei.

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The lagging elements are included in the daughter cells, too, but a considerable proportion is transformed into one or several secondary nuclei, which are, as a rule, much smaller than the principal nucleus and are therefore called micronuclei.³

DISCUSSION: Squamous cell carcinoma of the oral mucosa accounts for 90% to 95% of all oral malignancies.³ Oral exfoliative cytology has been used extensively for screening cellular alteration in oral squamous cell carcinoma cases. An accuracy of 95% and a reliability of more than 96% in detection of squamous cell carcinoma in mass screening have been reported in the literature.⁴ Oral exfoliative cytology can reveal various cellular alterations in squamous cell carcinoma. It includes karyorrhexis, karyolysis, micronucleus formation, pyknosis, binucleation, broken-egg nucleus, anucleation, etc.^{5,6}

Micronuclei in oral exfoliated cells is a marker of chromosomal damage caused by genotoxic agents from tobacco and tobacco-related substances, alcohol, etc.^{7,13} The micronucleus assay has been used to assess the genotoxic damage in oral squamous cell carcinoma and oral premalignancies.^{8,9} It has been established that genomic damage is produced by genotoxic substances, medical procedures (radiation, chemicals), micronutrient deficiency (folic acid), lifestyle factors (alcohol, smoking, stress, drugs), and genetic factors such as defects in metabolism and/or in repair of DNA.^{10,11}

The Micronuclei assay has been reported to correlate well with the histological grading of oral squamous cell carcinoma and leukoplakia. Incidence of micronuclei has been analyzed by various studies in normal patients, oral premalignancies, and oral squamous cell carcinoma.¹² Micronuclei has been used as a biomarker for assessment of DNA damage.¹⁴ When compared with other body sites, mouth provides with a distinct opportunity for defining biomarkers because the mouth permits noninvasive, repetitive examinations in longitudinal studies of tobacco-associated acute and chronic diseases.¹⁵

There are many studies (more than 200) in which epithelial cells from other site such as nasal mucosa, cervix, bladder, esophagus and bronchi had been used for micronuclei assay.¹⁶ Biomarkers help to detect high-risk patients. They are divided into three groups: First to define the exposure to carcinogenic agents, the second to show biological effects on the target tissue and the third to give information about the individual susceptibility.¹⁷ The micronucleus assay in exfoliated buccal cells is a useful and minimally invasive method for monitoring genetic damage in humans.¹⁸

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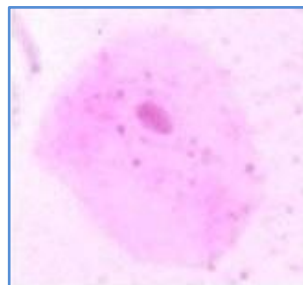


Figure 1

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