

Morphological analysis of the acute effects of cigarette smoke on normal human oral mucosa explants

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Cigarette smoke is one of the five leading risk factors for mortality in the world and smoking related lung cancer is the main cause of deaths from cancer in both sexes in the United States. This habit is particularly popular in Western low- and middle- income countries, with about one billion males and 250 million females smoking in the world. Human oral mucosa is the combustion chamber of cigarette, but scanty evidence is available about the early smoke effects.

The present work aimed at evaluating from a morphological point of view whole smoke early effects on epithelial intercellular adhesion and keratinocyte terminal differentiation in a three-dimensional model of human oral mucosa. Biopsies of keratinized oral mucosa of healthy non smoking women ($n = 5$) were collected. After culturing in a Transwell system, one fragment of each biopsy was exposed to the smoke of one single cigarette; the remnant represented the internal control. The distribution of epithelial differentiation markers (keratin-10, K10, and keratin-14, K14, for suprabasal and basal cells respectively), desmosomes (desmoglein-1, desmoglein-3), tight junctions (occludin), adherens junctions (E-cadherin, β -catenin), and apoptotic cells (p53, caspase-3) were evaluated by immunofluorescence.

Quantitative analysis of K14 immunolabeling revealed an over expression in the suprabasal layers as early as 3 hours after smoke exposure, without impairment of the epithelial junctional apparatus and apoptosis induction.

The present study showed that the early response of the normal human oral mucosa to acute exposure to the smoke of one single cigarette induced K14 expression in suprabasal oral keratinocytes, without impairment of the epithelial junctional apparatus and apoptosis induction, suggesting that the first significant response to cigarette smoke arise from the basal and suprabasal layers of the human oral epithelium.

The novelty of the present work consists in the combination of human oral explants with a non hermetic smoke exposure system. The main improvement offered by this setting is the ability of reproducing the cyclic condition by which cigarette smoke normally comes in contact with the oral mucosa. Furthermore, it allows administering simultaneously both gaseous phase and particulate matter of cigarette smoke.

Keywords: Cigarette smoke, epithelial differentiation markers.