Histopathological Changes of Vocal Cord Polyps Induced by Smoking

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Abstract

Background: Histopathological changes of the respiratory epithelium in response to cigarette smoking have been studied in depth in the lungs and oral cavity, but in the Vocal Cord Polyps (VCP). The aim of this study was to investigate the histological changes that occur in the VCP of smokers compared with non-smokers.

Patients: The files of patients who underwent VC polypectomy during 1/2013 to 12/2017 were reviewed. Polyp’s tissue samples were collected and examined. Goblet cells were counted, the inflammation degree, congestion, and edema was graded as mild, moderate, or severe. Epithelial thickness was measured as well. Findings were compared between smokers and non-smokers.

Results: A 73 patients underwent VCP resection during the study period. Exclusion criteria included: carcinoma in situ, post-radiotherapy, incomplete data, and lack of follow up. The 66 patients (70 polyps to 4 bilateral) were included. Mean age was 48 years. On statistical analysis, Non-significant differences were found between the smokers and non-smokers in mean number of goblet cells in the nasal epithelium (p<0.64), and mean epithelial thickness (p<0.68). The corresponding mean values of congestion were similar in both groups (p<0.35), the same also with the inflammation grade, (p<0.31). The only significant difference was the mean edema grade (p<0.1).

Conclusions: The histopathological findings in the VCPs of smokers resemble reported no special findings in the respiratory epithelium between the two groups. Surprisingly these findings are neither in line with the reported smoking-induced changes in nasal mucosa nor the lung respiratory epithelium. More data should be investigated.

Keywords: Vocal cord; Polyps; Smoking; Goblet cells

Introduction

Tobacco smoke is known to be toxic and carcinogenic. It has been implicated in many acute and chronic medical problems. Changes in the histopathology of the respiratory epithelium caused by tobacco smoke have been studied in greater depth in the lungs than in the nasal lining or another upper respiratory epithelium. In the lungs, smoke inhalation was found to lead to an increased number of goblet cells and submucosal gland hyperplasia, with excessive mucus production [1,2].

Given the morphological similarity of the respiratory and naso-pharyngeal epithelium, researchers have suggested that tobacco smoke exposure may cause headache, nose irritation, nasal congestion, postnasal drip, and sneezing [3]. Hamm et al., [4] noted that exposure to cigarette smoke was associated with hyperplasia, metaplasia, and inflammation of the nose and larynx, in addition to proliferative lesions of the lungs. From our data published [5]. Investigating the changes in the nasal mucosa of smokers and non-smokers, the main differences from nonsmokers are greater goblet cell hyperplasia and thicker epithelium. The aim of the present study was to investigate Histopathological changes in the resected vocal cord polyps of smokers compared with non-smokers, and to look for gender differentiations if exists.
Patients and Methods

Patients: The computerized database of the Department of Otolaryngology-Head and Neck Surgery of a major referral university-affiliated medical center was retrospectively reviewed for all patients ≥ 18 years of age that underwent Direct Laryngoscopy (DL) for vocal cord surgery due to polyps from January 2013 to December 2017.

The 73 patients underwent DL for Vocal cord polypectomy during the study period. The 66 patients were included in the study (70 vocal cords), 12 were women and the mean age at surgery was 45.7 years ± 13.5 years for smokers and 51.4 ± 14.8 for non-smokers. Of these, 36 patients (51.4%) were smokers. The histological samples were evaluated for the purpose of this study.

Exclusion criteria were carcinoma or carcinoma in situ, prior radiation therapy to the neck, lack of follow-up, incomplete data, not suitable samples for revision. The study protocol was approved by the Institutional Review Board, with waiver of informed consent.

Microscopic examination: The resected polyps were fixed in 10% buffered formalin, and were paraffin embedded and processed for examination by light microscope. Sequential 5 μm sections were stained with Hematoxylin Eosin (H&E) and Alcian blue. The slides stained with H&E were for blinded histologic evaluation. Degree of inflammation, congestion, and edema was graded as mild (+1), moderate (+2), or severe (+3). The mean grades of the smokers and non-smokers were calculated. Measurements of the thickness of the epithelium were made from the basement membrane by using an eyepiece equipped with a linear micrometer, at a magnification × 400, under an Olympus LM50 microscope (Olympus Corp., Tokyo, Japan), three times in different linear areas, and the average was calculated [5]. Sections stained with Alcian blue 1%, diluted with acetic acid 3% (final pH 2.5), were examined for the presence of mucus-secreting goblet cells. Findings were considered positive when the cell cytoplasm stained dark blue. The number of goblet cells was counted in areas of linear respiratory epithelium. The meticulous, semi-quantitative light microscope study was performed by an experienced pathologist (L.W), and the results expressed as number of goblet cells in the largest diameter of a high-power field (× 400) (goblet cell index). The mean index was calculated separately for smokers and nonsmokers.

Statistical analysis: Group data are expressed as mean and Standard Deviation (SD). Differences in mean parameters between groups were analyzed with Student’s t-test or Mann-Whitney test. All reported p values are two-sided. A p value of ≤ 0.05 was considered statistically significant.

Results

Light microscopy examination showed fragments of respiratory epithelium (respiratory-tract type) and mucus-secreting goblet cells with foci of hyperplasia. The stroma showed edema, congestion, and diffuse lymphocytic infiltration accompanied by some plasma cells and/or neutrophils. The mean number of goblet cells in the polyp epithelium was 1.05 ± 3.66 in the smokers group and 0.18 ± 0.87 in the non-smokers group; this difference was not statistically significant (p<0.64) (Figure 1). The edema in the smokers group was graded as severe in 11 cases, moderate in 10, and mild in 12, and in the non-smokers group, moderate in ten and mild in 11 (Figure 2). The mean grade between the two groups was statistically significant (p<0.1). Congestion was graded as severe in five cases in smokers. Moderate in 12 cases and mild in eight, and in the non-smokers group, also 5 cases were graded as sever, moderate in seven, and mild in 3 (Figure 3). The corresponding values were not statistically significant (p<0.35) unless we exclude the severe cases. Inflammation in the smokers group was both severe and moderate in one case each and mild in eleven cases, and in the non-smokers, severe in three cases, moderate in four, and mild in eight (Figure 4). The corresponding values were statistically non-significant (p<0.31). Epithelial thickness measured 0.28 mm ± 0.16 mm in the smokers group and 0.24 mm ± 14 mm in the non-
smokers (Figure 5). This difference wasn’t statistically significant (p<0.68).

Discussion

We present a study, which we believe the first to be published in literature, examining and investigating the histopathological changing on the vocal cord epithelium due to cigarette smoke exposure and the comparison between smokers and non-smokers also seeking for changes in between genders. Studies in rats have shown that lifetime exposure to cigarette smoke is associated with the development of tumors in the nasal passages and lung [6]. Sells et al., [7] reported that the administration of chemicals by non-inhalation routes induced changes in the nasal mucosa, including respiratory epithelial hyperplasia, degeneration. Causing necrosis of the olfactory epithelium, olfactory epithelium metaplasia, adenoma, adenocarcinoma, and squamous cell carcinoma. More research have been done in the domain, more and more information are learned and understood regarding the cigarettes smoke effect on respiratory mucosa.

As known, the mucosa of the nose is histologically similar to the bronchial mucosa, which is characterized predominantly by a pseudostratified ciliated columnar epithelium. Goblet cells are unicellular mucous glands with basal nuclei. They are distributed throughout the surface of the respiratory epithelium and constitute the glandular component of the epithelial layer.

These changes are mediated by various cytokines, such as Interleukins IL-4 and IL-13, and growth factors [8,9]. Previous histological studies of the lungs of cigarette smokers reported hyper secretion in the airways and an increased number of goblet cells found that smokers with symptoms of both chronic bronchitis and chronic airflow limitation had an increased number of goblet cells in addition to inflammatory cells in the epithelium of the peripheral airways [10-14].

Still, little is known regarding the histopathological changing’s of vocal cord epithelium due to smoking and less regarding gender differentiations. A paper published in 2009 from our department showed that the nasal mucosa of smokers is also characterized by a significantly increased number of goblet cells, edema and epithelium thickness compared with non-smokers (p<0.0001) [15].

However, the present study showed no significant histopathological changes on the vocal cord polyp’s mucosa due to tobacco smoke. Some little changing’s regarding the grade of inflammation, epithelial thickness and the number of Goblet cells were observed but NOT characterized as statistically significant. The only parameter statistically significantly was the increased grade of edema, compared with nonsmokers (p<0.1). These findings are NOT in line with the reported smoking-induced changes in the nasal and lung respiratory epithelium [11,15].

To be added, non-significant changes between the two genders (men vs. women) have been reported in our study [15-19]. Epithelium thickness (p=0.25), inflammation (p=0.16), edema (p=0.49), Number of goblet cells (p=0.61), congestion (p=0.16) (Table 1).

Conclusion

To the best of our knowledge this is the first article to be published in literature to examine the histopathological changing’s of vocal cord epithelium due to smoke exposure. Beside we believe to be the first to compare changes, if founded, between genders.

Interestingly, although tobacco smoking is associated with acute and chronic rhinitis, nasal and sinus symptoms may be exacerbated by tobacco smoking nasal mucosa remodeling, increased goblet cells, edema, inflammation and grade of congestion were recently demonstrated. Yet result showed no significant changes.

Several limitations to this study should be mentioned. The retrospective design could cause selection bias. Furthermore, patients with smoking duration of 2 years to 20 years were grouped together, however no changes have been found. Comparison between genders findings was not practical in our small sample; further studies and hormonal immunohistochemical staining should be performed.
References


