

The Specific Role of Periodontal Disease in Lung Cancer Pathogenesis

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Editorial

It has been proposed that poor oral hygiene, especially in high risk patients could be a predatory factor for respiratory diseases. Oral cavity that coincides with trachea could be a natural gate for colonization by respiratory pathogens. Dental plaque can be colonized by those that have been inhaled from the oro pharynx cavity to the upper airways and then can approach the lower airway and adhere to the bronchial or alveolar epithelium [1,2]. Periodontal Disease (PD) has been associated with chronic lung diseases, such as Chronic Obstructive Pulmonary Disease (COPD) [3,4]. It has also been recorded that pulmonary function in COPD patient's decreases with increasing Clinical Attachment Loss (CAL), and an association between poor oral hygiene and COPD was recorded after controlling for potential confounders, such as gender, age, smoking and socio-economic level [5]. The mentioned findings were in accordance with those that carried out from previous case-control and prospective studies [6-10].

However, only one similar investigation has not confirmed such observations [11]. Epidemiological researches have investigated the association between COPD and lung cancer (LC) [12-14]. Cigarette smoking is the principle risk factor for developing COPD [15] and LC [12-16]. Smokers with COPD are at a higher risk of developing LC, suggesting that an association exists between the processes that causes both diseases [17,18]. However, the majority of smokers do not develop COPD or LC despite the fact that the accumulated smoking history increases the risk of developing PD and cancer [17-20]. The contribution of smoking to PD development requires poor oral hygiene whereas in cases of established PD, smoking accelerates its progression. Similarly, smoking consists an important risk factor for LC development, however does not cause the disease to all smokers [21].

It is possible that the link between both diseases is mediated by a pre-existing chronic pulmonary disease such as idiopathic pulmonary fibrosis, COPD, and tuberculosis that are associated with an increased risk of LC development. A limited exploration

exists regarding the association between COPD and LC risk, especially in non-smokers, as they develop COPD rarely [13]. In a prospective study in health professionals with a PD history a slightly higher cancer incidence compared to those who did not have PD at the time of the study initiation and after controlling for known risk factors, was observed. It was also found that PD was statistically significantly associated with an increased risk for LC. Specifically, regarding LC, a strong association was recorded in individuals with a small number of remaining teeth and it was remained strong among non-smokers although it was weaker and statistically insignificant. However, many limitations were existed especially the self-reported assessment of PD [22]. Hujoel et al. [23] observed an increased risk of death from all types of cancer when the assessment of PD was based on other indicators. Specifically, it was found a statistically increased risk of LC, however it was not confirmed in non-smokers. It was suggested that periodontitis could include an unlimited percentage of smoking history, and therefore its relationship with the LC was invalid. In the same study, gingivitis that reflects the presence of inflammatory load, in individuals with natural teeth showed increased risk levels of death from LC.

Periodontitis could be a substitute indicator for the effects of smoking and therefore provides a link to LC.

The follow-up of NHANES III patients was shown that periodontitis was associated with an increased mortality from respiratory cancers. There was an increased risk tendency in relation to periodontitis severity [24]. Chrysanthakopoulos [25] was recorded that probing pocket depth as an index for PD severity was statistically significantly associated with the risk of developing LC after controlling for potential confounders. In addition to the suspected effect of COPD and smoking on the interpretation of the association between PD and the risk for developing of LC, the mechanisms that could link the two diseases have not been elucidated. Therefore, future studies are required, and they could be based on the

overall association between chronic inflammation and the risk of cancer development.

The inflammatory response to periodontal inflammation extends beyond the oral cavity and leads to increased levels of circulating inflammatory biomarkers [26,27], a finding that is supported from the highest incidence of cancer cases in individuals with chronic inflammatory conditions [28] and the efficacy of anti-inflammatory drugs in the prevention of certain types of cancer [29], how-ever that finding has not been confirmed in all studies [30,31], nor in LC. A possible mechanism can be supported on the basis of the PD pathogenesis and is characterized by a wide variety of microorganisms, bacteria and their products such as endotoxins, enzymes and metabolic products that are toxic to surrounding cells and can directly induce mutations in tumor suppressor genes and proto-oncogenes or can alter signaling pathways that affect cell proliferation and/or epithelial cell survival [32,33].

Other mechanisms that have been proposed include the immune system deflection and the production of carcinogenic products by periodontal tissues pathogens [34].

In addition, under-lying genetic factors may increase the sensitivity in both situations or may alter the relationship of environmental risk factors such as smoking, with PD and cancer. The role of the common genetic risk factors between the two situations, however, remains unclear. The sensitivity to the disease could be influenced by predetermined factors such as genetic polymorphisms that also need to be investigated [35,36]. Another possible mechanism could be attributed to the large inflammatory load caused by the PD and could be associated with the risk of LC through the mechanisms that are involved and lead to oxidative stress that causes damage to the tissues. The oxidative stress induces mechanisms in the progression of PD and cancer. Various types of PD are characterized by significant inflammation load that could affect the evolution of systematic conditions, including carcinogenesis in the lung [23].

It should be noted that the research regarding the possible association of PD with cancer is limited by the problems of controlling of confounders such as smoking and the socio-economic level. Smoking seems to be the main confounding factor in studies that examine cancer, such as LC. Other possible confounders are gender, age, nationality, diabetes mellitus and genetic factors. The definition of periodontitis in a number of large epidemiological studies was based on substitute indicators [24]. However, despite several limitations, periodontitis has been identified as a potential risk factor for gastrointestinal, respiratory and pancreatic cancer and possibly for cancer in other organs. Therefore, it exists an obvious need for further investigation.

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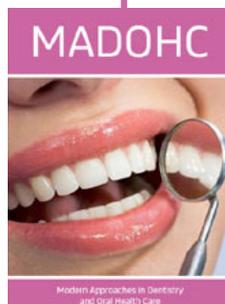
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