Letter to the Editor

Another point of view for meta-analysis studies focused on protective inhaled corticosteroids and the risk of lung cancer

Gabriel Costa de Carvalho

Resarch Department of Associação Fundo de Incentivo a Pesquisa-AFIP, São Paulo, Brazil

Correspondence to: Gabriel Costa de Carvalho, PhD. Associação Fundo de Incentivo a Pesquisa-AFIP, Street Pe. Machado 1040, 04127-015 São Paulo, Brazil. Email: gabriel.carvalho@afip.com.br.

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With great interest, I read the article entitled "*Inhaled corticosteroids and risk of lung cancer among chronic obstructive pulmonary disease patients*: *a comprehensive analysis of nine prospective cohorts*" by Ge and colleagues in *Translational Lung Cancer Research* (1). The authors presented a work aimed to see whether inhaled corticosteroids (ICs) protect against lung cancer in chronic obstructive pulmonary disease (COPD) patients. They observed that ICs were linked to a lower risk of lung cancer in COPD patients and the results were compatible across age and region groups. Considering their findings may have an impact on current clinical practice, some questions should be addressed.

Firstly, we note that all information was constructed from a unique and specific point of view of human biology in which the protective effect of ICs in COPD patients was discussed. The authors conducted the work using a meta-analysis of nine studies and found that ICs have protective effects against lung cancer in COPD patients with a mean follow-up time of fewer than 10 years (1). In agreement that ICs are useful for the treatment of COPD, additional observations on the side effects of using ICs in the immunology and infectious diseases fields will be required.

Secondly, the relationship between long-term ICs exposure and lung cancer risk in patients with COPD should be evaluated with more studies. Despite other authors suggesting that proinflammatory cytokines and cytotoxic chemicals produced by $CD8^+$ T cells in the lungs play a role in the pathophysiology of COPD, in the field of immunology, cytotoxic T $CD8^+$ cells (CTLs) as well as natural killer cells (NK), are also defined as specialized leukocyte populations that produce cytotoxic granules that act as antitumor factors (2,3). However, long-term use of ICs could favor the opposite scenario and conduct patients at risk of lung cancer. This point of view needs further consideration.

Thirdly, in the article, Ge *et al.*, mention the benefits of ICs, especially decreasing the effectiveness of epithelial-mesenchymal transition (EMT), avoiding no migratory phenotype, and consequently more adherent cells (1). The group also describes that characteristics of EMT are followed by increased expression of the danger-associated molecular patterns (DAMP) S100A4, MMP-9, and all the physiological progression EMT that we observe in nature (4). In my point of view, the authors forgot to explain that suppressor drugs could favor the invasion of infectious agents. Some adverse effects are connected to the long-term usage of ICs in COPD, like respiratory infections, such as oral candidiasis and mycobacterial disease (tuberculosis) that can lead to dysphonia not limited to systemic outcomes such as the increased risk of pneumonia. Diabetes-related problems are another example of systemic adverse effects, and at high dosages, ICSs are also followed by bone fractures (5-7).

In conclusion, regular ICs use may have a protective effect on COPD patients to reduce the risk of lung cancer. Although, more research is needed to evaluate this potential link from both immunohistopathological and infectious perspectives.

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Footnote

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