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Editorial Open Access

Advanced Glycation End Products (Ages) and Its Soluble Receptor in Smokers and Mild/Moderate COPD

Caram LMO[1*], **Ferrari R**[1] **and Rasslan Z**[2]

[1]*Department of Internal Medicine, Botucatu Medical School, UNESP-Univ Estadual Paulista, Pneumology Area, São Paulo, Brazil*

[2]*Internal Medicine Department, The Santa Casa Medical School, São Paulo, Brazil*

[*]**Corresponding author:** Caram LMO, Department of Internal Medicine, Botucatu Medical School, UNESP-Univ Estadual Paulista, Pneumology Area-UNESP, Distrito de Rubião Junior s/n, Botucatu, São Paulo, Brazil, Tel: +551438801171; Fax: +551438822238; E-mail: laucaram@hotmail.com

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Editorial

Smoking and COPD are associated with oxidative stress [1,2], which is classically defined as the result of an imbalance between oxidants and antioxidants substances. The advanced glycation end products (AGEs) are the result of protein carbonyls, a reaction that stems from lipid peroxidation and glycoxidation which release products that will react with proteins damaging them and are responsible for various manifestations associated with aging, diabetes mellitus, cardiovascular disease and the development of cancer and metastases [3,4]. In addition, toxic products of glycation are also present in aqueous extracts of tobacco and can react rapidly with proteins to form AGEs and products as methylglyoxal and glyoxal (AGEs precursors) are found in tobacco smoke [5]. In this direction, it was found that the concentration of AGEs is higher in smokers and COPD patients compared to nonsmokers, independently of the presence of diabetes [5-8].

Cerami et al. [5] found induction of AGEs after *in vitro* preparation of aqueous extract and in condensate of tobacco and increased concentrations of AGEs *in vivo* when compared nonsmokers and smokers. This result is in agreement with study showing positive association between smoking history and AGEs concentrations evaluated by skin auto-fluorescence technique. Meerwaldt et al. [6] found that in addition to the significant increase in AGEs concentrations among smokers, there was a positive association between smoking history and AGEs. Hoonhorst et al. [7] showed that smoking history correlates more closely with AGEs in the skin than with active smoking and the authors suggest that the deposition of AGEs in the skin is likely to occur after long-term oxidative insult (cumulative).

The increase of AGEs in COPD patients is also consistent with results of previous studies. Wu et al. [8] evaluated the presence of AGEs in lung tissue after lobectomy in subjects without COPD moderate disease and found increased concentrations in airway and alveolar wall in the group with the disease [7]. A recent study evaluated AGEs concentrations in the skin (autofluorescence technique) and showed higher values of AGEs in COPD patients (mild to very severe) compared to smokers and controls, but the authors found no difference between the stages according to the GOLD classification [8]. Thus, AGEs on the skin were elevated in COPD patients with any severity of the disease, when compared to controls irrespective of smoking status and age [8].

These glycation end products can be eliminated by the kidneys and bind to specific receptors such as the RAGE (receptor for advanced glycation end products), a transmembrane receptor that belongs to the family of the immunoglobulins. The connection AGE/RAGE results in the activation of nuclear factor kappa B (NFkB), which triggers the production of proinflammatory cytokines leading inflammation in various organs [9]. Studies evaluated the concentrations of AGEs, RAGE and sRAGE in smokers and in COPD patients, however the interaction between these oxidative stress indicators is not well established [7,8].

Several factors can influence the concentration of sRAGE. Research suggests that the release of sRAGE by the body exerts a protective role that attenuates the progression of the disease. Smith et al. [10] speculated that the high expression of mRAGE (RAGE expressed on the cell membrane in the lung) of COPD patients may be associated with low concentrations of sRAGE and can be a loss of control of inflammatory marker [10]. Alternatively, reduced levels of sRAGE can identify individuals exposed to high levels of RAGE ligands or other inflammatory mediators [10]. Thus, smokers with diminished sRAGE values could be predisposed to increased inflammation and tissue injury, and thus more likely to develop COPD. In the analysis of Tesra data was not identified differences in sRAGE concentrations compared COPD II vs. III; however, an association was found between sRAGE and emphysema after adjustment for spirometry and demographic variables. According to the data from the study Tesra, Cheng et al. [11] sRAGE biomarker may be associated with emphysema, regardless of the stage of disease. In summary, the sRAGE concentrations have been associated with severe emphysema, impaired diffusion capacity and airway inflammation, which support a possible role of sRAGE in cellular integrity and its protective properties [11,12].

As shown, some markers of oxidative stress are increased in smokers and COPD patients; however the identification of markers and the mechanism that may differentiate between smokers and patients with early disease remain unknown.

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