Receptor for Advanced Glycation End-Products and Environmental Exposure Related Obstructive Airways Disease: A Systematic Review

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Introduction: The development of obstructive airways disease (OAD) following environmental exposure is a complex and heterogeneous process. Our group has identified receptor for advanced glycation end-products (RAGE) as a predictor of World Trade Center particulate matter associated lung Injury (WTC-LI). RAGE has been shown to be a mediator of inflammation and pathogenesis in the lungs, however its association with OAD is poorly understood. Prior reviews have focused on RAGE as a biomarker of emphysema and smoking-related lung disease. Our objective was to conduct a systematic review of studies assessing the relationship between RAGE and OAD secondary to environmental exposure. Methods: A comprehensive search using PubMed and EMBASE was performed on 01/05/2018. Databases were searched for keywords focusing on environmental exposure, obstructive airways disease, and RAGE. We only included original human research studies in English, focusing on pulmonary end-points associated with RAGE and environmental exposure. The final systematic review was registered with PROSPERO (2018 CRD42018093834). Results: A total of 213 studies were identified on the initial search according to the aforementioned keywords. After removing the duplicates and application of exclusion criteria, we screened the titles and abstracts of 61 studies. Finally, 19 full text articles were included. The exposures discussed in these articles include, particulate matter (n=2) and cigarette smoke (n=17). Six studies discuss RAGE as a biomarker of OAD activity, seven evaluate its association with OAD, four are genome wide association studies, and two discuss the role of RAGE in different end-organ outcomes (Table 1). Conclusions: RAGE is a mediator of inflammation and involved in development of end-organ dysfunction such as obstructive airways disease. Soluble form of RAGE appears to function as a decoy receptor and has a protective effect. Only a few articles have identified RAGE as biologically relevant in environmental exposure associated lung disease. Future investigations should focus on further understanding of the role and therapeutic potential of RAGE in particulate matter exposure associated lung disease.