High exposure to Advanced Glycation End-products could facilitate the occurrence of pediatric Eosinophilic Esophagitis

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Objectives and Study. Eosinophilic esophagitis (EoE) is a major cause of upper gastrointestinal morbidity in the pediatric age. It has been hypothesized that the interaction between genetic and environmental factors (i.e., dietary habits) may induce the development of EoE. Among dietary factors, it has been postulated that advanced glycation end-products (AGEs), present at high level in ultra-processed foods (UPFs), could be involved in the pathogenesis of several inflammatory diseases, including food allergy. AGEs are ligands to the RAGE receptor and, mimicking signals provoked by tissue damage, are capable to increase tissue permeability, inflammation and Th2 response. We aimed to evaluate the potential pathogenic role elicited by AGEs in pediatric EoE.

Methods. Esophageal biopsy samples obtained through esophagogastroduodenoscopy from 6 active EoE pediatric patients (3 males and 3 females, age 8-18 yrs) and from 6 aged-sex matched controls were analyzed. Baseline features of esophageal samples of EoE patients were compared with those

observed in control subjects at baseline and after 24h exposure to AGEs (AGE-BSA, 500µg/ml) or bovine serum albumin (BSA) as control. Peripheral blood mononuclear cells (PBMCs) were also collected from healthy controls and stimulated with same of AGE-BSA or BSA concentrations. Eosinophils and eotaxin-3 were analyzed for immunohistochemistry. Th2 cytokines (IL-4, IL-5, IL-13), IL-33, and eotaxin-3 production was analyzed by ELISA in culture supernatants. Esophageal permeability (biotin-assay) and occludin expression were evaluated by immunofluorescence. Flow cytometry analysis was performed to evaluate the number of activated eosinophils (CD16- CD11b+ CD69+ cells) in PBMCs.

Results. AGEs exposure in esophageal samples from control children resulted in increased eosinophils density, IL-4, IL-5, IL-13 IL-33, eotaxin-3 production, esophageal permeability, occludin redistribution resembling the features observed in samples collected from active EoE patients. An increased number of activated eosinophils in PBMCs from healthy controls was also observed after stimulation with AGEs.

Conclusion. Our data suggest a potential role of dietary AGEs exposure in facilitating the occurrence of EoE in the pediatric age. Limiting the exposure to UPFs could be an effective preventive and therapeutic strategy against pediatric EoE.