Association between aryl hydrocarbon receptor and 4-hydroxynonenal in oxidative stress-mediated chronic rhinosinusitis with nasal polyps

Aigerim Kvarantan¹, Vedran Balta², Neven Zarkovic³, Tea Horvat⁴, Tea Vukovic⁴, Kamelija Zarkovic⁵, Livije Kalogjera⁶

 ¹Department of Otorhinolaryngology & Oral Surgery, General Hospital Ivo Pedisic Sisak, Sisak, Croatia, ²Department of Biology, Faculty of Science, Zagreb University, Zagreb, Croatia,
³Department of Molecular Medicine, Laboratory for Oxidative Stress, Ruder Boskovic Research Institute, Zagreb, Croatia, ⁴Department of Molecular Medicine, Laboratory for Oxidative Stress, Ruder Boskovic Research Institute, Zagreb, Croatia, ⁵ Department of Pathology, University Hospital Zagreb, Zagreb, Croatia, ⁶Department of ENT & Head and Neck Surgery, University Hospital Sestre Milosrdnice

Correspondence address: Aigerim Kvarantan, azhumabayeva7@gmail.com

Background: Chronic rhinosinusitis with nasal polyps (CRSwNPs) is a distinct entity within the chronic rhinosinusitis group of diseases, which are chronic upper airway diseases with several pheno- and endotypes. Oxidative stress plays an important role in the pathogenesis of CRSwNPs.

Aim: The aim was to assess the association between the expression of the aryl hydrocarbon receptor (AhR) and 4-hydroxynonenal (4-HNE) in patients with CRSwNPs.

Methods: The study included 26 patients who underwent endoscopic sinus surgery -14 patients with CRSwNPs, and 12 controls with healthy sinus mucosa. The expression of AhR and 4-HNE was assessed in tissue samples using immunohistochemistry. The level of 4-HNE in serum samples was measured using the ELISA assay. The total oxidative capacity (TOC) was assessed by measuring the peroxidase activity.

Results: Higher levels of 4-HNE expression were observed in tissues (3, range 1-3 vs. 0, range 0-0, p<0.001) and serum (27.7 \pm 11.5 vs. 9.8 \pm 7.7 pmol/mg, p<0.001) samples of CRSwNPs patients, as compared to healthy controls. A higher expression of AhR was found in inflammatory cells (plasma cells, lymphocytes, eosinopholes) of CRSwNPs patients, compared to controls (3, range 1-3 vs. 2, range 1-2, p=0.001). There were no differences in TOC across groups (0.0285 \pm 0.0207 vs. 0.02978 \pm 0.0197 μ M H2O2 eq., p=0.848). Patients with bronchial asthma (57%) had abundant eosinophiles in tissue samples. Patients with recalcitrant CRSwNPs had higher 4-HNE serum levels, compared to non-recalcitrant cases (27.3 vs. 24.2 pmol/mg, p=0.339).

Conclusion: Patients suffering from CRSwNPs have oxidative stress mediated overexpression of AhR, which is linked to a chronic inflammatory response in the paranasal sinus tissues.

Keywords: chronic rhinosinusitis, nasal polyps, oxidative stress