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MOLECULAR GENETIC ANALYSIS OF COX2 GENE POLYMORPHISM IN CHRONIC POLYPOSIS RHINOSINUSITIS

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Abstract

Analysis of the contribution of the COX2 gene polymorphism to the frequency of occurrence, development and clinical course. The prevalence of the rs20417 76 G/C polymorphism in the COX2 gene was analyzed among patients with chronic polyposis rhinosinusitis and chronic rhinosinusitis and in the control group. We can conclude that there are no significant differences in the frequency of detection of allelic and genotypic variants of the 76 G/C polymorphic locus in the COX2 gene.

Keywords. Polymorphism, encoded gene, inflammatory response, COX2 gene, homozygous.

CRSwP is a complex multifactorial disease that involves several genetic, immunological, environmental, and mucosal changes in the body, but still the etiology remains unclear. Many potential factors have been identified, such as various allergic reactions, impaired secretion of mucous membranes, decreased immunity, impaired epithelial protection, exposure to microbes and the environment. Further studies are needed to determine the role of genetic factors and their interaction with these factors in the pathophysiology of CRSwP disease. The lack of appropriate animal models, difficulties in standardizing phenotypes, the need for large controlled cohorts, and the high cost and low reproducibility of studies are major obstacles to elucidating the pathophysiology of CRSwP[5,16].

There is convincing evidence of the influence of genetic factors on the pathophysiology of CRSwP. Mutations in the cystic fibrosis transmembrane regulator (CFTR) gene cause cystic fibrosis (CF), which is the most frequently duplicated gene associated with CRS. There is a high prevalence of CRSwP in cystic fibrosis carriers, but some studies show that CFTR mutations also occur in CRSwP patients without cystic fibrosis[14,8]. Family studies suggest a genetic factor in the

pathogenesis of CRSwP, but environmental factors also play an important role in the development of nasal polyps. For example, observations have shown that even twins developed from the same egg have been studied to have different polyp tissue[18].

This part of the work is devoted to the study of the distribution frequencies of polymorphism of the COX2 gene, as well as to the analysis of the contribution of this polymorphism to the occurrence, development and clinical course of CRSwP and CRS[5,23].

DNA code information is given to us for life, so we have a growing interest in genetic markers. Recurrence in another person in the family of a patient with CRSwP due to genetic predisposition is 15-50%. When genetic predisposition was studied by American researchers, it was found that; the first-degree relative of an infected patient was 4.1 times more likely to be infected, and the second-degree relatives were 3.3 times more likely to be infected. In the research of Swedish scientists, it was found that the frequency of recurrence in the family of an infected patient is 5 times higher than in the rest of the population. In another study by scientists, monozygotic twins were observed, in this case, SPRS recurrence was not observed, from which we can conclude that the role of external environmental factors is not always dependent on heredity[10,27].

In polyp tissues and intranasal secretions, an increase in the concentration of various inflammatory mediators, in particular interleukins, is observed due to an increase in their synthesis by de novo effector cells [29]. Eosinophils (IL-4, IL-12, IL-13, GM-CSF), the main pro-inflammatory cytokines (IL-1, IL-2, FNO-α, IL-10) that contribute to the chronic inflammation in the nasal cavity, regulator special importance is given to the increase in the concentration of cytokines involved in the development, recruitment and activation of cytokines (IL-10, TLR2b)[8,3].

The distribution of allele gene frequencies of resistance predisposition, which forms the risk of development or resistance to multifactorial pathology, is determined by the racial and ethnic origin of the studied group [18].

Cytokine system is a universal regulatory network of mediators designed to control reproduction, differentiation and functional activity of cellular elements in all homeostatic systems of the body, depending on which the immune system plays a very important role in the occurrence and development of diseases[12].

Cytokines - leukocyte mediators of inflammation are included in pro-inflammatory or anti-inflammatory regulatory peptides. IL-1 and TNF-α play the biggest role in pro-inflammatory processes. The mechanisms by which these cytokines participate in the inflammatory response are largely common[13]. They can increase the

expression of the COX-2 gene with the increase in the production of leukotrienes and prostaglandins and their inclusion in the pathological process, thereby increasing the migration of leukocytes and inflammatory infiltration and activating the endothelium. IL-6 and IL-8 also have anti-inflammatory properties[2,21]. Anti-inflammatory cytokines are active antagonists of IL-1 and TNF-α, the most active of which are IL-4 and IL-10. Their anti-inflammatory activity is manifested by suppressing the production of IL-1 and TNF-α, colony-stimulating factors, and reducing the cytotoxicity of macrophages[24].

Summarizing the obtained results, we can conclude that there are no significant differences in the frequency of detection of allelic and genotypic variants of the 76 G/C polymorphic locus of the COX2 gene in the 1st and 2nd groups of patients and the control group. There is no significant contribution of this locus in the formation and development of any form of CRS. However, there is a significant trend toward an increased frequency of the G/G genotype in patients with CRSwP compared with controls.

References

1. Thomas Horn, Kumar Reddy Kakularam, Monika Anton, Constanze Richter, Pallu Reddanna, Hartmut Kuhn. Functional characterization of genetic enzyme variations in human lipoxygenases,Redox Biology,Volume 1, Issue 1,2013,Pages 566-577
2. Hsu, J., Pedro, C.A., Robert, C.K., et al., Genetics of chronic rhinosinusitis: state of the field and directions forward, J. Allergy Clin. Immunol., 2013, vol. 131, no. 4, pp. 977–993. doi 10.1016/j.jaci.2013.01.028CrossRefPubMedPubMedCentralGoogle Scholar
3. Vereshchagin, M.Yu. and Minkin, A.U., Polypoid rhinosinusitis, Ekol. Chel., 2012, no. 8, pp. 54–58.
4. Endam, L.M., Cormier, C., Bossé, Y., et al., Association of IL1A, IL1B and TNF gene polymorphisms with chronic rhinosinusitis with and without nasal polyposis: a replication study, Arch. Otolaryngol. Head Neck Surg., 2010, vol. 136, no. 2, pp. 187–192. doi 10.1001/archoto.2009.219
5. Bosse, Y., Bacot, F., Montpetit, A., et al., Identification of susceptibility genes for complex diseases using pooling-based genome-wide association scans, Hum. Genet., 2009, vol. 125, no. 3, pp. 305–318. doi 10.1007/s00439-009-0626-9

6. Pescador, D.B., Isidoro-García, M., and García-Solaesa, V., Genetic association study in nasal polyposis, J. Invest. Allergol. Clin. Immunol., 2012, vol. 22, no. 5, pp. 331–340.
7. Oakley, G., Curtin, K., and Orb, Q., Familial risk of chronic rhinosinusitis with and without nasal polyposis: genetics or environment, Int. Forum Allergy Rhinol., 2015, vol. 5, no. 2, pp. 276–282. doi 10.1002/alr.21469
8. Alexiou, A., Sourtzi, P., Dimakopoulou, K., et al., Nasal polyps: heredity, allergies, and environmental and occupational exposure, J. Otolaryngol. Head Neck Surg., 2011, no. 40, pp. 58–63.
9. Zhang, Y., Desrosiers, M., Mfuna-Endam, L., et al., Demonstration of a common genetic basis to CRS in Chinese and Caucasian populations, J. Allergy Clin. Immunol., 2011, vol. 127, no. 2, p. AB121. doi S0091-6749(10)02424-3
10. Henmyr, V., Vandeplas, G., Halldén, C. et al., Replication study of genetic variants associated with chronic rhinosinusitis and nasal polyposis, J. Allergy Clin. Immunol., 2014, vol. 133, no. 1, pp. 273–275.
11. Slavin, Raymond G., et al. "The diagnosis and management of sinusitis: a practice parameter update." Journal of Allergy and Clinical Immunology 116.6 (2005): S13-S47.
12. Palikhe, N.S., Kim, S.H., Cho, B.Y., et al., IL-13 gene polymorphisms are associated with rhinosinusitis and eosinophilic inflammation in aspirin intolerant asthma, Allergy Asthma Immunol. Res., 2010, vol. 2, no. 2, pp. 134–140.
13. Ober, C. and Yao, T.C., The genetics of asthma and allergic disease: a 21st century perspective, Immunol. Rev., 2011, vol. 242, pp. 10–30.
14. Tournas, A., Mfuna, L., Bossé, Y., and Filali-Mouhim, A., A pooling-based genome-wide association study implicates the p73 gene in chronic rhinosinusitis, J. Otolaryngol. Head Neck Surg., 2010, vol. 39, no. 2, pp. 188–195.
15. Castano, R., Bossé, Y., Endam, L.M., et al., Evidence of association of interleukin-1 receptor-like 1 gene polymorphisms with chronic rhinosinusitis, Am. J. Rhinol. Allergy., 2009, vol. 23, no. 4, pp. 377–384. doi 10.2500/ajra.2009.23.3303
16. Zhang, M., Ni, P., Cai, C., et al., The association between genetic polymorphisms of IL-6 and the susceptibility of chronic rhinosinusitis, J. Clin. Otorhinolaryngol. Head Neck Surg., 2012, vol. 26, no. 5, pp. 197–200.

17. Endam, L.M., Saud, A., and Bossé, Y., CD8A gene polymorphisms predict severity factors in chronic rhinosinusitis, Allergy Rhinol., 2013, vol. 1, no. 8, pp. 605–611. doi 10.1002/alr.21174
18. Buysschaert, I.D., Grulois, V., Eloy, P., et al., Genetic evidence for a role of IL33 in nasal polyposis, Allergy, 2010, vol. 65, no. 5, pp. 616–622.
19. Endo, Y., Hirahara, K., Iinuma, T., et al., The interleukin-33-p38 kinase axis confers memory T helper 2 cell pathogenicity in the airway, Immunity, 2015, vol. 42, no. 2, pp. 294–308. doi 10.1016/j.immuni.2015.01.016.