Abstract

Introduction: Celiac disease is a complex autoimmune disease induced in genetically predisposed individuals after ingestion of cereals containing gluten. Monocytes, as the main effector cells of innate immunity, play a non-negligible role in the development of the immune response in response to pathogenic and foreign agents as well as in the pathogenesis of celiac disease. The only effective treatment for celiac disease is strict and lifelong adherence to a gluten-free diet, while dietary choices are of key importance in the regulation of this disease. Oats have emerged as a controversial but nutritionally rich option to supplement a gluten-free diet with a source rich in fiber, micro- and macronutrients. Therefore, in this thesis, we focused on how the innate immune system, specifically monocytes, interact with the avenin peptides of a selected gluten-free oat cultivar and whether an immune reaction detectable at the molecular level occurs in response to its consumption.

Materials and methods: 39 patients with stabilized celiac disease were included in the study, who consumed 50 g of raw oatmeal of the selected cultivar daily for 14 days. $CD14^+$ monocytes were isolated from whole blood before the start of the study and after its completion using immunomagnetic separation, in which TLR2, TLR4, TNFα, IL8 and IL1β mRNA expressions were determined using quantitative polymerase chain reaction with *PGK1* gene mRNA as an endogenous control. Peripheral blood mononuclear cells were also isolated from whole blood using gradient centrifugation. Using flow cytometry, we analyzed the number of lymphocytes and monocytes, and the evaluation of the expression of surface markers TLR2, TLR4, HLA-DR, CD80 and CD86 made it possible to investigate the phenotype of leukocytes.

Results: Analysis and comparison of mRNA expressions before and after 14-day oat consumption revealed a slight increase in IL1β ($p = 0,005$) and TNFα ($p = 0,053$) expression levels. No change was detected in TLR2, TLR4, or IL8 mRNA following the 14-day dietary intervention, while TLR2 expression on the surface of $CD14^+$ monocytes decreased slightly but statistically significantly. The total number of monocytes, their individual subtypes and lymphocytes separated from whole blood either did not change after the diet or even decreased insignificantly. The same effect of the oat diet was also observed in leukocytes defined by the expression of surface markers TLR2, TLR4, HLA-DR, CD80; only the decrease in the number of $CD14^+CD86^+$ cells was statistically significant ($p = 0,029$).

Conclusion: The results suggest that at the level of the innate immune system, a weak immune response probably occurs through an increase in mRNA production of the pro-inflammatory cytokines TNFα and IL1β by monocytes, probably in connection with the 14-day oat consumption. However, it seems that at the cellular and protein level we do not detect this activation of the immune system through changes in the number or phenotype of monocytes after consuming oats in patients with celiac disease.

Key words: celiac disease, monocytes, innate immunity, oats, proinflammatory cytokines