Streszczenie w języku angielskim

Atherosclerosis is a chronic inflammatory process of blood vessels, which is the leading cause of cardiovascular diseases, including ischemic heart disease. Classic risk factors for the development of atherosclerosis include hypertension, hypercholesterolemia, type 2 diabetes, and smoking. Increasing attention is being paid to so-called non-classical risk factors, such as chronic inflammation caused by infectious agents. These disrupt metabolism and activate the immune system. One such contagious agent is *Helicobacter pylori*, a Gram-negative bacillus that colonizes the gastric mucosa. Interestingly, studies indicate that H. pylori is more common in patients with ischemic heart disease. Metabolic fatty liver disease (MAFLD), associated with lipid disorders and chronic inflammation, is also increasingly recognized as playing a role in the pathogenesis of atherosclerosis. MAFLD promotes the development of atherosclerosis through the overproduction of proatherogenic lipoproteins and damage to the vascular endothelium. Gastrointestinal infections, including those caused by *H. pylori*, may further exacerbate metabolic disorders and intestinal dysbiosis, thereby increasing cardiovascular risk.

In this doctoral dissertation, an in vivo model using domestic guinea pigs was employed to evaluate the effects of *Helicobacter pylori* infection and a high-fat diet on the development of pro-atherosclerotic changes and metabolic syndrome. It was demonstrated that both diet and *H. pylori* infection lead to increased LDL levels, enhanced lipid peroxidation, endothelial cell apoptosis, and the deposition of oxLDL in blood vessel walls. The most advanced changes were observed in animals simultaneously infected with *H. pylori* and fed a highfat diet. A significant association was also found between the presence of infection and a high-fat diet and the severity of liver steatosis in animals, confirming the involvement of these factors in the development of MASLD and atherosclerosis. These findings may have potential applications in identifying early markers of developing atherosclerotic changes.

In addition, an in vitro cell model using human monocytes confirmed the involvement of bacterial components of *H. pylori* and oxidized sterols in activating the NLRP3 inflammasome, as well as in enhancing the transformation of monocytes into foam cells. The critical role of the NLRP3 inflammasome itself in the transformation of macrophages into foam cells was also demonstrated, which may be an essential basis for the search for new therapeutic strategies in the treatment of atherosclerosis.

The presented studies also suggested the possibility of using colchicine encapsulated in polymeric nanocarriers as a potential anti-inflammatory therapy in atherosclerosis. Low doses

of colchicine (0.5 mg/day) have been approved by the FDA since 2023 for the prevention of cardiovascular events in patients with atherosclerosis. However, in its classic form, it has strong side effects, especially on the digestive system. Encapsulating colchicine in polymer nanoparticles reduced its cytotoxic effect on eukaryotic cells compared to the classic, unmodified form of the drug. In addition, colchicine-loaded nanoparticles showed comparable efficacy in inhibiting the transformation of macrophages into foam cells as free colchicine, with simultaneously lower cytotoxicity. Furthermore, the absence of hepatotoxic, nephrotoxic, and cardiotoxic effects of colchicine encapsulated in nanoparticles was confirmed in an animal model.

In summary, the results obtained indicate that *H. pylori* infection and metabolic disorders characteristic of MAFLD may act synergistically, exacerbating the inflammatory response in the vessel wall and promoting the development of atherosclerosis. The NLRP3 inflammasome, which contributes to the transformation of macrophages into foam cells, plays a crucial role in the development of proatherogenic inflammatory processes. Its activity can be effectively reduced by colchicine encapsulated in polymer nanoparticles, indicating the potential of this drug form in anti-atherosclerotic therapy.

Agata Tomaszewska