Streszczenie w języku angielskim

In skeletal muscles, lipids serve as a major energy source as well as important intracellular signal mediators. Within the cells, fatty acids become bound to FABPc or are activated by coenzyme A. In the latter form, most of them are oxidized, while the rest undergoes esterification to triacylglycerols for transient storage. Although skeletal muscles have a high capacity for fatty acid oxidation, they are also susceptible to lipid overload. A marked rise in muscle triacylglycerol deposition can be attributed to the imbalance between fatty acid oxidation and lipid storage, and can protect against the synthesis of lipotoxic metabolites. Indeed, the abnormal accumulation of diacylglycerols and ceramides can directly inhibit insulin-stimulated glucose transport and contribute to the activation of inflammatory processes. For these reasons, pharmacological regulation of lipid metabolism is an important goal of scientific studies.

The peroxisome proliferator-activated receptor γ co-activator 1α (PGC-1α) is a major protein controlling fatty acid metabolism in skeletal muscle. This co-activator interacts with a number of nuclear receptors and transcription factors, thereby increasing the expression of target genes encoding enzymes involved in β-oxidation and lipogenesis. Much attention is currently focused on the role of PGC-1α in the regulation of energy metabolism. However, the net effect on lipid content in skeletal muscle cells has not been established. Therefore, the aim of the study was to determine the impact of PGC-1α activation on lipid metabolism in skeletal muscle cells.

The research was performed on L6 myotubes subjected to the pharmacological stimulation of PGC-1α with the use of pyrroloquinoline quinone (PQQ) in the concentrations of 0.5, 1 and 3 μM in two time periods (i.e., 2 h and 24 h). The effectiveness of PGC-1α stimulation was evaluated at mRNA and protein levels by real-time PCR and Western Blot methods, respectively. The intracellular uptake of radioactive palmitic acid was determined using a scintillation counter. The content of specific lipid fractions was analyzed by means of gas-liquid chromatography (GLC) and high performance liquid chromatography (HPLC). In addition, the expression of selected enzymes of sphingolipid metabolic pathway was determined by the Western Blot technique.

As expected, the efficiency of PGC-1α stimulation depended on both concentration and time of cell treatment with PQQ. The highest PGC-1α protein expression was observed for 0.5 μM (2 h: + 24%; 24 h: +22 %, $p < 0.05$), while PGC-1α mRNA content reached a peak for 1 μM of PQQ (2 h: + 123%, 24 h: + 208%, $p < 0.05$). Solely long-term (24 h) incubation with 0.5

μM of PQQ significantly increased palmitic acid uptake. The incubation of L6 myotubes with PQQ resulted in the increased content of intracellular lipids in a triacylglycerol fraction in all studied groups, which was accompanied by a decrease in free fatty acids level (i.e., after 2 h exposure to 0.5 μM and 24 h treatment with 0.5, 1 and 3 μM), without significant changes in diacylglycerol level. Regarding sphingolipid metabolism, an increase in the intracellular content of ceramides was observed after 2 h incubation with 0.5 μM of PQQ and 24 h treatment with all tested PQQ concentrations. At the same time, the level of sphinganine and sphinganine-1-phosphate was reduced in the case of short-term stimulation of PGC-1α, while an increase in sphingosine content was noticed after prolonged incubation with the studied PQQ concentrations. Both short and long terms of incubation, caused a reduction in sphingomyelin level in skeletal muscle cells.

In conclusion, the pharmacological stimulation of PGC-1α in skeletal muscle cells leads to increased lipid content mainly in triacylglycerol and ceramide fractions.