

SUMMARY

Protein catabolism and muscle wasting are basic features characterizing the complex metabolic syndrome, called cachexia, which is a severe complication of many diseases, in whose pathogenesis are often participant the systemic inflammatory response and endotoxemia.

Branched-chain amino acids (leucine, isoleucine and valine) are not only an important substrate for protein synthesis, but they are also involved in the regulation of protein metabolism, insulin synthesis and secretion, and serve as the source of amino group in the alanine and glutamine formation in the muscle. Not only leucine but also some of its metabolites, α - ketoisocaproic acid (KIC) and β -hydroxy- β -methylbutyrate (HMB), have protein anabolic activity and thus some of leucine effects could be induced by these metabolites. In the last years there is paid attention to the HMB, which is used as a supplement for athletes and tested for its potential use in cachexia treatment.

The aim of our experiments was to study: 1) endotoxin-induced effect on metabolism of proteins and amino acids in different types of skeletal muscle and the dose dependence of these changes; 2) effects of selected leucine metabolites (KIC and HMB) on the metabolism of proteins and amino acids – in different types of skeletal muscle; under *in vivo* and *in vitro* conditions; in healthy rats and in the endotoxin model of sepsis.

The Wistar rats were used in our experiments. We used two types of skeletal muscles with the aim of assessment of differences in effects on muscles varying in muscle fibre composition – m. soleus (SOL) composed mostly of type I (slow-twitch, red) fibres and m. extensor digitorum longus (EDL) composed mostly of type II (fast-twitch, white) fibres. As the main parameters of protein metabolism we used the total and myofibrillar proteolysis, protein synthesis, leucine oxidation, proteolytic activity of proteasome and cathepsins B and L and proteasome α -subunits expression.

The endotoxin application induced the protein catabolism in skeletal muscle due to the increase in proteolysis and it was especially caused by proteasome proteolytic activity stimulation. EDL was more sensitive against the endotoxin effect than SOL. The proteasome proteolytic activity was stimulated not only in the skeletal muscle, but also in other tissues. The dose 5 mg of endotoxin/kg of body weight was the most suitable for protein catabolism development in skeletal muscle.

We have not demonstrated the effect of KIC on the measured parameters of protein metabolism in healthy and septic animals. HMB treatment of healthy rats lead to the decrease in the whole-body protein turnover and the proteasome proteolytic activity in skeletal muscle; treatment of septic rats attenuated the increase in skeletal muscle protein degradation and proteasome proteolytic activity. More intensive decline of values of the most parameters of protein degradation was observed in EDL; on the other hand the myofibrillar proteolysis decreased more dramatically in SOL. These results demonstrate the positive effect of HMB on rat skeletal muscle protein metabolism in protein catabolic state induced by endotoxin treatment.