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Optimization of therapeutic approach to the application of water-soluble C_{60} fullerenes for correction of ischemia-reperfusion injury in skeletal muscle of limbs: mechano-kinetic and biochemical aspects

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The therapeutic usage of pristine C_{60} fullerene aqueous colloid solution (C_{60}FAS) for correction of tourniquet-induced acute ischemia-reperfusion injury effects in skeletal muscle of limbs of male rats of the 'Wistar' line within 1 h was investigated. Effect of pathology inducing factor is much as possible approached to the physiological factors and the minimum duration of it can cause pronounced *in vivo* ischemia-reperfusion syndrome that manifests itself in 40 min after ischemia beginning.

The dose-dependent therapeutic effects of C_{60}FAS, which were identified through mechano-kinetic and biochemical markers, were studied in detail. The main goal of these experiments was to optimize the strategy of C_{60}FAS usage for therapeutic purposes.

The ability to realize tetanic efferent stimulation within 6 s and the speed of muscle contraction by repeated single stimulus with 1 and 2 Hz were chosen as mechano-kinetic markers of pathogenesis, on the one hand, and as markers of treatment efficacy, on the other hand. For the biochemical markers were selected following indices: CPK (creatine phosphokinase), LDH (lactate dehydrogenase), general bilirubin, ALT (alanine aminotransferase), AST (aspartate aminotransferase) and creatinine. All they are general markers for pathological states and indicate the destruction of muscle cells, cell membranes and myoglobin.

It was shown experimentally that in control (animals with ischemia without C_{60}FAS injection) a reduction of the absolute values of all investigated mechano-kinetic markers took place, that indicates a pronounced degradation effects in muscle tissue. At the same time, the value of all biochemical markers significantly increased. Intraperitoneal administration of C_{60}FAS in doses 1, 2 and 3 ml/kg per animal body weight (an initial concentration of C_{60} fullerenes in water was 0.15 mg / mL) causes the decrease in pathological changes, which were recorded in control, after 1 h, namely: C_{60}FAS therapeutic effect at a dose of 1 ml/kg was more than 50% compared to ischemic animals; increasing doses up to 2 and 3 mg/kg led to increase in therapeutic effect of C_{60}FAS only up to 10% and 15%, respectively. These results are strongly correlated with changes in biochemical markers in the studied animals.

Thus, therapeutic administration of C_{60}FAS at a dose of 1 ml/kg is physiologically optimal for the studied pathology. This opens up the real prospect of water-soluble C_{60} fullerenes application as effective therapeutic agents for the correction of ischemic damage at the level of mechano-kinetic pathological changes in skeletal muscle functioning and induced biochemical pathological changes in the blood composition.