Acetyl-L-Carnitine Improves Cell Bioenergetics

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Introduction: Acetyl-L-Carnitine (ALC), a natural occurring compound in all mammalian species, plays a variety of vital functions in the body. The most important are related to mitochondria, namely the transport of fatty acids for energy production through β oxidation and the control of acyl-CoA/CoA ratio. Due to this close interaction with cell bioenergetics, it plays a role in many diseases, especially those related to the mitochondria. We propose to characterize the action of ALC in mitochondrial bioenergetics and functional integrity.

Material and Methods: Rat pheochromocytoma cells (PC12) were exposed to the toxic effects of methamphetamine (METH 1 and 100 μM) and pretreated with different doses of ALC (0.01, 0.1 and 1.0 mM). After 24 or 72h of incubation, mitochondrial function, ATP production, intracellular reactive oxygen species (ROS) and mitochondrial membrane potential were assessed by using, respectively, Mitotracker CMXRos, CellTiter-Glo® kit, dichlorofluorescein diacetate probe (DCF-DA) and ^{99m}Tc-sestamibi uptake. Mitochondrial function and intracellular ROS were assessed by flow cytometry and fluorescence microscopy, ATP production was assessed by luminescence and mitochondrial membrane potential was assessed through the quantification of ^{99m}Tc-sestamibi uptake by the cells after a period of 45 minutes of incubation with 740 kBq/mL.

Results: ALC was effective in preventing the deleterious effects of METH on mitochondrial function caused by a 72h exposure, particularly significant when cells were treated with 1.0 μM of METH ($p<0.01$). Cells treated with ALC alone or in combination with METH exhibited consistently lower ATP levels comparing to control cells, with higher significance for 72h exposure. METH enhanced the production of intracellular ROS which was reduced by pre-treating cells with ALC, particularly when cells were treated with the ALC 0.01 mM. Although not enough to reach significance, exposure to METH 100 μM for 72h increases ^{99m}Tc-sestamibi uptake, indicating mitochondrial membrane potential augmentation. This may represent

mitochondrial metabolism hyperactivation in order to counteract the damaging effect of METH. Lower doses of ALC decreases slightly ^{99m}Tc-sestamibi utpake for the 72h exposure to METH 100 μM.

Conclusion: ALC exert its protective role by acting at the mitochondrial level, being able not only to improve mitochondrial function but also to improve cell bioenergetics, being effective in protecting cells against a variety of drugs known to cause oxidative stress, such as METH.

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