L-CARNITINE PREVENTS DNA DAMAGE INDUCED *IN VITRO* BY PROPIONIC AND L-METHYLMALONIC ACIDS IN HUMAN PERIPHERAL LEUKOCYTES.

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Introduction: The organic acids, propionic (PA) and L-methylmalonic (MMA), are found at high amounts in blood and urine of patients with propionic acidemia (PAemia) and methylmalonic acidemia (MMAemia), respectively. Patients with PAemia and MMAemia present severe metabolic complications in the neonatal period and long-term neurological manifestations. Treatment for these disorders consists of a protein restricted diet supplemented with synthetic formulas of amino acids, and L-carnitine to promote detoxification. In recent years, some *in vitro* and *in vivo* studies have demonstrated that lipid and protein oxidative damage may be involved in the pathophysiology of these diseases, but DNA damage has not been fully investigated.
Objectives: In this work we aimed to investigate the *in vitro* effect of L-carnitine (30-150 μM) on DNA damage induced *in vitro* by PA and MMA.
Materials and Methods: The alkaline version of the comet assay was used to evaluate the DNA damage index (DI) induced in human peripheral leukocytes after incubation for 6 hours at 37°C with PA (2.0, 3.0 or 5.0 mM) and MMA (0.50, 2.0 or 5.0 mM). DNA damage induced by 5 mM PA and MMA also was evaluated in the presence of different concentrations of L-carnitine (30, 60, 90, 120 and 150 μM). These L-carnitine concentrations were similar to those detected in our laboratory, by tandem mass spectrometry, in blood from patients with PAemia and MMAemia, which can vary from 30 μmol/L in patients at diagnosis to more than 100 μmol/L in patients under treatment.
Results and Discussion: Our results showed that PA and MMA, at all concentrations analyzed, induced a DNA damage index (DI) significantly higher than the control group. *In vitro* treatment with L-carnitine significantly reduced PA- and MMA-induced DNA damage in a concentration-dependent manner, being totally reversed with 150 μM of L-carnitine. No effect was observed with 30 μM L-carnitine, which is the concentration detected in the blood of patients with PAemia and MMAemia at diagnosis. Besides, L-carnitine prevented cells with damage classes 3 and 4 induced by 5 mM MMA.
Conclusions: Our present *in vitro* findings indicate that DNA damage is induced by PA and MMA and that L-carnitine is able to prevent this damage.

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