Protective effect of acetyl-L-carnitine on the apoptotic pathway of peripheral neuropathy.

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BACKGROUND: Peripheral neuropathies are widespread disorders induced by autoimmune diseases, drug or toxin exposure, infections, metabolic insults or trauma. Nerve damage may cause muscle weakness, altered functionalities and sensitivity, and a chronic pain syndrome characterized by allodynia and hyperalgesia. Pathophysiological mechanisms related to neuropathic disease are associated with mitochondrial dysfunctions that lead to the activation of the apoptotic cascade.

OBJECTIVE: In a model of peripheral neuropathy, obtained by the loose ligation of the rat sciatic nerve (CCI), we describe a nerve apoptotic state that encompasses the release of cytochrome C in the cytosol, the activation of caspase 3, and the fragmentation of the genome.

RESULTS: Animal treatment with acetyl-L-carnitine (ALCAR), but not with L-carnitine (L-Carn) or Gabapentin, prevents apoptosis induction. ALCAR reduces cytosolic cytochrome C and caspase 3 active fragments expression in a significant manner with respect to saline treatment. Accordingly, ALCAR treatment impairs caspase 3 protease activity, as demonstrated by reduced levels of cleaved PARP. Finally, ALCAR decreases the number of piknotic nuclei. This protection correlates with the induction of X-linked inhibitor apoptosis protein (XIAP).

CONCLUSION: Taken together these results show that CCI is a valuable model to investigate neuropathies-related apoptosis phenomena and that ALCAR is able to prevent regulated cell death in the damaged sciatic nerve.

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