

Abstract

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Prevention of paclitaxel-evoked painful peripheral neuropathy by acetyl-L-carnitine: effects on axonal mitochondria, sensory nerve fiber terminal arbors, and cutaneous Langerhans cells.

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BACKGROUND: Prophylactic treatment with acetyl-L-carnitine (ALCAR) prevents the neuropathic pain syndrome that is evoked by the chemotherapeutic agent, paclitaxel. The paclitaxel-evoked pain syndrome is associated with degeneration of the intraepidermal terminal arbors of primary afferent neurons, with the activation of cutaneous Langerhans cells, and with an increased incidence of swollen and vacuolated axonal mitochondria in A-fibers and C-fibers. Previous work suggests that ALCAR is neuroprotective in other nerve injury models and that it improves mitochondrial dysfunction.

OBJECTIVE: Thus, we examined whether the prophylactic efficacy of ALCAR was associated with the prevention of intraepidermal terminal arbor degeneration, the inhibition of Langerhans cell activation, or the inhibition of swelling and vacuolation of axonal mitochondria.

RESULTS: In animals with a confirmed ALCAR effect, we found no evidence of a neuroprotective effect on the paclitaxel-evoked degeneration of sensory terminal arbors or an inhibition of the paclitaxel-evoked activation of Langerhans cells. However, ALCAR treatment completely prevented the paclitaxel-evoked increase in the incidence of swollen and vacuolated C-fiber mitochondria, while having no effect on the paclitaxel-evoked changes in A-fiber mitochondria.

CONCLUSION: Our results suggest that the efficacy of prophylactic ALCAR treatment against the paclitaxel-evoked pain may be related to a protective effect on C-fiber mitochondria.

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