

Carnitine supplementation improves insulin sensitivity and skeletal muscle acetylcarnitine formation in type 2 diabetes patients

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Background: We have previously shown that increasing free carnitine availability (via oral carnitine supplementation) resulted in elevated skeletal muscle acetylcarnitine concentrations and restored metabolic flexibility in impaired glucose tolerant (IGT) individuals. Therefore, we here investigated if carnitine supplementation elevates skeletal muscle acetylcarnitine formation and thereby improves insulin sensitivity and glucose homeostasis in type 2 diabetes patients.

Methods: 32 type 2 diabetes patients followed a 12-week L-carnitine treatment (2970 mg/day). A two-step hyperinsulinemic-euglycemic clamp was performed to assess hepatic and peripheral insulin sensitivity. *In vivo* skeletal muscle acetylcarnitine concentrations at rest and post exercise (30 minutes 70% Wmax), as well as intrahepatic lipid content (IHL) was determined by proton magnetic resonance spectroscopy (¹H-MRS). All measurements were performed before and after carnitine supplementation.

Results: Carnitine supplementation increased plasma free carnitine levels (from 35.6±1.3 to 54.7±1.7 μmol/L, p<0.01) indicating good compliance. Furthermore, we reported improvements in insulin-induced suppression of endogenous glucose (31.9±2.9 vs. 39.9±3.2 %, p=0.020) and peripheral insulin sensitivity (Δ rate of disappearance, ΔRd: 10.53±1.85 vs. 13.83±2.02 μmol/kg/min, p=0.005). Resting and post-exercise skeletal muscle acetylcarnitine concentrations were both elevated after carnitine supplementation (1.18±0.13 vs 1.54±0.17 mmol/kgww, p=0.008 and 3.70±0.22 vs. 4.53±0.30 mmol/kgww, p<0.001, respectively). A trend towards reduced plasma glucose levels (from 8.1±0.3 to 7.7±0.3 mmol/L, p=0.083) and IHL (from 14.7±2.6 to 12.8±2.2%, p=0.098) was found after carnitine supplementation.

Conclusion: The current study revealed very pronounced positive effects of carnitine supplementation on insulin sensitivity and a trend for an effect on intrahepatic lipid content and fasting plasma glucose levels in type 2 diabetes patients. Furthermore, we demonstrated that carnitine supplementation increases acetylcarnitine concentration in muscle, which may be underlying the beneficial effect on insulin sensitivity.