

Abstract

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Ameliorating hypertension and insulin resistance in subjects at increased cardiovascular risk: effects of acetyl-L-carnitine therapy.

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BACKGROUND: Insulin resistance, a key component of the metabolic syndrome, is a risk factor for diabetes mellitus and cardiovascular disease. Acetyl-L-carnitine infusion acutely ameliorated insulin sensitivity in type 2 diabetics with insulin resistance.

METHODS: In this sequential off-on-off pilot study, we prospectively evaluated the effects of 24-week oral acetyl-L-carnitine (1 g twice daily) therapy on the glucose disposal rate (GDR), assessed by hyperinsulinemic euglycemic clamps, and components of the metabolic syndrome in nondiabetic subjects at increased cardiovascular risk a priori segregated into 2 groups with GDR \leq 7.9 (n=16) or $>$ 7.9 (n=16) mg/kg per minute, respectively.

RESULTS: Baseline GDR and systolic blood pressure were negatively correlated (n=32; P=0.001; $r=-0.545$), and patients with GDR \leq 7.9 mg/kg per minute had higher systolic/diastolic blood pressure than those with higher GDR. Acetyl-L-carnitine increased GDR from 4.89 ± 1.47 to 6.72 ± 3.12 mg/kg per minute (P=0.003, Bonferroni-adjusted) and improved glucose tolerance in patients with GDR \leq 7.9 mg/kg per minute, whereas it had no effects in those with higher GDRs. Changes in GDR were significantly different between groups (P=0.017, ANCOVA). Systolic blood pressure decreased from 144.0 ± 13.6 to 135.1 ± 8.4 mm Hg and from 130.8 ± 12.4 to 123.8 ± 10.8 mm Hg in the lower and higher GDR groups, respectively (P<0.05 for both; P<0.001 overall) and progressively recovered toward baseline over 8 weeks posttreatment. Total and high molecular weight adiponectin levels followed specular trends. Diastolic blood pressure significantly decreased only in those with higher GDRs. Treatment was well tolerated in all of the patients.

CONCLUSION: Acetyl-L-carnitine safely ameliorated arterial hypertension, insulin resistance, impaired glucose tolerance, and hypoadiponectinemia in subjects at increased cardiovascular risk. Whether these effects may translate into long-term cardioprotection is worth investigating.

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