Letter to the Editor

Oral Acetyl-L-Carnitine Therapy and Insulin Resistance

To the Editor:

We reported recently that oral acetyl-L-carnitine supplementation improved hypertension in patients at increased cardiovascular risk, as well as whole body glucose use in those with advanced insulin resistance, but not yet diabetes mellitus. These findings led us to suggest that acetyl-L-carnitine treatment corrects a relative carnitine deficiency in this population. However, in a recent letter to the editor, Muniyappa states that oral L-carnitine supplementation cannot achieve the plasma carnitine levels required to increase skeletal muscle carnitine concentration and improve insulin sensitivity. He refers to previous studies suggesting an insulin-sensitizing effect of intravenous L-carnitine that he reports obtained plasma carnitine levels of ~600 μmol/L. It is unfortunate, however, that for those studies plasma carnitine concentrations were in fact not provided, whereas the actual concentrations obtained with the intravenous dose that was used in one of them had been reported previously to be ~160 μmol/L. Furthermore, although little is known about the bioavailability of oral acetyl-L-carnitine, the relevance of achieved plasma levels in explaining its mechanism of action is questionable, because this compound has already been reported to ameliorate other various disease states, including diabetic neuropathy.

Muniyappa is unaware of human studies suggesting that the insulin-resistant state is associated with carnitine deficiency. It is known that carnitine levels are low in patients with type 1 and type 2 diabetes mellitus and that they are lower in patients with chronic complications compared with patients without such complications. In rats, free intramuscular carnitine levels were lower in conditions related to insulin resistance, such as aging and obesity, and they correlated inversely with insulin resistance, as assessed by the homeostatic assessment model. Thus, it is reasonable to assume that in humans there is also a (relative) carnitine deficiency in the insulin resistant state and that oral acetyl-L-carnitine supplementation may improve this condition. Consistently in our study the antihypertensive effect of acetyl-L-carnitine increased with duration of treatment and only gradually decreased after oral supplementation was suspended. Moreover, 3 of 4 patients who regained normal glucose tolerance on acetyl-L-carnitine supplementation returned to their previous state of impaired glucose tolerance after acetyl-L-carnitine withdrawal.

As stated in our article, we performed a pilot study aimed to explore the hypothesis that chronic acetyl-L-carnitine supplementation may have beneficial hemodynamic and metabolic effects in subjects at increased cardiovascular risk. The results confirmed the hypothesis and provided the background for a randomized, double-blind clinical trial, which we are currently running (identifier NCT00984750), to formally test the effects of acetyl-L-carnitine compared with placebo on blood pressure, lipid and metabolic profile, and kidney function in type 2 diabetes mellitus hypertensive patients. This trial will also offer the opportunity to explore the possible mechanisms mediating these effects. However, the major task at this stage is to confirm the beneficial effects of acetyl-L-carnitine in subjects with diabetes mellitus. Because acetyl-L-carnitine is a cheap and remarkably well-tolerated drug, we hope it will prove to be a valuable addition to the still-limited possibilities that we have to treat diabetes mellitus and its associated comorbidity, independent of involved mechanisms.

Disclosures

None.

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