Improving the vitamin D status of vitamin D deficient adults is associated with improved mitochondrial oxidative function in skeletal muscle.
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Abstract
Objective: Suboptimal mitochondrial function has been implicated in several disorders in which fatigue is a prominent feature. Vitamin D deficiency is a well-recognized cause of fatigue and myopathy. The aim of this study was to examine the effects of cholecalciferol therapy on skeletal mitochondrial oxidative function in symptomatic, vitamin D-deficient individuals. Design: This longitudinal study assessed mitochondrial oxidative phosphorylation in the gastrosoleus compartment using phosphorus-31 magnetic resonance spectroscopy measurements of phosphocreatine recovery kinetics in 12 symptomatic, severely vitamin D-deficient subjects before and after treatment with cholecalciferol. All subjects had serum assays before and after cholecalciferol therapy to document serum 25-hydroxyvitamin D (25OHD) and bone profiles. Fifteen healthy controls also underwent P-31 magnetic resonance spectroscopy and serum 25OHD assessment. Results: The phosphocreatine recovery half-time ($\tau_{PCr}$) was significantly reduced after cholecalciferol therapy in the subjects indicating an improvement in maximal oxidative phosphorylation (34.44 ± 8.18 sec to 27.84 ± 9.54 sec, $P < .001$). This was associated with an improvement in mean serum 25OHD levels (8.8 ± 4.2 nmol/L to 113.8 ± 51.5 nmol/L, $P < .001$). There was no difference in phosphate metabolites at rest. A linear regression model showed that decreasing serum 25OHD levels was associated with increasing $\tau_{PCr}$ ($r = -0.41$, $P = .009$). All patients reported an improvement in fatigue after cholecalciferol therapy. Conclusions: Cholecalciferol therapy augments muscle mitochondrial maximal oxidative phosphorylation after exercise in symptomatic, vitamin D-deficient individuals. This finding suggests that changes in mitochondrial oxidative phosphorylation in skeletal muscle could at least be partly responsible for the fatigue experienced by these patients. For the first time, we demonstrate a link between vitamin D and the mitochondria in human skeletal muscle.