A Placebo-Controlled Trial of Acetyl-L-Carnitine and α-Lipoic Acid in the Treatment of Bipolar Depression

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Background: Bipolar disorder may be associated with mitochondrial dysfunction. Therefore, agents that enhance mitochondrial functioning may be efficacious in bipolar disorder. We performed a randomized placebo-controlled trial of the mitochondrial enhancers acetyl-L-carnitine (ALCAR) and α-lipoic acid (ALA) in patients with bipolar depression, and assessed markers of cerebral energy metabolism using phosphorus magnetic resonance spectroscopy.

Methods: We administered ALCAR (1000–3000 mg daily) plus ALA (600–1800 mg daily) or placebo for 12 weeks to 40 patients with bipolar depression and obtained imaging data at baseline, week 1, and week 12 of treatment in 20 patients using phosphorus 3-dimensional chemical-shift imaging at 4 T. Statistical analysis used random effects mixed models.

Results: We found no significant difference between ALCAR/ALA and placebo on change from baseline in the Montgomery-Asberg Depression Rating Scale in both the longitudinal (mean difference [95% confidence interval], −1.4 [−6.2 to 3.4], $P = 0.58$) and last-observation-carried-forward (−3.2 [−7.2 to 0.9], $P = 0.12$) analyses. ALCAR/ALA treatment significantly reduced phosphocreatine levels in the parieto-occipital cortex at week 12 ($P = 0.002$). Reduction in whole brain total nucleoside triphosphate levels from baseline to week 1 was associated with reduction in Montgomery-Asberg Depression Rating Scale scores ($P = 0.02$) in patients treated with ALCAR/ALA. However, this was likely a chance finding attributable to multiple statistical comparisons.

Conclusions: Treatment with ALCAR and ALA at the dose and duration used in this study does not have antidepressant effects in depressed bipolar patients and does not significantly enhance mitochondrial functioning in this patient group.

Key Words: bipolar disorder, depression; mitochondria, acetyl-L-carnitine, α-lipoic acid

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