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Dodecanedioic Acid Treatment in VLCAD Fibroblasts

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Abstract

Very-long-chain acyl-CoA dehydrogenase deficiency is the second most common disorder of fatty acid oxidation in the USA, with an incidence of 1:25,000-1:100,000 newborns (Tucci, Floegel, Beermann, Behringer, Spiekerkoetter, 2017, pg. 196). The current dietary therapeutic strategies are designed to avoid long chain fatty acids, instead providing carbohydrates and medium chain triglycerides as an energy source. Despite the controlled and biochemically balanced diet, it has a limited success in treatment of clinical symptoms and metabolic decompensations in VLCAD affected individuals. It has been proposed that defect in long chain fatty acids catabolic pathway leads to the severe energy deficiency, that primary reflected by depletion of citric acid cycle (TCA) intermediates. This research study explores the effect of dodecanedioic acid (DODA) as potential anaplerotic reagent in fibroblasts from healthy and documented VLCAD individuals. To investigate effect of DODA cells were depleted from glucose and supplemented with L-Carnitine and palmitic acid. Cells were treated for 16 hours with 50μM of DODA. Then, we analyzed levels of acylcarnitine TCA intermediates, fatty acids and glucose.

We found accumulation of long chain acyl carnitines (C14 and C16) in VLCAD fibroblasts which is consistent with the VLCAD presentation in human. We also observed increase in TCA intermediates levels, post DODA treatment indicating DODA anaplerotic effect, however, glucose levels were not rescued post DODA treatment. In conclusion, our data support that hypothesis that DODA can replenish TCA and thus it represents a potential anaplerotic therapy for VLCAD disorder.

Further studies in vitro are warranted to further explore DODA effects on energy metabolism.

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