No effect of oral ketone ester supplementation on exercise capacity in patients with McArdle disease: a randomized placebo-controlled cross-over study

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Patients with glycogen-storage-disease type V or McArdle disease (GSDV) have blocked glycogen utilization in skeletal muscle, leading to exercise intolerance, muscle pain and muscle damage. Ketone bodies (KBs) constitute an alternative fuel source, that potentially could fuel the working muscle independent of glycogenolysis. This study aimed to explore the effects of a drink with exogenous KBs on exercise capacity in patients with GSDV.

Eight GSDV-patients and four matched controls (HC) were included in this placebo-controlled cross-over study and randomized to receive either an oral supplement with 395mg/kg ketone esters (KE) or placebo first on two separate days 25 minutes prior to a submaximal cycle exercise test. The primary outcome measure was heart rate (HR) response to exercise. Secondary outcomes included perceived exertion (PE) and KB-, carbohydrate- and fat-metabolism as measured using stable isotope technique and changes in blood metabolites during submaximal exercise.

In GSDV, the KE-drink increased plasma KBs from 78.6 to 3289.9µmol/L (p=0.00008) and KB-oxidation (p=0.0001) but did not improve exercise capacity as judged by the primary outcome measure HR (p=0.120) and the secondary outcome measure PE (p=0.109) compared to placebo. Other secondary outcomes showed significantly lower concentrations of free-fatty-acids, glycerol and glucose with KE vs. placebo drink. Similar results were found in the HC-group.

This study indicates that an increase in KB-oxidation by oral KE-supplementation cannot fully compensate the KB-induced inhibition of lipolysis and glycolysis, explaining why the drink failed to improve exercise capacity. Thus, oral KE-supplementation alone cannot be recommended as treatment option for patients with GSDV.