Study into the effect of Triheptanoin in adults with McArdle Disease

Copenhagen Neuromuscular Centre, Denmark

My participation in the study

- David Thompson -

The aim of the research

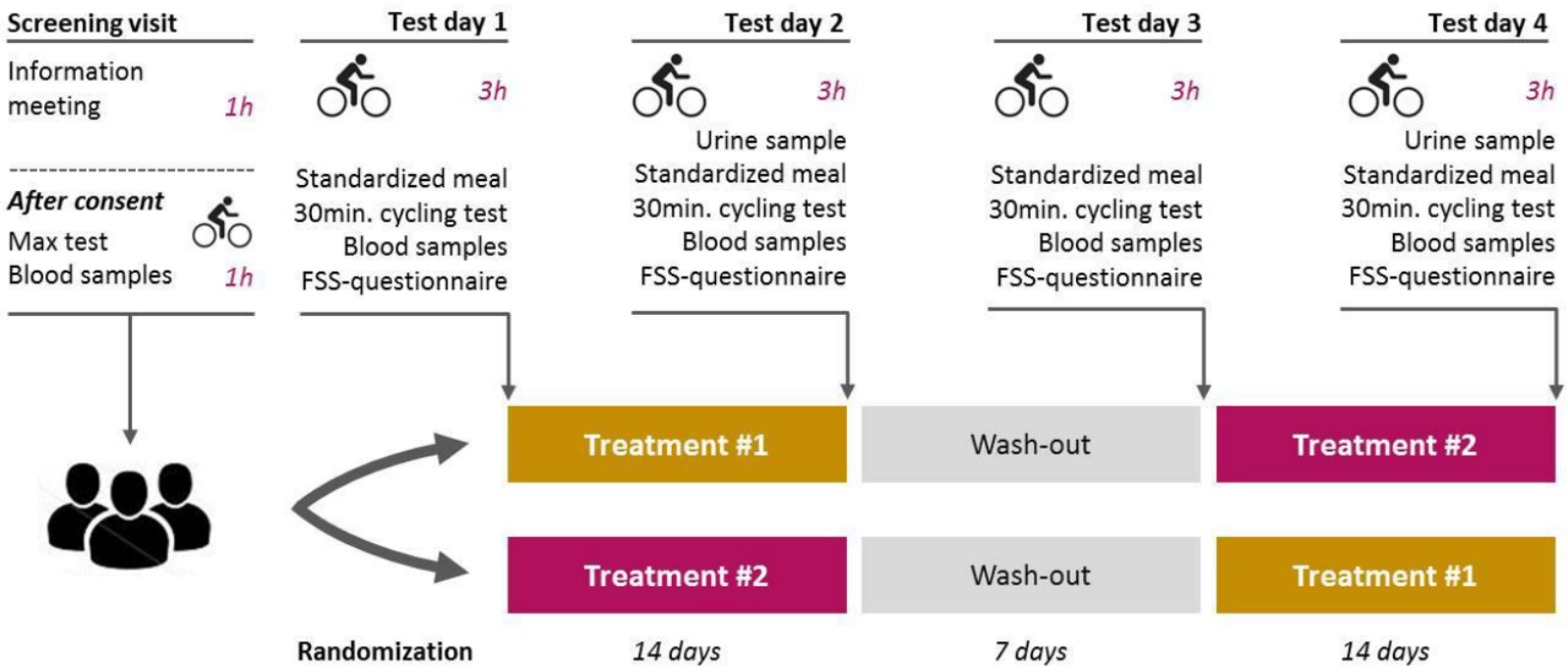
Triheptanoin is an oil with a special composition of fatty acids.

The study looked at whether Triheptanoin treatment could boost the breakdown of fat and increase the energy available for working muscles in McArdle patients.

What did it entail?

- For me the study period entailed four weekends in Copenhagen during February and March
- There were two treatment periods of 2 weeks separated by a 2 week wash-out period in between.
- During the first period, each participant took Triheptanoin oil or a placebo oil. *I had to take 95ml per day.* In the next period, we each took the opposite oil (Triheptanoin or placebo).
- During the treatment periods, we had to follow a diet low on sugar and fat and take the Triheptanoin oil as a supplement to our diet.
- Cycling tests in the laboratory were used to assess the effect of the treatment on our muscle performance.

Study overview



Max Test - This test was performed on the first day on a cycle-ergometer. I exercised for about 15 minutes with increasing resistance until I reached exhaustion. This test determined my maximal physical capacity.

- A facial mask was connected to a machine measuring oxygen (O2) consumption and CO2 production during exercise.
- Data was used to design the correct exercise test for the following visits.
- Blood samples were taken before exercise and at maximum exercise to measure metabolic products.

The “Cycle-ergometer”

Test Days

- Flight from Heathrow to Copenhagen in the evening.
- Overnight stay at the patient hotel.
- Standardized meal - *breakfast the next morning*.
- 30 minutes cycling test to evaluate physical performance and metabolism whilst measuring our O2-consumption and heart rate.
  - The initial 20 minutes was at a constant load corresponding to 65-70% of my maximal capacity. After 20 minutes, the load was increased gradually until it reached my maximal workload capacity.
  - O2-consumption and CO2 production were be measured, blood samples were taken from a small venous catheter in my elbow vein before and during the test. Urine samples were also taken.
- Taxi back to the airport and lunchtime flight back to Heathrow.

My Results

	After 20 min. exercise, constant load			At maximal load		
	Load (0-20 min)	Heart rate	Oxygen consumption	Load	Puls	Max. oxygen consumption
	Watts	*bpm*	*$L_{(O2)}$/kg/min*	*Watts*	*bpm*	*$L_{(O2)}$/kg/min*
Max-test				100	186	21.4
Visit 1	60	129	16.9	138	193	24.7
Visit 2	60	133	18.4	138	197	27.2
Visit 3	60	132	16.8	138	192	28.4
Visit 4	60	135	17.7	125	195	27.5

Published Results

No effect of triheptanoin on exercise performance in patients with McArdle disease - a double blind placebo-controlled crossover study

K. Madsen [1], P. Laforêt [2], A. Buch [1], M. Stemmerik [1], S. Hatem [2], D. Raaschou-Pedersen [1], N. Poulsen [1], M. Atencio [2], C. Ottolenghi [3], C. Jardel [2], R. Quinlivan [4], F. Mochel [2], J. Vissing [1]

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Patients with McArdle disease have blocked muscle glycogen breakdown due to an inherited defect myophosphorylase. This causes exercise intolerance with muscle pain, contractures and rhabdomyolysis. McArdle patients cannot increase fat oxidation to fully compensate for the energy deficiency due to a slow turnover in the tricarboxylic acid cycle (TCA). Metabolism of the 7-carbon fatty acid, triheptanoin, generates acetyl-CoA and propionyl-CoA, which enter the TCA and can therefore potentially boost fat oxidation in McArdle patients. In this double blind, placebo-controlled, crossover study we included 22 patients. Participants completed two 2-week treatment periods with a diet on triheptanoin or placebo oil (1g × kg-1 × day-1) separated by 1-2 weeks of washout. At baseline and at the end of the treatment periods, patients performed 20 minutes of submaximal exercise on a cycle ergometer followed by increments until exhaustion. Blood metabolites were measured every 10 minutes and exchange of O2. and CO2 was measured breath-by-breath. Nineteen patients completed the trial and qualified for data analysis. The patients had similar mean heart rates during submaximal exercise with triheptanoin (120±SD16 bpm) and with placebo treatment (121±SD16 bpm). Submaximal respiratory quotients were the same with triheptanoin (0.82±SD0.05) and placebo (0.84±SD0.03). They reached the same maximal workloads with treatment vs. placebo (105±SD38 vs. 102±SD31 Watts) and maximal oxygen uptake (1938±SD499 *vs.* 1977±SD380 mL × kg-1 × day-1). Blood glucose dropped with exercise to 4.6±SD0.8 *vs.* 4.4±SD1.0 mM and there was no difference in the production of ammonia with exercise (167±SD88 *vs.* 202±SD111 μM). Biochemical analyses of plasma TCA intermediates and fatty acids are ongoing. These preliminary data show no effect of triheptanoin treatment on exercise capacity and tolerance or muscle energy metabolism in McArdle patients.