Effects of a single oral dose of Ketone ester ON Exercise performance in patients with chronic Heart Failure

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON54508

Source
ToetsingOnline

Brief title
KETONE-HF

Condition

- Heart failures

Synonym
Heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: exercise performance, Heartfailure, Ketone ester

Outcome measures

Primary outcome

Rate and magnitude of change in PCr and Pi concentrations from baseline to maximum exercise. These parameters inform on the integrated homeostatic performance of oxidative and glycolytic ATP synthetic networks in muscle during exercise.

Secondary outcome

- Post-exercise recovery rate of PCr and Pi concentrations. These rates inform on mitochondrial ATP synthetic function

- Rates and magnitude of change in intramuscular pH during exercise and recovery. These parameters inform on the magnitude of anaerobic, glycolytic ATP synthesis.

- Maximal exercise performance.

Study description

Background summary

Heart Failure (HF) remains a devastating disease that is characterized with severe symptoms, frequent hospital admissions and a grim prognosis. HF currently affects 10% of the European population over 60 years of age and this number is expected to increase by 50% within the next decade, particularly among women (ref 1,2) Furthermore, 75 % of HF patients die within 8 years of the initial diagnosis, making the mortality for HF much higher than for most types of cancer (ref 1,2). New strategies to treat or prevent HF are therefore urgently needed.

Recent evidence from failing human and mouse hearts has suggested that the

reductions in carbohydrate and fatty acid metabolism are partially overcome by a compensatory increase in the ketone body oxidation. Moreover, the cardiac uptake of ketone bodies is increased in HF patients with both preserved and reduced ejection fraction.

Study objective

It has recently been demonstrated that the increase in ketone oxidation in the myocardium is protective and that ketone delivery to the heart can restore myocardial energetics (ref 9) Ketones are often referred to as efficient *super fuels* because ketone oxidation produces more net molecules of ATP per atom of oxygen than glucose and fatty acidsis. An additional merit of stimulating myocardial ketone oxidation in HF is that it does not influence the oxidation rates of glucose or fatty acid and therefore provide a true supplemental source of fuel.

Exercise intolerance is a hallmark of HF and is one of the earliest and most debilitating consequences of this syndrome. The current study will test if a simple sports drink containing ketones can improve exercise performance in HF patients

Study design

We will use a randomized, double-blind, placebo-controlled cross over design. Subjects will undergo the exercise MR examination twice, where they will be randomized to receive either a ketone ester or a placebo drink and subsequently undergo an exercise MR-spectroscopy study. After one to two weeks, subjects will cross-over and the exercise MR protocol will be repeated, this time receiving the other treatment

Intervention

ketone ester drink vs. placebo

Study burden and risks

The present study will provide insight into the change in oxidative skeletal muscle metabolism in patients with HF. The study aims to determine whether an oral dose of ketones can improve exercise performance in heart failure patients. The single oral administration of this potentially powerful nutritional compound will not be able to prevent or cure heart failure, but will hopefully improve quality of life by extending exercise capacity short term. Subjects do not directly benefit from participating in the present study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

HFrEF
- Chronic Heart Failure NYHA II - III
- LVEF<=40%
- Stable for the last 1 months prior to the study

HFpEF
- Chronic Heart Failure NYHA II - III
- HFpEF based on HFaPEFF score >= 5
- LVEF >= 45 %
- Stable for the last 1 month prior to the study

Exclusion criteria

HFrEF
- Age <18 years;
- Unable or unwilling to undergo exercise MRI (physical disabilities, claustrophobia);
- VO2peak >80% of expected and or/a cycling time of <8 minutes on recent exercise testing;
- Comorbidities which can influence study results such as muscular dystrophies, peripheral artery disease, insulin dependent diabetes mellitus, severe anaemia (defined as Hb <=6 mmol/L);
- Pregnant/trying to get pregnant/breastfeeding during the period from the first exercise test until 4 weeks after the last exercise test);
- Absolute contra-indications to undergo MRI according to the current UMCG protocols and guidelines (e.g. non-conditional medical device, recent device implantation, incompatible ferromagnetic objects in the body);
- BMI < 16 kg/m2; BMI > 40 kg/m2;
- Unable to understand study procedures;
- Unable or unwilling to provide informed consent.

HFpEF
- Age <18 years;
- Unable or unwilling to undergo exercise MRI (physical disabilities, claustrophobia);
- VO2peak >80% of expected and or/a cycling time of <8 minutes on recent exercise testing;
- Comorbidities which can influence study results such as muscular dystrophies, peripheral artery disease, insulin dependent diabetes mellitus, severe anaemia (defined as Hb <=6 mmol/L), hypertrophic cardiomyopathy with outflow tract obstruction and/or moderate to severe heart valve disease;
- Pregnant/trying to get pregnant/breastfeeding during the period from the first exercise test until 4 weeks after the last exercise test);
- Absolute contra-indications to undergo MRI according to the current UMCG protocols and guidelines (e.g. non-conditional medical device, recent device implantation, incompatible ferromagnetic objects in the body).
- BMI < 16 kg/m2; BMI > 40 kg/m2
- Estimated glomular filtration rate <30
- Unable to understand study procedures;
- Unable or unwilling to provide informed consent.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-03-2022
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	25-06-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL72044.042.19