Ketogenic diet therapy in patients with acromegaly

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To determine the effect of a 6-month eucaloric very-low-carbohydrate ketogenic diet on IGF-I levels in adult acromegaly patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53303

Source
ToetsingOnline

Brief title
KetoAcro trial

Condition

- Other condition

Synonym
acromegaly, giantism

Health condition

neuro-endocriene/hypofyse aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acromegaly, Diet, Ketogenic diet

Outcome measures

Primary outcome

Difference in IGF-1 (expressed as times the upper limit of the normal range (xULN)) between control and intervention group during 6 months of dieting (continuous).

Secondary outcome

Quality of Life (AcroQol), diet adherence, change in body weight, body composition, resting energy expenditure, handgrip strength and plasma parameters.

Study description

Background summary

Acromegaly is caused by a tumour located at the base of the brain in the pituitary gland that produces too much growth hormone (GH). Symptoms caused by the excess of GH, and consequently increased insulin like growth factor 1 (IGF-1), are disproportionate growth of body parts, fluid retention, snoring and excessive perspiration. The various metabolic changes that occur due to acromegaly increase the risk for insulin resistance, diabetes mellitus, arterial hypertension, sleep apnoea and thus an increased risk of cardiovascular disease if left untreated. The result is signs and symptoms, increased mortality, morbidity, and greatly reduced quality of life (QoL). Normalisation of GH and IGF-1 gives a normalisation of mortality, however morbidity and QoL do not (completely) normalise. After surgery, a somatostatin analogue is the primary medical treatment, however, normalisation occurs in only 40% of patients.
Recently, in a proof-of-principle study, we showed that a 2-week ketogenic diet (low in carbohydrates) in patients with somatostatin analogues could significantly reduce IGF-1 values. Patients felt better and sometimes even needed less somatostatin analogues. This proof of concept led to the new hypothesis that acromegaly patients with somatostatin analogues should possibly

be treated with a eucaloric low-carbohydrate ketogenic diet for a longer period of time to improve their biochemistry, symptoms and QoL. Additionally, this diet can make a significant contribution in the treatment of insulin resistance and glucose intolerance that often occur in this patient group.

In active acromegaly, glucose levels tend to be elevated, which is accompanied by high insulin levels. This GH-driven hyperinsulinemia results in an unwanted situation; the liver becomes even more GH sensitive. Redundant GH impairs insulin secretion and reduces glucose uptake, on behalf of lipolysis, release of free fatty acid (FFA), and hepatic glucose production. Insulin resistance is characteristic for the development of diabetes mellitus in patients with acromegaly.
Treatment with somatostatin analogs (SSAs) will suppress GH secretion from the adenoma and insulin secretion from pancreatic B cells. SSAs reduce insulin levels and increase HbA1c and postprandial glucose, with neutral effects on fasting plasma glucose (FPG). The effect of ketogenic diet therapy on glucose tolerance in acromegaly patients treated with SSAs is currently unknown.
Another treatment option for uncontrolled acromegaly is the GH receptor blocker pegvisomant. Pegvisomant treatment has favorable effects on glucose metabolism, lowering plasma glucose (FPG) and HbA1c. Unknown is whether under the circumstances of a ketogenic diet,if proteolysis or ketogenesis will prevail in acromegaly patients treated with pegvisomant, thus what will be the effect of the ketogenic diet.

Study objective

To determine the effect of a 6-month eucaloric very-low-carbohydrate ketogenic diet on IGF-I levels in adult acromegaly patients.

Study design

A single-centre randomised controlled trial

Intervention

A eucaloric ketogenic diet (30-40 g carbohydrate per day) for 3 months, followed by a less strict ketogenic diet (50-60 g carbohydrate per day) for another 3 months. The control group will receive a eucaloric diet according to the national healthy food guidelines/Mediterranean diet.

Study burden and risks

The extent of the burden of our study is considered low. Dietary restriction and the ketogenic diet have been proven feasible and safe in previous studies. For this study, three extra blood samples by 3 venepunctures are taken. No extra visits to the hospital or imaging studies are needed in order to obtain

all the information required for this study. Several standardized questionnaires are asked to be filled in during and after the diet. Mentioned questionnaires take about 30 minutes to complete. No other risks concerning the dietary intervention are to be expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Main study population
Patients (>=18 years) with active acromegaly will be recruited from the Pituitary Centre Rotterdam outpatient clinic of the Erasmus MC and via the *Nederlandse Hypofyse Stichting*, the national patient association. Our own cohort follows over fifty patients with acromegaly on somatostatin analogue monotherapy, and the National Patient Association approximately has 400 active members with acromegaly, making it likely that we will be able to reach the

planned number of patients.

Sub study population
Patients with uncontrolled acromegaly with pegvismant treatment, will start with ketogenic diet for three months, as a pilot study, with the same recruitement strategy and the same in- and exclusion criteria only without exclusion of pegvisomant.

Exclusion criteria

- Pregnancy or breastfeeding
- Pegvisomant treatment (not for subpopulation)
- Has undergone pituitary surgery or radiotherapy within 6 months prior to study entry;
- It is anticipated that the patient will receive pituitary surgery or radiotherapy during the study;
- History or presence of epilepsy;
- Participation in a trail of an experimental drug or device within 30 days prior to screening;
- Has a mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study
- Screening HbA1c > 6,5%;
- Use of systemic corticosteroids within 60 days prior to screening

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-06-2023

Enrollment:	70
Type:	Actual

Ethics review

Approved WMO Date:	24-04-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-06-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL83841.078.23