Short-term effects of a eucaloric ketogenic diet in acromegaly patients

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To assess the efficacy of two weeks eucaloric ketogenic diet on GH and IGF-I levels in acromegaly patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON46800

Source
ToetsingOnline

Brief title
Ketogenic diet in acromegaly

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Acromegaly

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acromegaly, Ketogenic diets

Outcome measures

Primary outcome

To assess the efficacy of two weeks eucaloric ketogenic diet on GH and IGF-I levels in acromegaly patients. The primary endpoints are the difference in GH and IGF-I levels before and after 2 weeks of ketogenic diet.

Secondary outcome

The secondary objective of the study is to evaluate whether ketogenic diet, might have a:

* blood glucose lowering effect;

* positive effect on the insulin secretion;

* induces weight loss;

* positive effect on the lipid profile, especially on triglycerides and free fatty acids

* broad safety range

This secondary objectives are measured by the following efficacy and safety parameters:

Blood biochemistry: (t0 =baseline, t1= week 1 and t2= week 2)

* IGF-1 levels

* GH levels

* IGF-BP1 levels

* Fasting plasma glucose, insulin, HbA1c levels, HOMA-IR

* Total cholesterol, HDL-cholesterol and LDL-cholesterol levels

* Triglycerides, free fatty acids

* AST, ALT, alkaline phosphatase, gamma-glutamyltransferase, lactate dehydrogenase (LDH)

Note: all the following laboratory evaluations will be performed at the study site.

Urine: (t1= week 1 and t2= week 2)

One voided sample of urine will be collected at the study site. One dipstick strip is used to measure ketones.

Vital signs: (t0 =baseline, t1= week 1 and t2= week 2)

Pulse rate and blood pressure were measured after 5 minutes of rest in the seated position at the outpatient clinic.

Anthropometric measurements: (t0 =baseline, t1= week 1 and t2= week 2)

Height and body weight were obtained at the outpatient clinic; patients will be weighted clothed without shoes. Body composition will be assessed at the outpatient clinic by Body Impedance Assessment. Waist-to-hip ratio were measured as follows. The waist was defined as the minimal abdominal circumference located midway between the lower rib margin and the iliac crest. The hip was defined as the wides circumference over the great trochanters. Circumferences were measured with the subjects in the standing position using

flexible tape measure and maintaining close contact with the skin without compression of underlying tissues.

One questionnaire: (t1= week 1 and t2= week 2) will be filled out at the outpatient clinic(*Vragenlijst gebruik en effecten dieetproduct*. In this questionnaire we assess the ease of use, safety and compliance.
One food diary (t0 =baseline, t1= week 1 and t2= week 2) will be filled out at the outpatient clinic. In this questionnaire we assess therapy compliance.

Study description

Background summary

In patients without biochemical control with LA-SSA monotherapy on maximum doses for at least 6 months, there are currently three therapy options: add or switch to Pegvisomant therapy, transsphenoidal surgery or radiotherapy. However, several studies shown in healthy subjects that when restricted carbohydrates are ingested, the decrease in portal vein insulin concentration can also lead to a reduction in IGF-I synthesis by the liver. The contribution of a eucaloric ketogenic diet, could provide the same decrease in IGF-I and GH levels in acromegaly patients. When ketogenic diet in acromegaly patients could provide normalisation of IGF-I levels and/or GH levels, it can be considered as fourth therapy option in patients without biochemical control with LA-SSA monotherapy. However, the effect of eucaloric ketogenic diet on IGF-I and GH secretion in acromegaly patients has not been studied yet.

Study objective

To assess the efficacy of two weeks eucaloric ketogenic diet on GH and IGF-I levels in acromegaly patients.

Study design

This will be a single-centre, prospective, proof-of-concept intervention study.

Intervention

All ten subjects received eucaloric ketogenic diet for two weeks (see figure 1 protocol). During this ad libitum ketogenic diet, emphasis is placed on polyunsaturated and monounsaturated fats (diet margarines, oils, fish, nuts). Moreover, we also supplement the diet with polyunsaturated and monounsaturated fats and therefore this diet is eucaloric (contains about the same number of calories subjects use each day).

Study burden and risks

Study participants will have 3 visits to the outpatient clinic over a period of 2 weeks. This comes down to 180 minutes in total. During this visits physical exam will be performed, 2 blood tubes of 2,5 cc and one voided sample of urine will be collected and two questionnaires will be filled out of 60 minutes in total. The usual burden for a single patient is 2-outpatient visits over a period of 1 year, which takes about 60 minutes in total and with the same volume of blood per visit.

Administering a eucaloric ketogenic diet did not produce any significant side effects for a longer period of time[1, 2]. Therefore, we expect it is safe to use a ketogenic diet for two weeks in our subjects. When ketogenic diet in acromegaly patients could provide normalisation of IGF-I levels and/or GH levels, it can be considered as fourth therapy option in patients without biochemical control with LA-SSA monotherapy on maximum doses for at least 6 months. Eucaloric ketogenic diet combined with LA-SSA and/or Pegvisomant therapy has potentially also the advantage that a lower LA-SSA or Pegvisomant dose is required to normalize IGF-I and/or GH levels .

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

-Written informed consent male or female aged * 18.
-Documentation supporting the diagnosis of acromegaly based on elevated GH and/or IGF-I levels due to a pituitary tumor
-The patient is treated with lanreotide Autogel or octreotide long-acting release (LAR) on maximum doses for at least 6 months and has a serum IGF-I level above 120% of the age- and sex adjusted normal limits.
-Subjects must be willing and able to comply with study restrictions and to remain at the clinic for the required duration during the study period and willing to return to the clinic for the follow-up evaluation as specified in the protocol.

Exclusion criteria

- 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.
- Has a history of epilepsy
- Has been treated with any unlicensed drug within the last 30 days before study entry.
- Has a mental condition rendering the subject unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude.
- Has abnormal baseline findings, any other medical condition(s) or laboratory findings that, in the opinion of the investigator, might jeopardize the subjects safety or decrease the chance of obtaining satisfactory data needed to achieve the objective(s) of the study.
- Diabetes type 1 or diabetes type 2 and using insulin
- Use of systemic corticosteroids within 60 days prior to screening
- Females of childbearing potential must be using contraception (we do not perform a pregnancy test), otherwise excluded from the study

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-08-2018
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	08-06-2018
Application type:	First submission
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

ID: 27621
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL64773.078.18
OMON	NL-OMON27621