KETOgenic diet therapy in patients with HEPatocellular adenoma

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to determine the effect of dietary restriction and the ketogenic diet on the regression of hepatocellular adenoma after 6 months.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatic and biliary neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON49811

Source
ToetsingOnline

Brief title
Ketohep(py)-Study

Condition

- Hepatic and biliary neoplasms benign

Synonym
Hepatocellular adenoma. Benign Livertumor

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: Dietary Restriction, Hepatocellular Adenoma, Ketogenic Diet, Weight loss

Outcome measures

Primary outcome

Our main study endpoint is the difference in tumour regression. The size (largest diameter in cm) of the largest hepatocellular adenoma found on MRI will be measured at T0 = time of inclusion and at T4= 6 months after start of the intervention. Mean regression will be calculated after which it will be compared to the regression in tumour size of our (earlier acquired) cohort and the subsequent internally validated model.

Secondary outcome

- Feasibility / Adherence to the ketogenic diet

- Change in plasma parameters: fasting glucose, fasting insulin, HbA1c, total cholesterol, HDL-cholesterol, LDL- cholesterol, free fatty acids, triglycerides levels, branched amino acids,

- Quality of life

- Change in body weight (kg)

- Change in body composition (fat mass / fat free mass)

- Resting Energy Expenditure

Study description

Background summary

Hepatocellular adenoma (HCA) is an uncommon, solid and benign liver lesion. Typically, it is a solitary lesion found in women within their reproductive years and it is strongly associated with the use of oral contraceptive medication (OC). Development of HCA is also associated with obesity and metabolic syndrome. More recently, studies have shown a rising incidence of HCA diagnosis, current prevalence is estimated to be between 0.001 and 0.004%. HCA

consists off several subtypes: inflammatory, steatotic, β-catenin mutation associated and unspecified. A higher BMI is associated with inflammatory HCA, which is also associated with multiple lesions. Steatotic HCA more often consist of single lesions.

Management of HCA requires a multidisciplinary approach. For female patients, it depends on the associated symptoms, lesion size and location. All female patients are advised to stop using OC and maintain a healthy body weight. Women with a HCA can be included in a surveillance period for 6 months, after which a contrast-enhanced magnetic resonance imaging (MRI) is performed. The aim is to predict if larger lesions (>5cm) will regress, thus avoiding unnecessary surgery. Treatment modalities to further enhance the regression and avoid surgery are an interesting research possibility. As overweight is frequently observed in women with liver adenoma, metabolic changes are assumed to play a role and diet may help to reduce tumor size.

Dietary restriction, defined as reduced intake of food without malnutrition, may be effective. It*s associated with metabolic changes, extended life span, lower risk of age associated diseases, improved fitness and increased resistance to acute stress. In combination with a ketogenic diet, it also reduces portal insulin concentrations, which down-regulate hepatic growth hormone receptors and reduces IGF-I synthesis. A recent study also shows the beneficial effect of eucaloric very-low-carbohydrate diet on disease control of acromegaly patients. Dietary restriction can be performed in different regimens such as short-term fasting or up to 30% reduced daily calorie intake. To explore the potential efficacy of dietary restriction, we aim to investigate whether the beneficial effects of a ketogenic diet with slight caloric restriction might increase the regression of HCA. This will further strengthen the treatment modality of close observation and avoid surgical resection.

Study objective

to determine the effect of dietary restriction and the ketogenic diet on the regression of hepatocellular adenoma after 6 months.

Study design

A single-centre pilot study

Intervention

Diet:
Month 1-3: Low carbohydrate, ketogenic diet containing approximately 1500 kcal, 35grams of carbohydrate and 0.8 g/kg of protein /day
Month 4-6: Moderate carbohydrate, ketogenic diet containing approximately 1500

kcal, 60grams of carbohydrate and 0.8 g/kg of protein /day

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 venous punctures 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 5-10 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:
Female subjects with a hepatocellular adenoma, who are advised to enter an initial surveillance period of 6 months after diagnosis, after reviewing their case by the multidisciplinary team of experts, including a hepatobiliary surgeon, a hepatologist and a liver radiologist.

Study subpopulation:
Female subjects with a hepatocellular adenoma, who after the initial surveillance period of 6 months including the regular treatment advice of losing weight and cessation of use of oral contraceptives, did not or only minimally (5mm) experience a reduction of the size of the HCA. Standard treatment for this subgroup after the 6 months of initial surveillance would consist of an additional surveillance period of 6 months, after which another MRI would be performed to assess the change in size of HCA.

Inclusion Criteria:
- Age 18-50 years
- BMI > 25 kg/m2
- Provide written consent

Exclusion criteria

- Current pregnancy or breastfeeding
- Diabetes Mellitus type 1 or 2
- Insufficient understanding of the Dutch language
- Participation in another clinical 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):	02-04-2021
Enrollment:	55
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	20-11-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-07-2024
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	NL75014.078.20