Safety and feasibility of the ketogenic diet in therapy resistand paediatric recurrent or progressive pontine glioma, a pilot study

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To establish the safety, feasibility and quality of life in children with recurrent of progressive pontine glioma who receive a ketogenic diet during a study period of 3 months

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON33175

Source
ToetsingOnline

Brief title
Pontine glioma and ketogenic diet

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
diffuse malignant brainstem glioma, malignant brain tumour

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: industrie,SHS International, Liverpool

Intervention

Keyword: child, ketogenic diet, pontine glioma, therapy resistant

Outcome measures

Primary outcome

determination of safety and feasibility of the ketogenic diet in children with

recurrent of progressive pontine glioma during study period of 3 months

Secondary outcome

stabilisation of neurological functioning

patient survival

Study description

Background summary

In the Netherlands each year approximately 150 children are newly diagnosed with a tumour of the central nervous system. 5% of these children are diagnosed with pontine glioma. Prognosis of children with malignant pontine glioma is extremely poor. With the present treatment protocol which consists of radiotherapy followed in case of tumour recurrence by oral Temozolomide the reported 2 year survival rate is only 5%.
Until now, no further treatment options remain after tumour recurrence or progressieve tumour growth during Temozolomide treatment. In a recent nation wide Dutch study on the effect of Temozolomide treatment of 40 children with recurrent ponsglioma after radiotherapy, survival after stop oral Temozolomide varied from 3-9 months.
New therapies to ameliorate survivalof this tumour with grim prognosis are urgently needed.
A high grade glioblastoma like pontine glioma is known for its high glucose consumption. Glucose is also the preffered energy stubstrate of normal neurons and glia but under fasting induced reductions of blood glucose these cells are also able to meet their energy requirement by metabolizing ketone bodies. In contrast, malignant brain tumour cells lack metabolic flexibility and for energy supply depend on glucose. When the patient is treated with a ketogenic diet (a high fat 70-90en% and low carbohydrate 5-19 en% diet) the glucose supply (read; energy supply) of the brain tumour in fact is beiing sabotaged.
The ketogenic diet as treatment for refractory childhood epilepsy has proven

its safety and efficacy and is widely acceptated as treatment modality in this patient group. There are two versions of the ketogenic diet widely used; the classical form (mainly in USA) and the MCT version of the diet (in Europe and Netherlands). There is no difference in effect of the two diets.
The work of the group of Prof Seyfridt USA has shown a 35-65 % reduction of braintumors on ketogenic diet in mousemodels with human braintumors A high grade glioblastoma.

Study objective

To establish the safety, feasibility and quality of life in children with recurrent of progressive pontine glioma who receive a ketogenic diet during a study period of 3 months

Study design

open label prospective pilot study (phase II)

Intervention

Ketogenic diet (first Classical version of the diet with shakes , soups and smoothies) after that the MCT version of the diet

Study burden and risks

The child has to use a stadaridized Ketocal formula for max of 2 weeks or until adequate level of ketosis (3-4+ blood ketones) is achieved. The ketocal formula consist of exchanges of shakes, soups and smoothies matching the individually calculated energy need of the child based on the results of a Indirect calorie measurement and a 3-days pre-diet food diary. At time of adequate and stable ketosis the child is allowed to substitute the shakes of soups into individually calculated meals based on the MCT version of the ketogenic diet.
Growth curve will be monitored closely.
Bloodglucose and bloodketones will be measured daily by parents until adequate and stable ketosis (3-4+) is reached and after that once a month.
Questionnair quality of life and Vineland behaviour scale will be noted at start of the study in outpatient clinic and at end of the study at home.
Adverse effects related to the diet will be noted on a questionnaire and communicated by mail or telephone by parents. In case of problems and worries parents can contact the nurse practioner by mobile phone. When necessary the nursepractioner will contact the dietitian or paediatric neurologist.
The child follows the diet as long as the child and parents want until the end of the study periode of 3 months which adequate ketosis (3-4+ bloodketones) is maintained.
Based on the results of this study the search for treatment therapies in

malignant and progressive brain tumours hopefully will set up new ways.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- recurrent or progressive pons glioma
- 1-18 years of age
- failure of treatment with radiotherapy and Temozolomide and no therapeutic options left
- good Dutch reading and writing (parents of caregivers)
- Informed Consent of parents/care givers and/or the child (when >12)
- willingness of children younger than 12 years to participate in the study

Exclusion criteria

- < 1 year or >17 year of age
- use of Temozolomide or other chemotherapeutic drug
- language barrier (parents or caregivers)
- current treatment with steroids of treated within 3 weeks before start of the study
- fatty acid disorders (like MCAD)
- Hypertrigyceridemia (> 10mmol/l)
- kidney stones
- diabetes mellitus
- pancreatitis
- gastro intestinal problems like persistent diarrhoea
- parents unable to handel dietary instructions

NB: use of tube feeding is NOT an exclusion criteria

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2010
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	02-02-2010

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

No registrations found.

In other registers

Register	ID
CCMO	NL28568.078.09