A comparison of Glycosade® and Uncooked Cornstarch (UCCS) for the dietary management of hepatic glycogen storage diseases (GSD)

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In light of the variability in response between UCCS and Glycosade® in patients with hepatic GSD (personal communication from authors and published data (Bhattacharya et al. 2007; Correia et al. 2008; Corrado M et al, 2013; Hubert A et al, 2013));...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON45944

Source
ToetsingOnline

Brief title
Glycosade® vs. UCCS in Hepatic GSD (GLYDE)

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
glycogenosis, metabolic disease

Research involving
Human

Sponsors and support

Primary sponsor: Vitaflo International Ltd
Source(s) of monetary or material Support: Vitaflo International Ltd.

Intervention

Keyword: dietary management, glycogen storage disease, uncooked cornstarch

Outcome measures

Primary outcome

The primary outcome for this study will be an increase in the duration of

normal blood sugar levels and / or delaying the development of significant

ketosis during dietary management with Glycosade® compared to dietary

management with UCCS (Part 1) as defined by:

a. Period of normal blood glucose levels (plasma glucose * 3.6 mmol/l)

increased by 60 minutes,

OR

b. A delay of 30 minutes in the development of significant ketosis in patients

with GSD III, VI, IX as defined by:

* BOHB * 1.0 mmol/L (participants < 14 years)

* BOHB * 0.4 mmol/L (participants * 14 years)

Secondary outcome

The secondary outcomes for this study will be:

1. The insulin area under the curve during dietary management with UCCS

compared to dietary management with Glycosade®.

2. The area under the curve in lactate, BOHB, during dietary management with

UCCS compared to dietary management with Glycosade®.

3. Tolerability & palatability of both Glycosade® and UCCS.

Study description

Background summary

The hepatic glycogen storage diseases (GSDs) comprise a group of rare inherited disorders of glycogen metabolism which arise due to one of a number of enzyme deficiencies. Hepatic GSDs comprise GSD I, GSD III, GSD VI & GSD IX. Patients are usually diagnosed in infancy and childhood and depending upon the type of GSD may present with:
* hypoglycaemia,
* hyperlipidaemia,
* hyperuricaemia,
* hyperlactataemia,
* hyperketosis,
* hepatomegaly
* lethargy,
* seizures
* faltering growth
(Chen 2001, Dagli, 2010).

The major metabolic consequence of hepatic GSD is hypoglycaemia provoked by relatively short fasts, and maintaining normal blood glucose has been shown to improve the secondary biochemical features;
* hyperlipidaemia,
* hyperuricaemia,
* hyperlactataemia,
* hyperketosis,
depending upon the individual enzyme deficiency, as well as some of the clinical parameters (Rake et al 2002a; Rake et al 2002b, Kishnani et al 2010). Thus the primary aim of dietary management of patients with GSD is achieving and maintaining normal blood glucose levels which have been shown to improve the secondary biochemical disturbances and promote normal growth.

The introduction of continuous overnight nasogastric glucose polymer feeds

demonstrated this clearly (Greene et al. 1976). The subsequent introduction of uncooked corn starch (UCCS) into the daily dietary management of these patients at least matched this improvement (Chen et al. 1993; Chen, Cornblath, & Sidbury 1984). Whilst the introduction of UCCS has dramatically improved the quality of life for patients with GSD, its use does have problems. For some, the duration of normal blood glucose levels can be very short with some studies suggesting that corn starch therapy only prevents hypoglycaemia for a median time of 4.25 hours in children (Weinstein & Wolfdorf 2002). Thus patients may need to be given another intake of UCCS through the night which has a considerable impact on the quality of life for the patient and families (Correia et al 2008). In addition many find UCCS neither palatable nor convenient, and for others there can be symptoms of bloating, flatulence and diarrhoea with large intakes (Lee, Dixon, & Leonard 1996). Whilst some of these gastrointestinal symptoms may be a feature of GSD itself they may be exacerbated by the use of UCCS (Sanderson et al 1991; Visser et al 2002). There is also some evidence that UCCS is only partially digested and can be associated with malabsorption (Bodamer et al. 2002).

The features of an ideal starch for the dietary management of patients with the hepatic GSDs include sustained normal blood glucose levels of approximately 8 hours without an excessive insulin rise and normalisation of other secondary biochemical abnormalities, palatability, convenience, well tolerated and maintenance of normal appetite (without excessive weight gain) (Correia et al 2008; Rake et al. 2002; Wolfsdorf et al 1990; Smit et al. 1984).

Recently, short and medium term studies conducted in patients with GSD I and III have found improved blood glucose control and improved nutritional outcomes with a physically modified corn starch, Glycosade® (manufactured by Vitaflo International Ltd, UK) (Bhattacharya et al. 2007; Correia et al. 2008). One study of GSD I patients showed that Glycosade® resulted in the improved maintenance of plasma glucose levels compared to UCCS (Correia 2008). Another study indicated a longer duration of normal blood glucose levels, a slower decrease in plasma glucose and a more rapid suppression of lactate with Glycosade® compared to UCCS (Bhattacharya et al. 2007). However, on an individual patient basis, not all patients have an increased duration of normal blood glucose levels with Glycosade® and some still appear to respond better to standard UCCS (personal communications from the investigators; Hubert A, 2013; Corrado M, 2013). The reasons for these potential differences in response remain unclear.

In light of the variability in response in patients with hepatic GSD, this study aims to establish if Glycosade® improves the dietary management of GSD. The trial is a randomised double blind cross over study comparing the short term changes in blood glucose, insulin and ketone levels of patients with hepatic GSD (Types I, III, VI and IX) following equivalent intakes of carbohydrate provided by UCCS and Glycosade® supplied by Vitaflo International Ltd, with the aim of identifying a starch which provides the greatest duration

of normal blood glucose levels for each patient.

Study objective

In light of the variability in response between UCCS and Glycosade® in patients with hepatic GSD (personal communication from authors and published data (Bhattacharya et al. 2007; Correia et al. 2008; Corrado M et al, 2013; Hubert A et al, 2013)); this study aims to establish whether Glycosade improves dietary management for patients with hepatic GSD (types I, III, VI & IX) compared to UCCS therapy by comparing the duration of normal blood sugars, lactate and ketone levels.

Study design

Participants will be randomised to receive either UCCS or Glycosade® for the initial intervention period crossing over to the other product for the second intervention period (part 1). Participants will continue in an open label part of the study for up to 24 months on the product considered most appropriate by the clinician and patient.

Intervention

At the end of the two intervention periods (i.e. the starch loads), the clinician will become unblinded to the dietary management and test starch the participant received in each period. The investigator/clinician will discuss which starch (Glycosade® or UCCS) and intake level is the most appropriate for the participant to continue for the open follow-up period of the study.

Study burden and risks

Participation in the trial puts patients at no greater risk than they would be exposed to outside of the trial, except for the additional DEXA forearm scan required at visit 5. However, this specific risk does not exist for patients at the UMCG, because -as discussed with the sponsor- MRI and DEXA scans will not be part of the trial protocol at the UMCG. These studies will only be performed after discussion with the patients, when they are indicated based on guidelines and clinical pathways. However the risks associated with this level of exposure are defined as Trivial (IPEM, 2002. Medical and Dental Guidance Notes. A Good Practice Guide on all Aspects of Ionising Radiation Protection in the Clinical Environment. Journal of Radiological Protection, 22(3), p.334. Available at: http://stacks.iop.org/0952-4746/22/i=3/a=705.). A greater dose increase would occur if someone, normally resident in York, took a holiday to Cornwall for 2 weeks.

During the open label phase of the study, participants will be regularly checking their blood sugar levels to assess glycaemic status as is routine

practice for this group of patients.

In respect of the starch load tests these will be carried out in a hospital setting and under the supervision of appropriately qualified study personnel.

In the UMCG the application of DEXCOM G4 subcutaneous continuous glucose sensor monitoring is standard of care. The system measures glucose each 5 minutes and is capable to alarm at low and/or quickly decreasing levels. The system will be provided during the entire trial when needed, for example during starch loading tests to improve safety.

Contacts

Public
Vitaflo International Ltd

Sefton Street 182
Liverpool L3 4BQ
GB
Scientific
Vitaflo International Ltd

Sefton Street 182
Liverpool L3 4BQ
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

See the study protocol, §6.1:;Patients with GSD I, III, VI or IX under the care of a metabolic centre meeting the following inclusion criteria:

* Diagnosed by either genetic mutation analysis or enzymology study (this includes patients with only a single mutation but who also have supportive enzymology consistent with the condition). For those whom mutation analysis is not completed this will be assessed during the study.
* Adults and children aged 2 years or older.
* Established on UCCS for at least 6 months to full dietary requirements as defined by local clinical practice.
* Freely given informed written consent from participant or parent/caregiver.

Exclusion criteria

See the study protocol, §6.2;* Evidence of any other medical condition which in the opinion of the Investigator makes it undesirable for the subject to participate in the trial or which would jeopardise compliance with the protocol.;* Women pregnant / breastfeeding at the start of the study or planning to become pregnant during its duration. ;Note: Women who become pregnant unexpectedly during this study can continue on the study product if they wish.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-04-2017
Enrollment:	16

Type:	Actual

Ethics review

Approved WMO Date:	30-11-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-07-2017
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
ClinicalTrials.gov	NCT02318966
CCMO	NL55112.042.15

Study results

Date completed:	14-08-2020
Actual enrolment:	12

Summary results

Trial is onging in other countries