Effects of sodium lactate infusion in patients with glucose transporter 1 deficiency syndrome (GLUT1DS)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders congenital
Study type	Interventional

Summary

ID

NL-OMON48362

Source
ToetsingOnline

Brief title
Lactate infusion in GLUT1DS

Condition

- Neurological disorders congenital
- Glucose metabolism disorders (incl diabetes mellitus)
- Seizures (incl subtypes)

Synonym
Glucose transporter 1 deficiency syndrome, GLUT1

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Children, Genetic disease, Glucose transporter 1 deficiency syndrome, GLUT1, Lactate infusion

Outcome measures

Primary outcome

Change in frequency or form of epileptic discharges on EEG.

The change in EEG will be measured by a neurologist experienced in reading

EEG*s.

Secondary outcome

Seizure frequency: Subjects will be recorded on video camera and seizures will

be monitored.

Laboratory measures: All measurements will be performed in blood samples, and

all samples will be analysed in laboratories of the Radboudumc.

- lactate concentration

- pH

- glucose

- sodium

- potassium

- chloride

- bicarbonate

Study description

Background summary

In glucose transporter 1 deficiency syndrome (GLUT1DS) cerebral glucose uptake from the systemic blood circulation is limited, because of deficient transport of glucose across the blood-brain barrier by the transporter protein (GLUT1). Classically patients present with developmental problems, movement disorders and severe epilepsy. There is no curative treatment for GLUT1DS, and anti-epileptic drugs usually have little to no effect. The ketogenic diet, providing ketones as an alternative energy substrate for the brain is an effective treatment option for the epilepsy and movement disorders in many GLUT1DS patients. Unfortunately, not in all GLUT1DS patients the ketogenic diet has a positive effect and other treatment options for these patients are very limited.
Traditionally, lactate is seen as a waste product of glycolysis during anaerobic conditions and a marker of ischemia. Interestingly, research has shown the beneficial side of lactate as an energy source for the brain, besides glucose and ketones. The aim of this study is to investigate whether lactate can be an alternative energy source for the brain of children with GLUT1DS, and as such can reduce seizures and epileptic discharges on EEG when intravenously administered in these patients.

Study objective

The purpose of this explorative study is to investigate whether treatment with lactate has any positive effect on the symptoms of GLUT1DS, especially the drug-resistant epilepsy.

Primary Objective:
- To assess changes in EEG during and shortly after the infusion of lactate.

Secondary Objective(s):
- To assess any changes in seizure frequency during and shortly after infusion of lactate.
- To assess any change in laboratory parameters during and shortly after infusion: lactate, pH, sodium, bicarbonate, chloride, potassium, glucose.

Study design

This is a single center, explorative, interventional, open-label proof of principle study in an hospital setting. The study will be conducted at the Radboudumc in Nijmegen and includes patients with GLUT1DS.
The duration of the study will be 4 months (1 month data collection, 3 months analyzing the data and writing an article). Patient participation is 1 day per patient.

Intervention

Sodium lactate will be administrated intravenously and we will use a primed

(0,10 mmol/kg/min for 15 minutes) continuous (0,06 mmol/kg/min for 105 minutes) infusion scheme, aiming at plasma lactate levels of 7,5-10 mmol/L. Dosage modifications will be performed if plasma lactate levels fall below 7 mmol/L or rise above 10.5 mmol/L.

Study burden and risks

Potential risks include hematomas and/or phlebitis following infusion, yet this is self-limiting. To reduce the risk of phlebitis, we will flush the catheter with 100 ml NaCl 0.9% after the lactate infusion. Some early studies have described that sodium lactate can induce panic attacks in patients with panic disorders, when a high dose of sodium lactate was rapidly infused, but substantial methodological problems (i.e. lack of specificity and sensitivity, disregard of baseline cofounders) render the evidence highly questionable. Such adverse effects have not been reported in later studies involving healthy volunteers and different patient groups
Based on all literature studied, (serious) adverse effects aren*t expected with the use of sodium lactate intravenously. Studies have showed that lactate concentration in blood can rise to more than 10 mmol/L during excersise, without any serious adverse effects. Multiple other studies have infused sodium lactate above physiologically rest values, without any (serious) side effects. Only mild shifts in electrolyte balance in blood, mild increase of pH blood are occasionally reported. No participants in earlier studies needed intervention for these effects, and values returned quickly to normal after treatment.
A benefit of participation in this study is that they could have a temporarily reduction of frequency of seizures and normalisation of their EEG. Most importantly, participation contributes to evidence based developing of new treatment options in the future, regarding the role of lactate in patients with GLUT1DS.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Diagnosed with GLUT1DS and known in our center.
Baseline characteristics include a high frequency of clinical seizures and epileptic discharges on EEG.
History of trying ketogenic diet with good compliance without beneficial effects.
Age > 6 years.
Informed consent.

Exclusion criteria

Additional medical condition or illness that impairs the patient*s ability to participate in the study (for example actual treatment of a malignancy, active infection, poorly controlled diabetes mellitus, hypertension, organ failure, clinically significant haematological or biochemical abnormalities).
Elevated serum sodium (> 145 mmol/L).
Participation in another interventional study at start of the study or during the study.
Presence of known panic disorders or a history of panic attacks.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-05-2022
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	09-06-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-05-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2019-003676-39-NL
ClinicalTrials.gov	NCT04112862
CCMO	NL71548.091.19