Clinical trial results:
The effect of lactate administration on cerebral blood flow during hypoglycemia

Summary

EudraCT number	2018-000684-82
Trial protocol	NL
Global end of trial date	14 May 2019

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022
Summary attachment (see zip file)	Paper Effect of lactate on CBF (Paper Effect of lactate on CBF.pdf)

Trial information

Trial identification

Sponsor protocol code	2017-3968

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03730909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands,
Public contact	clinical research centre nijmegen, Radboud umc, crcn@radboudumc.nl
Scientific contact	clinical research centre nijmegen, Radboud umc, crcn@radboudumc.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2019
Global end of trial reached?	Yes
Global end of trial date	14 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of intravenous lactate administration, compared to placebo, on thalamic (regional) CBF during euglycemia and hypoglycemia in patients with T1DM and normal awareness of hypoglycemia.

Protection of trial subjects:

We did not use specific measures to protect trial subjects

Background therapy:

-

Evidence for comparator:

We used saline 0.9% infusion as a comparator. This is often used as a placebo to compare results to the test product. We can use the same amount of saline as the test product and it looks the same (from the outside) so it is suitable to use in a blinded study.

Actual start date of recruitment	11 June 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	9
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment of patients between 11th of June 2018 and 14th of May in 2019.

Pre-assignment

Screening details:

Inclusion criteria: type 1 diabetes, age <50 years, BMI <30 kg/m2, and HbA1c levels not exceeding 9.0% (75 mmol/mol). Exclusion criteria:
medication other than insulin, presence of any other medical condition, micro- and macrovascular complications of diabetes en contraindications for MRI. Three participants withdrawn, two were replaced.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

We used bags to cover the sodium lactate and sodium chloride infusion fluids

Arms

Are arms mutually exclusive?	Yes
Arm title	Sodium lactate

Arm description:

Sodium lactate infusion day

Arm type	Experimental
Investigational medicinal product name	Sodium lactate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Sodium lactate 600 mmol/L
Sodium lactate infusion was started in a dose of 40 µmol/kg/min for 15 min, and then continued in a dose of 25 µmol/kg/min for
the remainder of the experiment

Arm title	Sodium chloride

Arm description:

Sodium chloride 0.9% infusion day

Arm type	Placebo
Investigational medicinal product name	Sodium chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Sodium chloride 0.9% 500 mL, administered in an equivalent volume as compared to lactate infusion

Number of subjects in period 1	Sodium lactate	Sodium chloride
Started	5	4
Completed	5	4

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description:

Ten subjects were included, three withdrew consent, two of them were replaced and therefore the results of nine subjects were analysed. Mean age was 23.0±3.6 years, 4 male and 5 female subjects. Mean weight was 75.1±13.7 kg, and BMI 23.6±2.8 kg/m2. Median duration of diabetes was 7.0 (3.0–10.5) years. Mean HbA1c was 7.1±1.0 % (54.2±11.1 mmol/mol).

Reporting group values	Overall trial	Total	
Number of subjects	9	9	
Age categorical			
Mean age 23.0±3.6 years			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	9	9	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
mean age 23.0±3.6 years			
Units: years			
geometric mean	23		
standard deviation	± 3.6	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	4	4	

End points

End points reporting groups

Reporting group title	Sodium lactate
Reporting group description: Sodium lactate infusion day	
Reporting group title	Sodium chloride
Reporting group description: Sodium chloride 0.9% infusion day	

Primary: Hypoglycemic symptom score

End point title	Hypoglycemic symptom score
End point description:	
End point type	Primary
End point timeframe: during hypoglycemia (45 minutes)	

End point values	Sodium lactate	Sodium chloride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: points				
number (not applicable)	26.7	26.1		

Statistical analyses

Statistical analysis title	T-test hypoglycemic symptom score
Comparison groups	Sodium lactate v Sodium chloride
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Notes:

[1] - Paired t-test for hypoglycemic symptoms during the two hypoglycemic glucose clamps

Secondary: Glucose infusion rates

End point title	Glucose infusion rates

End point description:

End point type	Secondary

End point timeframe:
during hypoglycemic glucose clamp

End point values	Sodium lactate	Sodium chloride		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	4		
Units: mg/kg/min				
number (not applicable)	3.7	3.5		

Statistical analyses

Statistical analysis title	T-test glucose infusion rate
Comparison groups	Sodium lactate v Sodium chloride
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 1 week after hypoglycemic clamp	
Assessment type	Systematic

Dictionary used	
Dictionary name	not used
Dictionary version	1

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)		
General disorders and administration site conditions			
Vasovagal syncope	Additional description: One participant experienced vasovagal syncope after cannulation of intravenous catheters. Duration several seconds and it resolved without any further interventions		
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Limitations: sample size, difference in electrolyte concentration between sodium chloride and sodium lactate

Notes: