Clinical trial results:
Effect of oral magnesium supplementation on insulin sensitivity in people with type 2 diabetes

Summary

EudraCT number	2021-001243-27
Trial protocol	NL
Global end of trial date	15 November 2022

Results information

Result version number	v1 (current)
This version publication date	23 November 2023
First version publication date	23 November 2023
Summary attachment (see zip file)	Magnesium study published manuscript (Published paper.pdf)

Trial information

Trial identification

Sponsor protocol code	77108

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1264-6218
Other trial identifiers	PaNaMa: 111728

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525 GA
Public contact	Internal Medicine, Radboudumc, +31 243618819, secretariaatstaf.aig@radboudumc.nl
Scientific contact	Internal Medicine, Radboudumc, +31 243618819, secretariaatstaf.aig@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	05 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2022
Global end of trial reached?	Yes
Global end of trial date	15 November 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of oral magnesium supplementation on insulin sensitivity in people with insulin-treated type 2 diabetes mellitus (T2DM) and a low serum magnesium concentration.

Protection of trial subjects:

Magnesium gluconate has a safe profile and the recruited subjects will receive magnesium in the same way as used in daily clinical care. Possible side effects of magnesium gluconate are gastro-intestinal symptoms like diarrhoea. Their was a weekly telephone consultation with the investigator to monitor possible side effects. The use of venous catheters may cause hematomas or phlebitis which are self-limiting. During the clamp there is a potential risk of developing hypoglycemia, yet this risk is very low because plasma glucose levels are frequently monitored and glucose 20% is continuously infused, the rate of which will be increased when glucose levels tend to fall. In ver 1000 clamps performed to date, severe hypoglycemia has never occurred.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2021
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: 14
Worldwide total number of subjects	14
EEA total number of subjects	14

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)	5

From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects will be recruited from the outpatient clinic of the Radboud University Medical Center. Patients will be asked to participate by their treating physician. Subjects are also recruited via social media and via advertisements on websites of patient associations.

Pre-assignment

Screening details:

A total of 30 participants were screened, 14 of whom were included (14 were excluded because their serum magnesium concentration was too high, 1 because of participation in another study, 1 because of a decreased renal function). First inclusion: 22-2-2022. Last inclusion: 3-8-2022.

Period 1

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

Blinding implementation details:

Randomisation to the order of treatment regimens will be performed by the pharmacy department to ensure the double blind study design.

Arms

Are arms mutually exclusive?	No
Arm title	Magnesium

Arm description:

Treatment with magnesium gluconate for 6 weeks, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml (15 mmol magnesium, equivalent to 360 mg).

Arm type	Experimental
Investigational medicinal product name	Magnesium gluconate oral solution 0.1 mmol/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution in bottle
Routes of administration	Oral use

Dosage and administration details:

50 ml three times a day, resulting in a daily dose of 150 ml (15 mmol magnesium, equivalent to 360 mg)

Arm title	Placebo

Arm description:

Treatment with placebo, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution in bottle
Routes of administration	Oral use

Dosage and administration details:

50 ml three times a day, resulting in a daily dose of 150 ml.
The placebo IMP fot this trial has the same qualitative composition as the "magnesium gluconate oral solution 0.1 mmol/ml", except magnesium gluconate. Furthermore, the placebo contains NaOH to adjust the pH to 5 (same pH as verum).

Number of subjects in period 1	Magnesium	Placebo
Started	14	14
Completed	14	14

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	14	14	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	67		
standard deviation	± 6	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	7	7	

End points

End points reporting groups

Reporting group title	Magnesium
Reporting group description:	
Treatment with magnesium gluconate for 6 weeks, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml (15 mmol magnesium, equivalent to 360 mg).	
Reporting group title	Placebo
Reporting group description:	
Treatment with placebo, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml.	

Primary: Change in insulin sensitivity after oral magnesium supplementation measured by the difference in mean glucose infusion rates during the final 30 minutes of a hyperinsulinemic euglycemic glucose clamp

End point title	Change in insulin sensitivity after oral magnesium supplementation measured by the difference in mean glucose infusion rates during the final 30 minutes of a hyperinsulinemic euglycemic glucose clamp
End point description:	
End point type	Primary
End point timeframe:	
During the final 30 minutes of a hyperinsulinemic euglycemic glucose clamp	

End point values	Magnesium	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	14		
Units: mg kg−1 min−1				
arithmetic mean (standard error)	4.6 (± 0.5)	4.4 (± 0.6)		

Statistical analyses

Statistical analysis title	Multilevel mixed-efects linear regression model
Comparison groups	Magnesium v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)

Notes:

[1] - It was a cross-over study, so 14 participants were included in the analysis because all participants participated in period 1 and period 2

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 22-02-2022 / 15-11-2022	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Magnesium
Reporting group description: Treatment with magnesium gluconate for 6 weeks, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml (15 mmol magnesium, equivalent to 360 mg).	
Reporting group title	Placebo
Reporting group description: Treatment with placebo, administered orally as a liquid solution of 50 ml three times a day, resulting in a daily dose of 150 ml.	

Serious adverse events	Magnesium	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Magnesium	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	3 / 14 (21.43%)	
Nervous system disorders			
Occipital neuralgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Gout			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			

Eczema	Additional description: Mycosis foot		
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2022	Inclusion criteria "serum magnesium concentration below or equal to 0.75 mmol/l" changed to "serum magnesium concentration below or equal to 0.79 mmol/l"

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/37922013