Effect of dapaglifozin on serum magnesium in HNF1β patients with renal hypomagnesemia

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This study has been transitioned to CTIS with ID 2024-518855-43-00 check the CTIS register for the current data. Primary objective: To evaluate the effect of SGLT2 inhibition with dapagliflozin 10 mg on serum magnesium in diabetic and non-diabetic...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON51437

Source
ToetsingOnline

Brief title
DAPA-MAG

Condition

- Nephropathies

Synonym
ADTKD-HNF1β, HNF1β-related ADTKD, HNF1β-related nephropathy

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Nierstichting

Intervention

Keyword: ADTKD-HNF1&beta, Dapagliflozin, Hypomagnesemia

Outcome measures

Primary outcome

Change in serum magnesium

Secondary outcome

- Renal fractional magnesium excretion

- Magnesium supplementation requirement

- Symptoms scored by symptom questionnaire

Study description

Background summary

Renal hypomagnesemia is caused by different inherited and acquired renal tubular disorders. One of these hereditary tubular defects leading to renal magnesium wasting is autosomal dominant tubulointerstitial kidney disease (ADTKD) subtype HNF1β. Patients with ADTKD-HNF1β can also suffer from diabetes mellitus (MODY5). Up till now, treatment of this renal hypomagnesemia only consists of magnesium supplementation, which is limited by the gastrointestinal side effects. Therefore, this treatment is often insufficient and an optimal treatment regimen for these patients is still lacking.
Sodium-glucose co-transporter type 2 (SGLT2) inhibitors are a relatively new type of glucose-lowering agents for patients with type 2 diabetes mellitus. SGLT2 inhibitors are also increasingly prescribed in patients with heart failure and chronic kidney disease, with and without diabetes mellitus, with beneficial effects on cardiovascular and renal outcomes. Furthermore, post hoc analyses of the large SGLT2 inhibitor trials in diabetes have demonstrated that treatment with SGLT2 inhibitors moderately increases serum magnesium. Recently, a case series reported three patients with diabetes and renal magnesium wasting (two patients had a genetically proven ADTKD-HNF1β) that were treated with SGLT2 inhibitors and had an even larger and clinically highly relevant increase in serum magnesium.
Since SGLT2 inhibitors have been demonstrated to increase serum magnesium and are also increasingly prescribed in non-diabetic patients without safety issues, these agents might be a novel treatment strategy for patients suffering

from renal magnesium wasting. We hypothesize that SGLT2 inhibition leads to a clinically relevant increase of serum magnesium in diabetic and non-diabetic ADTKD-HNF1β patients with renal hypomagnesemia.

Study objective

This study has been transitioned to CTIS with ID 2024-518855-43-00 check the CTIS register for the current data.

Primary objective:
To evaluate the effect of SGLT2 inhibition with dapagliflozin 10 mg on serum magnesium in diabetic and non-diabetic ADTKD-HNF1β patients with renal hypomagnesemia.

Secondary objectives:
- To evaluate the effect of SGLT2 inhibition with dapagliflozin 10 mg on renal fractional magnesium excretion in diabetic and non-diabetic ADTKD-HNF1β patients with renal hypomagnesemia.

- To evaluate the effect of SGLT2 inhibition with dapagliflozin 10 mg on symptoms in diabetic and non-diabetic ADTKD-HNF1β patients with renal hypomagnesemia.

Study design

Multicenter, crossover, placebo-controlled, randomized, double-blinded trial.
The study will take place at three hospitals in the Netherlands, namely at Radboudumc (Nijmegen), Erasmus MC (Rotterdam), and Amsterdam UMC (Amsterdam).

Intervention

Dapagliflozin 10 mg or placebo tablet, one tablet per day. Participants will receive dapagliflozin during one period and placebo during the other period.

Study burden and risks

The study comprises 4 study visits which include measurement of weight and blood pressure, blood sampling, 24-hour urine collection, 2-hour spot urine collection, and filling out a personalized symptom questionnaire. Furthermore, participants have to make two additional visits to the hospital for blood sampling and a 2-hour spot urine collection. At this timepoint, the investigator will also contact the participant by phone. Participants will have to take study medication for 8 weeks (2x 4 weeks), 1 tablet per day. The risks of treatment with dapagliflozin are considered to be minimal. Dapagliflozin is a registered drug in the treatment of patients with diabetes mellitus, heart failure and, chronic kidney disease. Therefore, a part of the participants will

already have a registered indication for treatment with dapagliflozin. The most important side effects of dapagliflozin are urinary tract infections, genital infections, back pain and polyuria. Due to the crossover design, all patients will be offered the interventional treatment with dapagliflozin, which means that all patients might benefit from the intervention. Based on the effect on serum magnesium described in recently published literature, we expect patients to benefit from the intervention. We expect that the chance of developing serious side effects outweighs the expected benefit for the participants.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Genetically proven ADTKD-HNF1β disease
- Renal hypomagnesemia (serum magnesium < 0.70 mmol/l)

- Age 16 - 75 years
- Informed consent

Exclusion criteria

- All other types of diabetes mellitus, including type 1 and type 2 diabetes
- History of kidney transplantation
- Receiving therapy with an SGLT2 inhibitor within 4 weeks prior to enrolment
- Previous intolerance for an SGLT2 inhibitor
- Pregnancy or lactation
- Use of loop diuretics or thiazide diuretics and inability to discontinue these medications before start of the trial
- eGFR < 30 ml/min/1,73m2
- Patients with severe hepatic impairment (Child-Pugh class C).

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-05-2023
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Forxiga

Generic name:	Dapagliflozin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-01-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2023
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
EU-CTR	CTIS2024-518855-43-00
EudraCT	EUCTR2022-000596-40-NL
CCMO	NL80578.091.22