Exploratory study into the effect of salt supplementation in Gitelman syndrome

Published: 08-09-2020
Last updated: 16-11-2024

To determine the effect of salt (NaCl) supplementation on (1) physiological parameters (such as serum potassium) and on (2) clinical signs and symptoms and quality of life.

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

Summary

ID

NL-OMON49231

Source
ToetsingOnline

Brief title
Salt supplementation in Gitelman syndrome

Condition

- Nephropathies

Synonym
Gitelman syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Gitelman syndrome, N-of-1 trial, Salt supplementation

Outcome measures

Primary outcome

- Serum potassium

- Personalized symptom scoresheet

- Gitelman symptom questionnaire (including the RAND SF-36 QoL score)

Secondary outcome

- Serum electrolytes (sodium, magnesium, chloride, bicarbonate, calcium),

aldosterone and renin

- Intracellular potassium (measured in erythrocytes)

- T helper 17 cell response in peripheral blood mononuclear cells (PBMC)

- 24-hour urinary excretion of potassium, sodium, chloride, magnesium, calcium,

creatinine, renin and aldosterone

- Blood pressure; including determination of orthostatic hypotension

- Body weight

- Bioimpedance measurement

- Muscle strength (measured by hand grip dynamometer)

- Potassium and magnesium supplementation requirement

Study description

Background summary

Gitelman syndrome is a rare, salt-losing tubulopathy due to inactivating mutations in genes encoding the thiazide-sensitive sodium chloride cotransporter (NCC). This leads to a decreased reabsorption of sodium chloride (NaCl) in the distal convoluted tubule, causing electrolyte disturbances and contraction of the extracellular volume. The clinical symptoms are mainly related to this contracted extracellular volume and ensuing electrolyte

disturbances, particularly hypokalemia and hypomagnesemia. Current treatment consists of advising a liberal dietary salt intake in combination with lifelong oral potassium and magnesium supplementation. Despite maximal tolerable treatment, normalisation of electrolytes is not achieved, patients often remain symptomatic and experience a reduced quality of life.
Since renal salt wasting is the primary cause of symptoms, high doses of salt supplementation added to an already liberal dietary salt intake might normalize extracellular volume, leading towards a better regulation of electrolytes, a reduction in symptoms and along with that an improvement of quality of life. Our preliminary data support this hypothesis.

Study objective

To determine the effect of salt (NaCl) supplementation on (1) physiological parameters (such as serum potassium) and on (2) clinical signs and symptoms and quality of life.

Study design

Multiple single-subject randomized double-blinded multi-crossover placebo-controlled trials (N-of-1 trials), executed at four collaborating centers. Each N-of-1 trial consists of 6 treatment blocks of 4 weeks (3 times intervention, 3 times placebo).

Intervention

Salt supplementation: 12 grams of NaCl per day. This will be administered in a double-blinded randomized order alternating with placebo capsules, each treatment block lasting for 4 weeks.

Study burden and risks

The burden comprises of taking extra capsules (NaCl capsules alternated with placebo), the collection of additional blood- and urine samples, filling out questionnaires and a few extra visits to the outpatient clinic (including measurement of blood pressure, bioimpedance and muscle strength during this visits). One of the theoretical risks of the study is the development of hypertension due to salt supplementation. However, it is not likely hypertension will occur because of the pathophysiology of Gitelman syndrome, being a salt-losing disorder characterized by a low blood pressure in which raising blood pressure is actually thought beneficial. All patients might benefit from the NaCl supplementation since all patients will get exposed to the intervention. Also, because of the N-of-1 trial design, this effect will be evaluated within each individual patient. If the intervention is successful in the individual patient, supplementation can be continued after finishing the

N-of-1 trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age: >= 16 years
- Genetically-proven Gitelman syndrome
- Informed consent

Exclusion criteria

- inability to discontinue potassium-sparing diuretics, MRAs and NSAIDs; this means inability to reach a potassium level of 2.5 mmol/L or higher with maximally tolerable potassium supplementation after discontinuation of potassium-sparing diuretics.
- patients who are pregnant at time of inclusion

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-04-2021
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	08-09-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-07-2021
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
CCMO	NL72495.091.19