Effect of amiloride on polyuria and well being in lithium treated patients

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Primary objective: to investigate the effect of amiloride on urine volume and urinary concentrating ability in patients on chronic lithium therapy suffering from polyuria.We hypothesize that amiloride therapy will improve urinary concentating...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Manic and bipolar mood disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON46002

Source
ToetsingOnline

Brief title
Polyuria in Lithium Treatment (PoLiTreat)

Condition

- Manic and bipolar mood disorders and disturbances
- Nephropathies

Synonym
Diabetes Insipidus. Frequent urination

Research involving
Human

Sponsors and support

Primary sponsor: Maasstadziekenhuis
Source(s) of monetary or material Support: Stichting Coolsingel;Wetenschapssubsidie Maasstad Ziekenhuis

Intervention

Keyword: Amiloride, Lithium, Polyuria, Treatment

Outcome measures

Primary outcome

Main endpoint is the change in 24 hour urine volume after intervention with amiloride therapy. To examine this, three 24 hour urine samples are collected. The first is collected at the beginning of the study, the second after first six weeks of treatment and the last after the final six weeks of treatment.

Secondary outcome

Assessment of quality of life (SF-36)

Frequency of sleep distrubance (ISI)

Assessment of the prevalence of diabetes insipidus in patients on lithium therapy

Other study parameters include changes in renal function or mean serum lithium concentration.

Change in urinary concentrating after study medication

Additionally changes in plasma renin and co-peptin will be assessed as measures of extracellular volume status and ADH activity.

Change in aquaporin clearance by urinary exosome excretion.

Study description

Background summary

Lithium is the most effective treatment for bipolar affective disorders. A frequently seen complication of lithium therapy is development of nephrogenic diabetes insipidus (DI). It occurs in 20% of all patients uring lithium. Oficially diabetes insipidus is diagnosed based on insufficient urine concentration. However in some reports up to 50% of patients using lithium report polyuria. In our experience patients reporting polyuria and polydipsia may benefit from therapy even as having partial diabetes insipidus. Typically amiloride is used to treat lithium-induced diabetes insipidus. We ai mto prove that amiloride therapy significantly reduces urine volume in patients that experience polyuria but do not necessarily classify as having diabetes insipidus. Additionally we aim to show that reduction in polyuria improves and sleep and increases quality of life.

Study objective

Primary objective: to investigate the effect of amiloride on urine volume and urinary concentrating ability in patients on chronic lithium therapy suffering from polyuria.

We hypothesize that amiloride therapy will improve urinary concentating ability and reduce polyuria in patients using lithium.

Study design

Patients will be approached in the psychiatric outpatient clinic of Antes, Delta Zorgboulevard. When patients report polyuria, a blood sample will be taken to obtain baseline measurements of sodium, potassium, lithium and creatinine, after which they will be screened by collecting a 24-hour urine sample. Patients with a 24-hour urine volume more than 3L, will be included in the study. Assessment of quality of life and sleep of participants will occur by means of filling out two questionnaires: the Short Form 36 Health Survey (SF-36) and the Insomnia Severity Index (ISI).
24-hour urine samples will be delivered at the outpatient department of nephrology and will be analyzed on volume, creatinine, albumin and aquaporin-2 excretion. An overnight water deprivation test will be performed on all participants to quantify renal concentrating ability. Patients will be instructed to deprive themselves of water intake during the night for at least 8 hours. Following water deprivation, patients will visit the outpatient department of nephrology for measurement of blood pressure, taking a blood sample (plasma sodium, potassium, creatinine, osmolarity, lithium, renin and co-peptin) and delivering a 24-hour urine sample (sodium, potassium, creatinine, osmolarity).

After randomization, patients will be assigned to a amiloride or placebo period. Patients will receive a daily dose of 10mg amiloride or placebo for 6 weeks. Two weeks after treatment initiation plasma lithium- and potassium

concentrations will be measured. If necessary, lithium dose will be adjusted. After 6 weeks, blood samples and 24-hour urine samples will be collected, SF-36 and ISI-questionnaires will be filled out and an overnight water deprivation test will be performed. Plasma lithium- and potassium concentrations will be measured again 2 weeks into the washout period. After a washout period of 6 weeks subjects will crossover to the other study arm. After 18 weeks, blood samples and 24-hour urine samples will be collected, questionnaires will be filled out and overnight water deprivation tests are performed. After 20 weeks final plasma lithium- and potassium concentrations will be measured.

In total each participant has 4 visits to the nephrology outpatient department to take blood samples, deliver urine samples, check blood pressure and evaluate general well being. Three more visits to the hospital are necessary to take blood samples for evaluation of lithium treatment, 2 weeks after initiation of the study, 2 weeks into the washout period and 2 weeks after completing the study. Outcome of blood and urinary analysis will be monitored and interpreted by the coordinating researcher. Any adjustment of lithium dosage will be performed by the treating psychiatrist.

Intervention

The intervention consists of 12 weeks of treatment, 6 weeks amiloride, 6 weeks placebo. Additionally, patients are instructed to undergo a water deprivation test three times, to fill out questionnaires three times and to collect 24-hour urine samples on four occasions.

Study burden and risks

The burden for all participants consists of filling out a questionnaire three times, taking a daily dose of one tablet for a total of 12 weeks (6 weeks placebo, 6 weeks amiloride), collecting 24 hour urine-volume on 4 different occasions performing an overnight water deprivation test three times, subsequently followed by hospital visits to take on blood sample and measure urine volume and osmolarity.

Additionally blood samples will be taken at baseline, after the first water deprivation test, 2 weeks after treatment initiation, at week 6, at week 8, at week 18 and at week 20

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the following criteria:
-Participant did not experience polyuria before commencing lithium therapy.
-All participants are aged 18 years and over.
-24 hour urine volume>3L

Exclusion criteria

-Inability to give informed consent
-Inability to complete overnight water deprivation test
-Patients aged under 18 years
-Pregnancy
-History of renal disease
-Usage of other diuretics that cannot be discontinued
-Presence of diabetes insipidus or other etiology
-Contraindications for amiloride therapy

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Amiloride
Generic name:	Amiloride
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	19-04-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	04-07-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2016-001107-23-NL
CCMO	NL57205.101.16