The effect of acetazolamide on lithium-induced nephrogenic diabetes insipidus in patients with an affective disorder: a pilot study

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To study the effect of acetazolamide on lithium-induced NDI.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON35668

Source
ToetsingOnline

Brief title
Acetazolamide in the treatment of nephrogenic diabetes insipidus

Condition

- Renal disorders (excl nephropathies)

Synonym
excessive urine production due to a diminished concentrating ability of the kidney as a result of the use of lithium, lithium-induced nephrogenic diabetes insipidus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: acetazolamide, lithium, nephrogenic diabetes insipidus, pilot study

Outcome measures

Primary outcome

Primary study parameters:

- maximal urine volume reduction after stimulation with dDAVP

- maximal urine osmolality after stimulation with dDAVP

Both parameters will be evaluated 7 days before and 28 days after the start of treatment with acetazolamide.

Secondary outcome

Secondary study parameters:

- subjective symptoms (frequency of micturition)

- vital signs (body weight and blood pressure)

- blood levels of sodium, potassium, chloride, bicarbonate, lithium, creatinine, haemoglobin and osmolality-

- urine levels of sodium, potassium, osmolality, urea and creatinine in morning spot urine samples

- side effects of acetazolamide treatment

- psychiatric outcome

All parameters will be evaluated 7 days before and on day 0, 7, 14, 21, 28 and 42 after the start of treatment with acetazolamide.

Study description

Background summary

In our lithium-induced nephrogenic diabetes insipidus mouse model we examined the effect of acetazolamide on water channel aquaporin-2 expression in vitro and its possible use as a therapeutic agents for lithium-induced nephrogenic diabetes insipidus in vivo. Our mouse model not only showed that acetazolamide had a beneficial effect on the development of lithium-induced neprogenic diabetes insipidus but also is a more potent drug than either thiazide, amiloride or a combination of both. Since acetazolamide is an already approved therapeutic drug we would like to test its efficacy in patients with lithium-induced nephrogenic diabetes insipidus.

Study objective

To study the effect of acetazolamide on lithium-induced NDI.

Study design

Phase II (pilot) study.

Intervention

After confirmation of the diagnosis lithium-induced neprogenic diabetes insipidus, eligible patients will be treated with acetazolamide for four week. The first two weeks, acetazolamide will be given in a dose of 1 x 250 mg/day. If no side effects occur, doses will be increased in the third and fourth week to 2 x 250 mg/day and 2x500 mg/day, respectively.

Study burden and risks

After an initial evaluation, patients will have to make six additional visits to the out patient clinic. At each visit, blood samples will be taken. In addition, patients will have to monitor their micturition frequency and urine volume by filling out the questionnaire each week. Patients will also undergo a dDAVP test at the first and last visit to examine their maximal urine concentration and to evaluate the efficacy of acetazolamide in improving this parameter.
No treatment benefits can be guaranteed to the study participants. However, patients may be rewarded from participation in the study. First, patients may benefit from a partial or complete recovery of the lithium-induced NDI. Furthermore, patients may also benefit from close monitoring that may be more than the standard of care. Finally, the information obtained from this study may improve the evaluation and further development of this therapy that may be helpful in treating patients with lithium induced NDI in the future. As a consequence of their participation in this study, patients may be exposed to adverse effects of acetazolamide. They will therefore be closely monitored

during and after treatment.

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

sex: men and women
age: 18 years and older
stable patients treated with lithium for an affective disorder
moderate to severe lithium-induced nephrogenic diabetes insipidus (max. urinary osmolality >150 and <600 mOsm/kg)

Exclusion criteria

pregnancy
diabetes mellitus
underlying renal disorders
significant cardiac/pulmonary comorbidity
heart rhythm disorders
pre-existent side effects of lithium treatment
treatment with hydrochlorothiazide or amiloride in the preceding 2 weeks
concomittant treatment with other diuretics
hypotension (systolic blood pressure <100 mm Hg)
renal insufficiency
hypo/hyperkalemia
hypercalcaemia
hypo/hyperthyroidism

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-01-2015
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Acetazolamide Sandoz 250
Generic name:	acetazolamide

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	08-02-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-02-2012
Application type:	First submission
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
EudraCT	EUCTR2011-005970-41-NL
CCMO	NL39068.091.11