Decline in renal concentration ability in lithium treated patients

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- to explore the decline in renal concentration ability (RCA) in a Dutch population of lithium treated patient - to explore the decline in kidney function

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nephropathies
Study type	Observational invasive

Summary

ID

NL-OMON50138

Source
ToetsingOnline

Brief title
Nephrogenic diabetes insipidus (NDI) in lithium treated patients

Condition

- Nephropathies

Synonym
lithium-induced nephrogenic diabetes insipidus; excessive

Research involving
Human

Sponsors and support

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

Intervention

Keyword: dDAVP, desmopressin, lithium, nephrogenic diabetes insipidus

Outcome measures

Primary outcome

Maximal urinary osmolality after intranasal administration of dDAVP.

Secondary outcome

- To determine the correlation between changes in kidney function and renal concentration ability

- To determine the number of patients with chronic kidney disease

- To determine the relation of the dDAVP test results with complaints (micturition history) and clinical parameters (duration of lithium therapy, plasma lithium concentration, baseline plasma creatinine, sodium and potassium concentration and baseline urinary osmolality) of lithium treated patients.

- To determine the correlation between renal concentration ability and clinical parameters (duration of lithium therapy, plasma lithium concentration, baseline plasma creatinine, sodium and potassium concentration and baseline urinary osmolality)

Study description

Background summary

Lithium is a common therapeutic agent used to treat patients with various mood disorders. In Western countries about 0.1% of humans are being treated with lithium. However, its use has been associated with several forms of renal injury. The most common presentation of lithium-induced nephrotoxicity is nephrogenic diabetes insipidus (NDI), characterized by resistance to vasopressin, polyuria, and polydipsia. Slightly impaired renal concentrating ability is found in about 50% of patients. Initially, the decreased urinary concentrating ability is largely reversible after cessation of lithium. However, continued treatment ultimately results in polyuria due to nephrogenic diabetes insipidus (NDI) in about 20% of patients. Nephrogenic diabetes

insipidus induced by lithium may even persist despite the cessation of treatment, indicating irreversible renal damage. This functional lesion is associated with chronic focal interstitial fibrosis predominantly in the medullary region of the kidney which may be progressive, leading to end-stage renal failure.
Lithium-induced nephrogenic diabetes insipidus results from accumulation of lithium in the collecting tubular cells after entry into these cells through the epithelial sodium channels (ENaC) in the luminal membrane. Lithium blocks vasopressin-induced reabsorption by inhibiting adenylate cyclase activity, and hence cyclic adenosine monophosphate production, and also by decreasing the apical membrane expression of aquaporin 2, the collecting tubule water channel. Besides polyuria due to nephrogenic diabetes insipidus, however, both central diabetes insipidus (CDI) and primary polydipsia have also been described in patients treated with lithium. Therefore, a dDAVP test should be performed to establish the correct diagnosis.
Lithium induced defects in urinary concentration can frequently be ameliorated by treatment with diuretics (thiazide, amiloride). In addition, early treatment with amiloride is thought to prevent the development of renal insufficiency. However, most patients with lithium induced nephrogenic diabetes insipidus only present with complaints in an advanced stage of the disease. Early recognition of an impaired urinary concentration may be helpful in selecting lithium treated patients at risk of severe nephrogenic diabetes insipidus and allow increased surveillance and an earlier start of treatment. In the current study we aim to explore the decline in renal concentration ability and nephrogenic diabetes insipidus in a Dutch population of lithium treated patients.

Study objective

- to explore the decline in renal concentration ability (RCA) in a Dutch population of lithium treated patient
- to explore the decline in kidney function

Study design

This is a retrospective cross-sectional study.

Study burden and risks

Patients may be exposed to the risk of adverse effects as a consequence of their participation in this study. Adverse reactions occurring most often (but still infrequently) include transient headache, nausea, nasal congestion, rhinitis nosebleed, sore throat, cough, upper respiratory infections and flushing occasionally along with mild abdominal cramps. In addition, intranasal DDAVP at high dosage infrequently produce a slight elevation of blood pressure. Since dDAVP is administered only once, there is no prolonged action and development of severe adverse reactions is thus unlikely. Furthermore, many of

these risks are substantially minimized by increased subject monitoring before, during, and after treatment.
Early recognition of an impaired urinary concentration may be helpful in selecting lithium treated patients at risk of severe nephrogenic diabetes insipidus and allow increased surveillance and an earlier start of treatment.
Finally, information obtained from this study may improve the evaluation and care for patients with lithium induced NDI in the future.

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

o included in the previous study
o men and women

o age >= 18 years

Exclusion criteria

general contra-indications for participation in a trial:
-inability to give informed consent
-pregnancy
-unstable psychiatric condition

alternative causes of (nephrogenic) diabetes insipidus:
- hypokalemia (plasma potassium < 3.5 mmol/l)
- severe hypercalcemia (albumin-corrected plasma calcium > 2.80 mmol/l)
- hyperglycemia (plasma glucose > 10.0 mmol/l)
- history of amyloidosis, Sjögren*s syndrome or Sickle cell anemia
- previous treatment with ifosfamide
- established primary polydipsia or central diabetes insipidus

contra-indications for dDAVP administration:
- inability to comply with water restriction
- renal insufficiency (GFR < 45 ml/min/1.73 m2)
- hyponatremia (plasma sodium < 130 mmol/l)
- instable angina pectoris
- decompensated cardial insufficiency
other:
- concomitant treatment with desmopressin or democlocycline

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-07-2022

Enrollment:	51
Type:	Actual

Ethics review

Approved WMO Date:	17-01-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-04-2022
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	NL72701.091.20