The role of Copeptin as a biomarker of volume status in pediatric polyuric tubulopathies

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To investigate copeptin levels in pediatric polyuric tubulopathies such as Nephrogenic Diabetes Insipidus (NDI), Renal Fanconi syndrome and Bartter syndrome to use it as biomarker for the volume state of these patients.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal and urinary tract disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON57173

Source
ToetsingOnline

Brief title
Copeptin study

Condition

- Renal and urinary tract disorders congenital
- Renal disorders (excl nephropathies)

Synonym
renal disease, tubulopathy

Research involving
Human

Sponsors and support

Primary sponsor: Cruces University Hospital
Source(s) of monetary or material Support: Beurs van ESPN (European Society for

Paediatric Nephrology)

Intervention

Keyword: Copeptin, Pediatric, Tubulopathy, Volume status

Outcome measures

Primary outcome

- To investigate copeptin levels in pediatric polyuric tubulopathies such as Nephrogenic Diabetes Insipidus (NDI), Renal Fanconi syndrome and Bartter syndrome to use it as biomarker for the volume state of these patients.

Secondary outcome

- Assess the relation between copeptin levels and other parameters of kidney function and water and salt homeostasis. In particular:

o eGFR;

o Serum electrolytes and acid base status;

o urine and plasma osmolality;

o urinary excretion of AQP2;

o urinary levels of cAMP;

o plasma renin and aldosterone levels;

o rate of growth.

Study description

Background summary

Polyuria is defined as an excessive urinary output of more than 40-50 mL per kg body weight per 24h, occurring as water or osmotic diuresis. Polyuria can be caused by excessive water intake, insufficient AVP secretion or kidney unresponsiveness to the hormone, and also as a consequence of several kidney

diseases. Some primary tubulopathies, such as nephrogenic diabetes insipidus, Bartter syndrome, cystinosis or Dent disease, frequently associate marked polyuria. In these entities, clinical measurement of volume status is relevant as chronic volume depletion has been associated with a permanent renin-angiotensin-aldosteron system activation. This, in turn may produce kidney fibrosis and kidney function deterioration over time. However, the assessment of volume status in clinical practice is difficult as measuring diuresis in children can be difficult, and other surrogates of volume status, such as plasma osmolality or arterial pressure rely on different factors other than intravascular volume. In this context, and knowing that copeptin can be easily measured and correlates with polyuria and volume status, the measurement of this molecule in patients with polyuric tubulopathies could help to differentiate patients who need a higher liquid intake to correct volume depletion.

Study objective

To investigate copeptin levels in pediatric polyuric tubulopathies such as Nephrogenic Diabetes Insipidus (NDI), Renal Fanconi syndrome and Bartter syndrome to use it as biomarker for the volume state of these patients.

Study design

The present study will be an explorative multicentric cohort study, conducted in the largest group of patients (50-100 patients) we will be able to involve in the study, in three different time points.

Methods:
- Sample collection and processing: Blood samples will be collected into chilled plastic tubes with disodium-EDTA and aprotinin and placed on ice before centrifugation (at 1600×g for 15 min at 4 °C) to collect the serum and stored at -80 °C Urine sample will be collected (added with proteasis inhibitors), centrifuged (3000rpm 10* at 4C) and stored at -80 °C.
- AQP2 excretion and cAMP measurements: The excretion of AQP2 in urine (u-AQP2) will be assessed by ELISA assay. The urinary excretion of AQP2 is proportional to its expression in the kidney and in the luminal membrane of collecting duct principal cells, representing a useful biomarker for the renal response to vasopressin (Valenti et al. 2000). Urinary cAMP levels will be measured by ELISA (Tsugawa et al. 1990).
- Measurement of serum copeptin: Serum copeptin levels will be assessed with TRACE (Time Resolved Amplified Cryptate Emission) technology (KRYPTOR COMPACT PLUS - THERMO FISHER).
- Measurement of serum renin and aldosterone: Serum renin and aldosteron levels will be assessed with CLIA (chemiluminescent immunoassay) technology (DiaSorin XL -PALEX).
- DDAVP test (once during any of 3 visits): Voluntary if not performed before,

as part of patient care.

Study burden and risks

Diary regarding intake and output: standard care in outpatient clinic visits (no additional burden)
Blood: 1 tube is drawn during blood collection for regular outpatient clinic visit (no additional burden)
Urine: 1 tube is collected durine planned urine collection for regular outpatient clinic visit (no additional burden)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Child <18 years of age;
• Diagnosis of polyuric tubulopathy including Nephrogenic Diabetes Insipidus (NDI), Renal Fanconi syndrome, Dent disease, cystinosis and Bartter syndrome, with molecular confirmation of the disease;
• Signed Informed Consent form;
• Native kidneys;
• eGFR >= 60 ml/min/1.73 m2 (for patients older than 1 year).

Exclusion criteria

• Advanced chronic kidney disease (CKD 3-5).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-01-2025
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	10-10-2024
Application type:	First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL85632.042.23