Overview

Useful For
The investigation of the differential diagnosis of patients with water balance disorders, including diabetes insipidus in conjunction with osmolality and hydration status

May aid in the evaluation of cardiovascular disease in conjunction with other cardiac markers.

Method Name
Immunofluorescent Assay

NY State Available
Yes

Specimen

Specimen Type
Plasma EDTA

Specimen Required

Patient Preparation: For water-deprived testing, have the patient fast and thirst for at least 8 hours (no liquids, including water, are allowed).

Collection Container/Tube: Lavender top (EDTA)

Submission Container/Tube: Plastic screw-top aliquot tube

Specimen Volume: 0.5 mL

Collection Information: Centrifuge and aliquot plasma. Do not submit in original tube.

Specimen Minimum Volume
0.3 mL

Reject Due To

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<tr>
<th>Gross hemolysis</th>
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<tbody>
<tr>
<td>Gross lipemia</td>
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<tr>
<td>Gross icterus</td>
<td>OK</td>
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<tr>
<td>Other</td>
<td>Original collection tube: plasma not poured off into an aliquot tube</td>
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Specimen Stability Information

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<th>Time</th>
<th>Special Container</th>
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Clinical and Interpretive

Clinical Information

Copeptin (also known as Copeptin proAVP or Copeptin AVP) and arginine vasopressin (AVP) are derived from the same precursor peptide. Copeptin has been proposed as a more stable, potentially superior, surrogate marker of AVP in the assessment of water balance disorders. Unlike AVP, copeptin is stable in plasma. Both copeptin and AVP are responsive to osmotic stimuli and increase in response to water deprivation. In healthy subjects, water deprivation causes the plasma osmolality to rise above approximately 280-290 mOsmol/kg, leading to the release of AVP and copeptin into the circulation. Copeptin increases gradually with fasting and water deprivation and declines rapidly after intake of water and/or food.

Diabetes insipidus (DI) is characterized by the inability to appropriately concentrate urine in response to volume and osmolar stimuli. The main causes for DI are decreased AVP production (central DI) or decreased renal response to AVP (nephrogenic DI).

The determination of the underlying disease pathology in patients with polyuria and altered plasma osmolality is often difficult. Polyuria can be related to insufficient AVP (central DI), reduced sensitivity to AVP (nephrogenic DI), or excessive water intake. Measurement of plasma copeptin concentration has been shown to be useful in the investigation of these AVP-related disorders. Additionally, utilization of copeptin has been proposed in the assessment of syndrome of inappropriate antidiuretic (SIADH).

Copeptin is also a marker of acute hemodynamic stress, and has been reported to aid in the prognosis or diagnosis of several cardiac disorders such as acute coronary syndrome, stable coronary artery disease, congestive heart failure, and acute ischemic stroke. Some studies have demonstrated that copeptin may improve prediction of mortality and heart disease outcome when combined with natriuretic peptides such as B-type natriuretic peptide (BNP) and N-terminal pro b-type natriuretic peptide (NT-proBNP).

Reference Values

Non-water deprived, non-fasting adults: <13.1 pmol/L

Water deprived, fasting adults: <15.2 pmol/L

Non-water deprived, non-fasting pediatric patients: <14.5 pmol/L

Note:


2. The reference interval for fasting and water deprived adults (at least 8 hours of fasting and water deprivation) was determined from an in-house Mayo study.


Interpretation

While secreted in equimolar concentrations in conjunction with arginine vasopressin (AVP), measured plasma
Concentrations of copeptin do not correlate strongly with AVP concentrations, due to in vivo and in vitro differences in stability. Copeptin is a more stable surrogate biomarker of AVP release. The clinical utility of copeptin, in conjunction with osmolality and hydration status, in the differentiation of polyuria and water balance disorders has been demonstrated in a number of studies.

In a prospective clinical study an algorithm was established based on patients with polyuria-polydipsia syndrome (n=55). A nonwater deprived baseline copeptin concentration of 21.4 pmol/L or greater was found to be consistent with the presence of nephrogenic diabetes insipidus (DI). In the algorithm found in Timper et al(3) patients with a copeptin concentrations of under 21.4 pmol/L, and a copeptin cut-off of 4.9 pmol/L after fluid deprivation was used to distinguish between complete or partial DI (<4.9 pmol/L) and primary polydipsia (> or =4.9 pmol/L).

Central DI may also be differentiated from nephrogenic DI by measuring copeptin during a stimulus for AVP release such as a water deprivation test. Copeptin concentrations obtained in the process of a water deprivation test can be difficult to interpret because of variation in water deprivation protocols. Patients with psychogenic polydipsia will either have a normal response to water deprivation or, in long-standing cases, will show a pattern suggestive of mild nephrogenic DI. Expert consultation is recommended in these circumstances.

Although the water-deprivation test is considered the reference standard for the evaluation of DI, measurement of saline stimulated copeptin was shown to be more accurate than the water-deprivation test.(4) In this indirect water deprivation test with a cutoff of 4.9 pmol/L or less indicated central DI while a concentration greater than 4.9 pmol/L indicated primary polydipsia.

An elevated plasma copeptin AVP concentration in a hyponatremic patient may be indicative of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). However copeptin determination alone is not typically sufficient to distinguish SIADH from other hyponatremic disorders.(5)

Elevations of plasma copeptin in patients with symptoms of heart failure may be prognostic of short and long term mortality. In patients with heart failure (HF) following a myocardial infarction (MI), elevations in copeptin are associated with severity of HF and poorer prognosis.(6) In a cohort of patients with class III or IV HF, copeptin concentrations of 40 pmol/L or greater significantly increased the risk of death or need for cardiac transplantation. The combination of elevated copeptin and hyponatremia was an even stronger predictor of heart failure, independent of B-type natriuretic peptide (BNP) and cardiac troponin (cTn) concentrations.(7)

**Cautions**

- Sepsis, severe sepsis, septic shock, lower respiratory tract infections and chronic obstructive pulmonary disease (COPD), cardiovascular diseases, ie, chronic heart failure may increase copeptin concentrations.

- Arginine vasopressin (AVP) receptor antagonist therapies and other diseases in which AVP has been shown to play an important pathophysiologic role may also increase copeptin concentration.

- In some cases bronchial carcinoma may lead to ectopic copeptin secretion.

- Mixed forms of diabetes insipidus (DI) can exist, and both central and peripheral DI may be incomplete, complicating the interpretation of results.

- Some patients who have been exposed to animal antigens, either in the environment or as part of treatment or imaging procedures, may have circulating antianimal antibodies present. These antibodies may interfere with the assay reagents to produce unreliable results.

**Clinical Reference**


Performance

Method Description

Copeptin proAVP is measured in this homogeneous automated immunofluorescent assay on the BRAHMS Kryptor Compact PLUS. The Kryptor Compact PLUS uses TRACE (Time Resolved Amplified Cryptate Emission) technology based on a nonradioactive transfer of energy. This transfer occurs between 2 fluorescent tracers: the donor (europium cryptate) and the acceptor (XL707). In the Copeptin proAVP assay, a sheep polyclonal antibody against C-terminal proAVP is labeled with europium cryptate and a mouse monoclonal antibody against C-terminal proAVP is labeled with XL707. Copeptin is sandwiched between the 2 antibodies, bringing them into close proximity. When the antigen-antibody complex is excited with a nitrogen laser at 337 nm, some fluorescent energy is emitted at 620 nm and the rest is transferred to XL707. This energy is then emitted as fluorescence at 707 nm. A ratio of the energy emitted at 707 nm to that emitted at 620 nm (internal reference) is calculated for each sample. Signal intensity is proportional to the number of antigen-antibody complexes formed, and therefore to antigen concentration.(Package insert: BRAHMS Copeptin proAVP Kryptor. ThermoFisher Scientific, Ver. R01 09/2015)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 8 a.m.-4 p.m.
Test Definition: CPAVP
Copeptin proAVP, P

Saturday; 8 a.m. -5 p.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
3 days

Specimen Retention Time
90 Days

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
84588

LOINC® Information

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