MAYO CLINIC LABORATORIES

Test Definition: CPAVP

Copeptin proAVP, Plasma

Overview

Useful For

Investigating the differential diagnosis for 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 (IFA)

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 vial
Specimen Volume: 0.5 mL
Collection Information: Centrifuge and aliquot plasma into plastic vial. Do **not** submit in original tube.

Specimen Minimum Volume

0.3 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Refrigerated (preferred)	7 days	

	Frozen	30 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

Arginine vasopressin (AVP) and copeptin (also known as copeptin proAVP or copeptin 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.

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 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:

*Keller T, Tzikas S, Zeller T, et al: Copeptin improves early diagnosis of acute myocardial infarction. J Am Coll Cardiol. 2010 May 11;55[19]:2096-2106. doi: 10.1016/j.jacc.2010.01.029

**In-house Mayo study.

***Du JM, Sang G, Jiang CM, He XJ, Han Y: Relationship between plasma copeptin levels and complications of community-acquired pneumonia in preschool children. Peptides. 2013 Jul;45:61-65. doi: 10.1016/j.peptides.2013.04.015

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 of differentiating polyuria and water balance disorders has been demonstrated in a number of studies, when used in conjunction with osmolality and hydration status.

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 a described algorithm,(1) 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, 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.(2) 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.(3)

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.(4) 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.(5)

Cautions

Sepsis, severe sepsis, septic shock, lower respiratory tract infections, chronic obstructive pulmonary disease, and cardiovascular diseases, eg, 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.

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human

anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Clinical Reference

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3. Fenske W, Stork S, Blechschmidt A, Maier SGK, Morgenthaler NG, Allolio B: Copeptin in the differential diagnosis of hyponatremia. J Clin Endocrinol Metab. 2009 Jan;94(1):123-129. doi: 10.1210/jc.2008-1426
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5. Miller WL, Grill DE, Struck J, Jaffe AS: Association of hyponatremia and elevated copeptin with death and need for transplantation in ambulatory patients with chronic heart failure. Am J Cardiol. 2013 Mar 15;111(6):880-885. doi: 10.1016/j.amjcard.2012.11.053
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10. Du JM, Sang G, Jiang CM, He XJ, Han Y: Relationship between plasma copeptin levels and complications of community-acquired pneumonia in preschool children. Peptides. 2013 Jul;45:61-65. doi: 10.1016/j.peptides.2013.04.015

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.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
Same day/1 to 3 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Rochester

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
84588

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CPAVP	Copeptin proAVP, P	78987-5

Result ID	Test Result Name	Result LOINC® Value
CPAVP	Copeptin proAVP, P	78987-5