Hypertonic Saline Infusion Test for Diabetes Insipidus

This is potentially dangerous and must be undertaken with great care. Patients unable to conserve water may rapidly become severely hypertonic during this test

An increase in serum osmolality is a strong stimulus for AVP release via the hypothalamic osmoreceptors. Administration of hypertonic saline intravenously will produce a hyperosmolar state, causing maximal stimulation of AVP secretion. Serum copeptin, the C-terminal glycoprotein of the AVP prohormone, is measured as a more stable marker of AVP secretion and is present in approximately equimolar concentrations. Serum copeptin is reported in relation to serum osmolality and assessed using a normogram. Serum copeptin and AVP levels have been shown to agree well.

Indications

To make a clear diagnosis of central diabetes insipidus (CDI) in subjects with polyuria and normal serum osmolality.
This is a specialist investigation and should only be conducted after referral to Endocrinology and performed as an inpatient.
Nephrogenic DI may be investigated using a paired random co-peptin and osmolality with co-peptin levels > 21.4pmol/L suggestive of nephrogenic DI.

Contraindications

Patients with epilepsy, cerebral or cardiovascular disease.

Side Effects

There is a serious risk of dehydration in patients with DI.
The hypertonic saline may induce thrombophlebitis at the site of the infusion.

Requirements

- 14 x brown top serum sample tubes
- 5% saline
- *iv* cannula
- (note orange Li Hep tubes also acceptable for co-peptin

Procedure

PATIENT PREPARATION

Fast from midnight prior to the test. Water only to be consumed, no more than 500ml. No tea, coffee, alcohol or smoking after midnight.

Weigh the patient.

TEST

Inform the Biochemistry laboratory that the samples for copeptin will be arriving so that samples can be processed promptly. Samples should arrive within 2hrs.

- A thirst chart should be completed throughout the test
- BP should be measured at regular intervals throughout the test

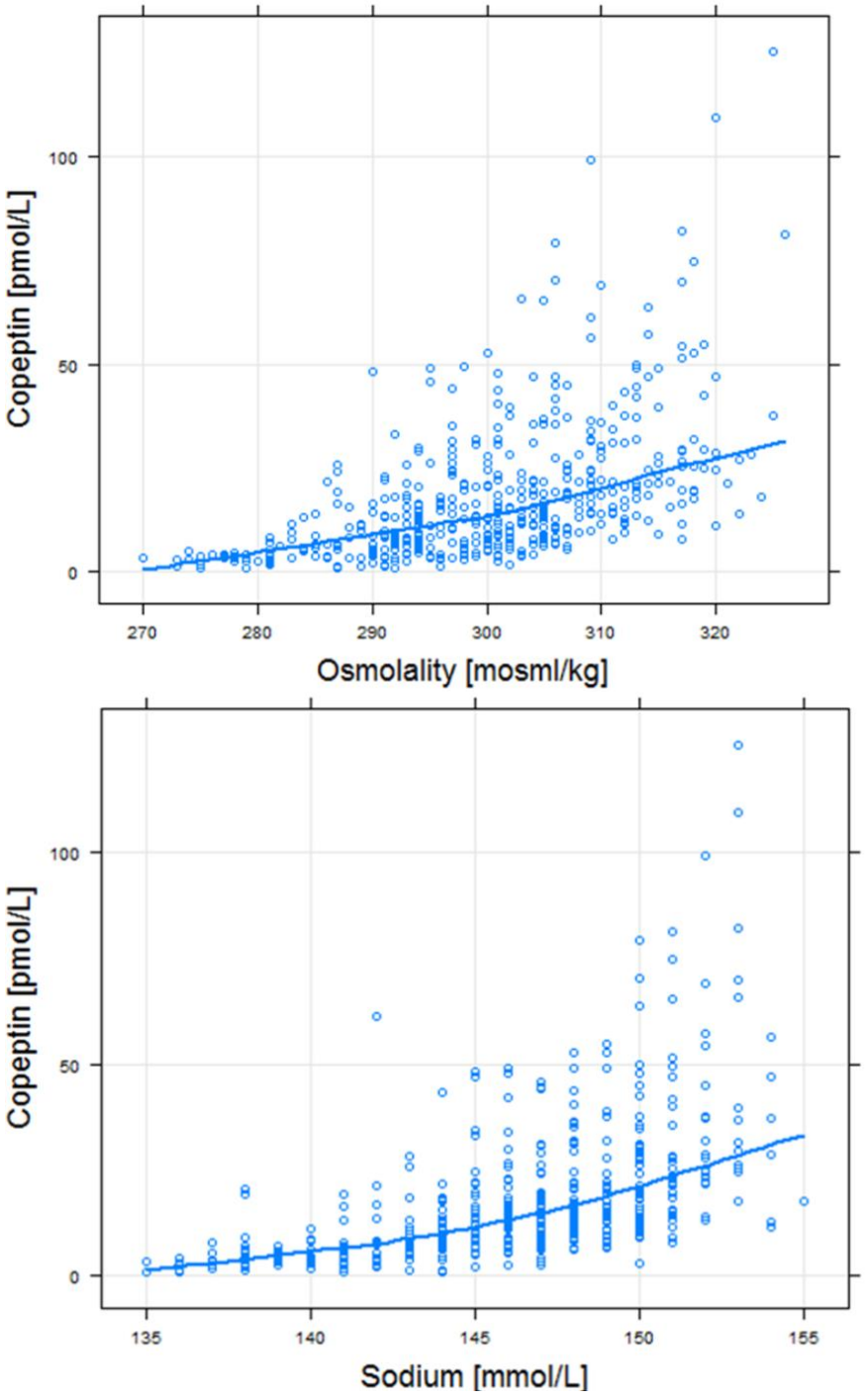
Minutes	Procedure	Samples
-30	Basal Sample	1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
0	Infuse 5% saline 0.06ml/kg/min for 2 hours	1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
30		1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
60		1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
90		1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
120	STOP SALINE INFUSION	1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)
135		1 x brown top serum (osmolality, Na) 1 x brown top serum (copeptin)

Note Copeptin samples are referred to Royal Victoria Hospital, Newcastle-upon-Tyne, for analysis and reported versus a normogram.

Interpretation of results
Patients with primary polydipsia have normal copeptin rise in response to the hyperosmolar state induced by the procedure. Patients with central diabetes insipidus have little or no rise in copeptin.

Results that fall within the central area of the graph indicate a normal response. Points falling to the right show decreased copeptin (and therefore AVP) relative to normal osmoregulation and indicate central DI.

Correlation of Co-peptin levels with plasma osmolality and sodium results from 91 healthy individuals (blue data points)[3]



Reference[3]

Schnyder et al.(2015) Physiological area of normality of co-peptin in normal-to-hyperosmolar states. Endocrine Abstracts 37:EP706.