Hypertonic Saline Infusion Test

Test Name: CHILD HYPERTONIC SALINE INFUSION TEST

Not commonly used

This test is potentially dangerous (it is very rarely used in children) and must be undertaken with great care. Patients unable to conserve water may rapidly become severely hypertonic during this test.
This test requires a doctor to be present throughout.

Principle

This test is designed to stress the integrity of the renal-AVP axis, in order to assess posterior pituitary function, providing reliable information regarding the relation between plasma osmolality and AVP. The infusion of hypertonic saline raises plasma osmolality and ensures maximal stimulation of AVP secretion. The failure of maximal renal concentration of urine does not help differentiate which organ is performing sub-optimally. The diagnosis can be seen by comparing the response of plasma AVP to plasma osmolality using the Newcastle chart (Prof P.H. Baylis).

Indication

- This test is performed if the results of the water deprivation test are equivocal: the test can be useful in differentiating partial forms of AVP disorders and to demonstrate normal osmoregulation in patients with primary polydipsia. This test is also indicated when investigating patients with adipsic or hypodipsic hypernatraemia. A subjective thirst score maybe performed at the same time and requires copies of the unit-less 100 mm linear visual analogue scale.

Precautions

- Contraindicated in patients with epilepsy, cerebral or cardiovascular disease.

Side Effects

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

Preparation

The laboratory MUST be notified AT LEAST 24 hrs before the test, ideally with more notice. Osmolality results are required as soon as possible after the specimens have been collected.

- Overnight food fast from midnight the day before the test
- Only water maybe drunk until the time of the test; other drinks are not permitted after midnight.
- No smoking during period of food fast
- Absolute food/fluid fast during the infusion period
- Assess to exclude the presence of any confounding factor e.g., hypercalcaemia, hypokalaemia, glycosuria or any other cause of a dilute solute diuresis, prior to commencing the test.
- Cortisol insufficiency must be treated prior to doing a water deprivation test as it interferes with the ability to excrete water and can mask AVP disorders.

Protocol

1. Patient instructed to empty bladder. Measure urine volume and osmolality
2. Weigh patient
3. Patient to lie supine where they will remain for the remainder of the test.
4. Insert cannula into antecubital veins of both arms. Allow patient to rest for 30 min.

5. Blood pressure monitored every 5 min during the 30 min preceding the test and throughout the infusion period.
6. Take blood for copeptin and osmolality
7. Repeat blood sample after 15 min
8. Begin infusion of 5% (0.85 mol/L) sodium chloride at 0.05 mL/kg/min for 2 hours into non-blood sampling arm via an indwelling cannula for a max of 3 hrs or until a plasma osmolality of 300 mmol/kg is achieved.
9. Take blood samples at 30 min intervals for copeptin and osmolality
10. Measure volume and osmolality on all urine passed.

Note time at which thirst is noted - if patient very thirsty during test, give ice chips

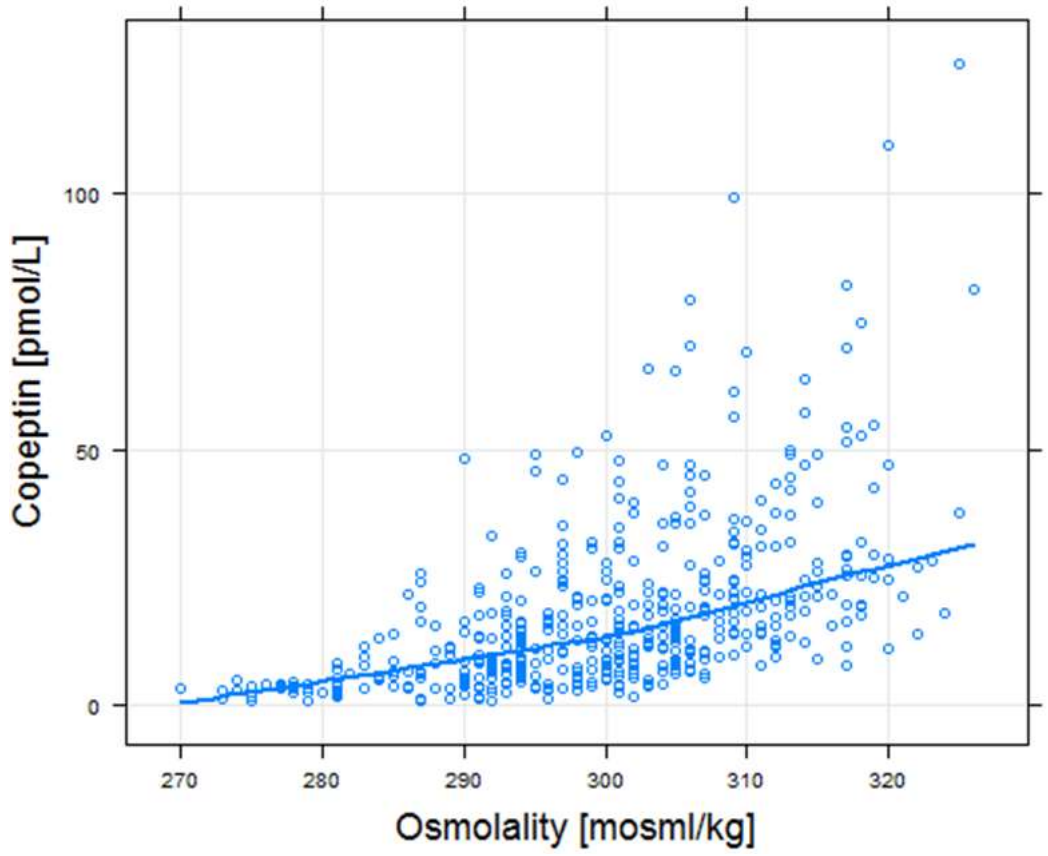
11. Take final blood sample 15 min after completion of infusion.
12. Record blood pressure, urine volume, blood sampling, patients' comments
13. Allow patient to drink after test. Avoid ingestion of large fluid volumes.

Samples

Plasma osmolality & sodium	1.2 mL lithium heparin blood (orange top)
Copeptin	1.2 mL lithium heparin blood (orange top)

Interpretation

Patients with primary polydipsia or AVP-resistance have normal AVP and copeptin release in response to the hyperosmolar state induced by this procedure. Patients AVP-deficiency have little or no rise in AVP and copeptin.



A. Correlation of Copeptin levels with plasma osmolality results from 91 healthy individuals (blue data points)[5]

Copeptin

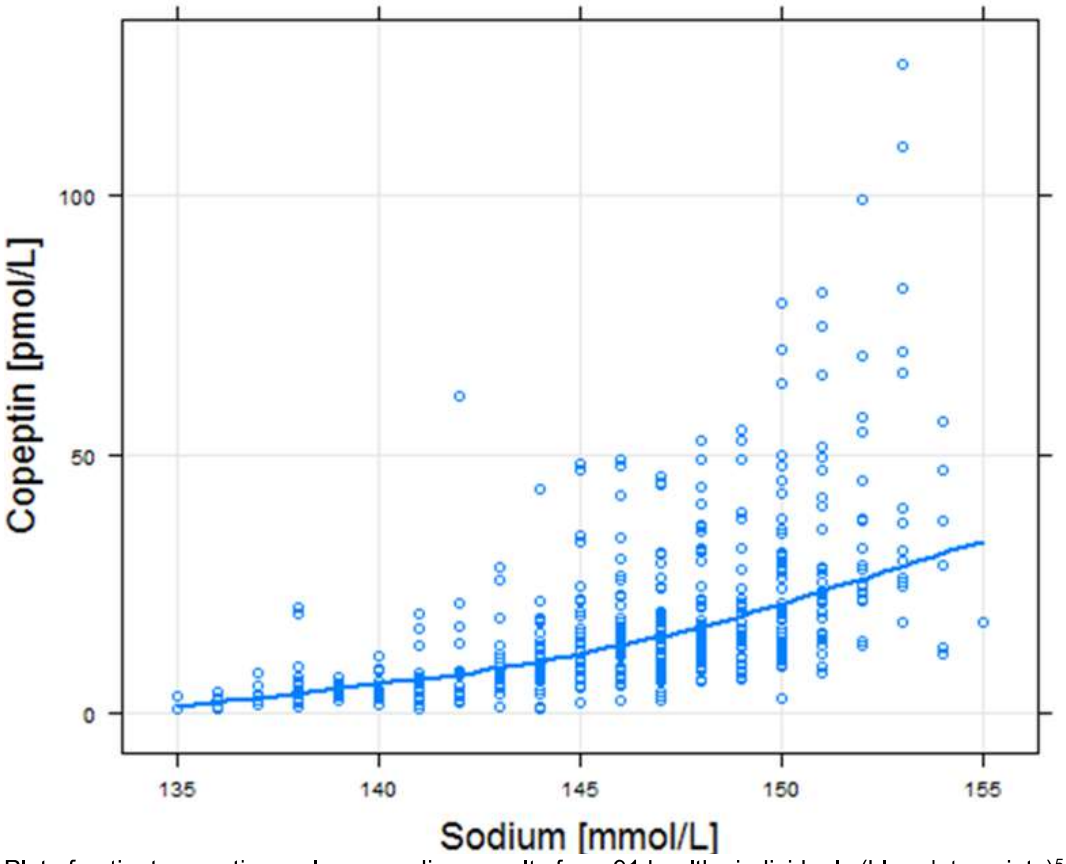
There are currently no reference ranges for copeptin in children.
The following ranges are derived from limited studies in adult populations:

Baseline plasma copeptin <2.6 pmol/L prior to hypertonic saline infusion - suggestive of complete AVP-deficiency.

Baseline plasma copeptin ≥21.4 pmol/L prior to hypertonic saline infusion suggestive of (partial or complete) AVP-resistance.

Baseline plasma copeptin >5 pmol/L – suggestive that AVP-deficiency is unlikely (even with a normal serum sodium/osmolality).
Plasma copeptin level of ≤4.9 pmol/L after hypertonic saline infusion - suggestive of partial or complete AVP deficiency.

Plasma copeptin level of >4.9 pmol/L after hypertonic saline infusion - suggestive of primary polydipsia. A higher cut-off value of 6.5 pmol/L distinguishes AVP-deficiency from primary polydipsia with increased accuracy based on newer data, with a value of >6.5 pmol/L being consistent with primary polydipsia[3].



Plot of patient copeptin vs plasma sodium results from 91 healthy individuals (blue data points)[5].

References

1. Baylis P.H. & Robertson G.L. (1980) Plasma vasopressin response to hypertonic saline infusion to assess posterior pituitary function. *J Roy Soc Med* **73**:255-60.
2. Baylis P.H. & Cheetham T. (1998) Diabetes insipidus. *Arch Dis Child* **79**: 84 – 89
3. Szinnai G et al. (2007) Changes in Plasma Copeptin, the C-Terminal Portion of Arginine Vasopressin during Water Deprivation and Excess in Healthy Subjects.
4. Fenske et al. (2018) A copeptin-based approach in the diagnosis of diabetes insipidus. New England Journal of Medicine. 2018;379(5):428–439
5. Schnyder et al.(2015) Physiological area of normality of copeptin in normal-to-hyperosmolar states. Endocrine Abstracts 37:EP706.