PENICILLIAMINE TEST FOR THE DIAGNOSIS OF WILSON'S DISEASE

INTRODUCTION

Wilson's disease is an autosomal recessive disorder resulting in impaired biliary excretion of copper and accumulation of copper in the brain, liver and cornea. Presenting symptoms include neurological dysfunction, liver disease and Kayser-Fleischer rings on ocular exam.

The diagnosis of Wilson's disease (hepato-lenticular degeneration) should be made on a combination of investigations including serum copper (< 12 µmol/L), caeruloplasmin concentration (< 0.2 g/L) and 24 h urine copper excretion (> 1.6 µmol/24 hours). Some recommendations suggest copper concentration of liver tissue to be the most important diagnostic criterion but this may be compromised by the inherent difficulty in obtaining both appropriate reference material and adequate patient samples. Despite these investigations, the possibility of Wilson's disease may still be unclear; hence the test described below may be of further use.

D-Penicillamine (D-β, β-dimethylcysteine), following oral administration, chelates the excess copper, which is loosely bound to tissue protein in patients with Wilson's disease. Hence there is enhanced excretion of copper in the urine.

CONTRAINDICATIONS AND SIDE EFFECTS

The use of penicillamine prior to the investigation will compromise this test since it will have reduced the copper stores. Since the extent to which the stores will have been depleted is unknown, it is best to avoid using this test within 6 months of penicillamine use.

Avoid if there is known allergy to penicillamine.

PATIENT PREPARATION

No special preparation is required.

PROTOCOL

Requirements

1. plain tube for blood sample
2. 3 x 24h urine containers with no preservatives (acid washed)
3. 2 x 500mg penicillamine tabs

Procedure

1. Take 2 baseline measurements of 24h urinary copper, and baseline serum copper and caeruloplasmin levels prior to this test.
2. At 0900 on the morning of the test start the 24 hour urine collection and administer 500mg D-Penicillamine.
3. At 2100 administer a second dose of 500mg D-Penicillamine.
4. At 0900 next day, complete the urine collection.

INTERPRETATION

The diagnosis of Wilson's disease should be entertained in the absence of other diseases of the liver, since the diagnostic accuracy of measurements of copper metabolism may be compromised by the latter.

The following threshold values are guidelines for Wilson's disease and a combination of abnormal results is best used for a diagnosis to be made.

Caeruloplasmin	< 0.2 g/L
Serum copper	< 12 µmol/L
Urine copper	> 1.6 µmol / 24 h in a symptomatic patient; > 0.64 µmol / 24h warrants further investigation
Urine copper post-penicillamine	> 25 µmol/24 h

SENSITIVITY & SPECIFICITY OF TEST

Low serum caeruloplasmin may be seen in all forms of chronic liver disease especially PBC, as well as in malnutrition, malabsorption and nephrotic syndrome. In inflammatory states, an increase of up to 30% in serum copper may disguise a low value.

If equivocal results are obtained from the penicillamine test, the next investigative step would be liver biopsy to measure tissue copper content. Some authorities believe that a liver copper measurement should be made on all diagnostic liver biopsies because of its strong diagnostic value.

CONTACTS

Basildon Hospital Biochemists: ext. 3029 / 3539 / 3095

Southend Hospital Biochemist: ext. 8795

REFERENCES

Up to date – Wilson's Disease: Diagnostic Tests. (accessed 19/08/2020, last updated May 2018)