SERUM TOTAL BILE ACIDS

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Introduction

The two major bile acids in the human, cholic acid and chenodeoxycholic acid, are synthesised in the hepatocyte by the cytochrome P450-mediated oxidation of cholesterol. These acids are secreted into the biliary canaliculi as sodium salts (primary bile salts) by means of a bile salt export pump, conjugated with glycine, taurine, sulphate or glucuronic acid, and stored in the gall bladder until excreted into the intestinal lumen in response to a fatty meal [1].

Within the intestinal lumen the primary bile salts are converted to secondary bile salts (deoxycholate and lithocholate), mostly by the action of bacterial enzymes. Pathogenic bacteria may also de-conjugate bile salts and promote their early re-absorption into the portal circulation. Secondary bile salts are c. 95% re-absorbed from the terminal ileum and colon, transported to the liver via the hepatic portal blood supply and re-excreted into the gall bladder. This process is referred to as the enterohepatic circulation of bile salts. Interruption of the enterohepatic circulation by means of bile acid sequestrants (e.g. Questran) can be used to promote cholesterol wasting from the body and lowering of the serum cholesterol concentration [2].

The total bile acid pool in humans is about 4 grams and it is re-circulated 5 to 10 times per day. Hepatic extraction of bile salts is highly efficient and, as a result, in health there are normally very low levels of bile salts in the peripheral circulation (less than 6.4 μmoles/L in the fasting state). Serum bile salts normally increase two to five-fold after eating, with a post-prandial peak at 60 – 90 minutes. It is therefore important for the subject to fast, or, in certain circumstances, to have both fasting and post-prandial bile acids measured.

Indications

Changes in serum bile acids are seen in quite mild liver disturbances. The test may be used with other parameters such as serum glutathione-S-transferase (GST) and gamma-glutamyl transferase (GGT) activities to provide a very sensitive test of liver function. Bile acid measurement is not indicated in subjects who are overtly cholestatic (jaundice with high serum bilirubin) as bile acids do not provide further information on hepatobiliary function in this setting.

Elevations in circulating bile salts can be a cause of pruritis, typically on the palms of the hands and the soles of the feet. The commonly accepted clinical indication for making this measurement is in the investigation of obstructive cholestasis in pregnancy [3].

Bile salts are, however, far more than gastro-intestinal detergents [4]; they are required for cholesterol and fat-soluble vitamin absorption, as well as conferring resistance to the overgrowth of pathogenic intestinal bacteria. They are required for the activation of enterokinase (an enzyme released by the enterocytes as food passes into the duodenum which activates the proteolytic enzymes secreted by the pancreas). Bile salts have also been shown to enhance glycaemic control and energy expenditure via cell signalling pathways. It is therefore interesting to read current research which suggests that there is a blunted bile salt response to feeding, with increased bile salt turnover, in obese subjects. These changes could result in more efficient absorption of dietary fat in such individuals [5].

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Serum total bile acids may therefore provide additional information in the investigation of a number of disturbances to the physiological functions described above.

Interpretation

The test is usually performed on a fasting sample, with normal fasting serum total bile acids being less than 6.4 μmoles/L. The measurement of bile acids in paired (fasting and 2 hour post-prandial) samples will increase the test sensitivity; two-hour post-prandial bile acid concentrations of > 20 μmol/L are suggestive of hepatobiliary disease.

Other variables, independent of hepatobiliary function, may affect serum bile acid concentrations:

- Inadequate fasting or decreased gastrointestinal transit time can increase fasting bile acid concentrations, which can, in some cases, be higher than the postprandial bile acid concentration.
- Prolonged fasting, intestinal malabsorption or increased transit time through the bowel (e.g. diarrhoea) can lower bile acid concentrations and hence decrease the sensitivity of the test as an indicator of hepatobiliary disease.

Synonyms:

Serum total bile acids, serum total bile salts

Methodology

Biolab measures serum total bile acids by an enzymatic method (using 3-alpha-hydroxysteroid dehydrogenase). The results are subject to both internal quality control and external quality assessment.

Turn around time: 4-5 working days.

Patient preparation

The patient should fast overnight before venipuncture.

Specimen requirements

Serum; blood should be collected into a serum separator tube. Lithium heparin plasma is also acceptable. Postal samples must reach Biolab within 3 days of collection.

References

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4. Crook MA. Bile salts and obesity. Ann Clin Biochem 2010; 47:482-484.
5. Glicksman G, Pournaras DJ, Wright M et al. Postprandial bile acid responses in normal weight and obese subjects. Ann Clin Biochem 2010;47:482-484.