CME CREDIT

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BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

Q: How should a patient with an isolated GGT elevation be evaluated?

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A: DO NOT BECOME overly concerned about it. Isolated GGT (gamma glutamyl transpeptidase) elevations are common, and do not indicate serious or progressive liver disease. No specific evaluation apart from a history and physical examination is needed. Although GGT is elevated in a number of liver conditions, in most of them other enzymes are elevated as well, and these other enzymes are more diagnostically useful than the GGT. Clinical laboratories should consider removing GGT from the panel of bundled liver tests to minimize the number of patients who end up on a merry-go-round of testing prompted by isolated GGT elevations.

GGT LACKS SPECIFICITY

As a screening test, the GGT level is very sensitive but has a very low specificity. GGT is found in highest concentrations in the liver (particularly in biliary tubular epithelium), but also in the kidneys, seminal vesicles, pancreas, spleen, heart, and brain.[1] Elevations of this enzyme occur therefore in a number of disparate clinical situations,[2] including all manner of liver disease—fatty liver, viral hepatitis, bile duct obstruction, and most drug reactions involving the liver.

GGT HAS LITTLE UTILITY

The combination of high sensitivity and very low specificity seriously hampers the utility of GGT. Clinically, the value of the GGT is marginal. If other hepatic enzymes are elevated, the GGT level provides no incremental information.

GGT measurement is often used to determine if elevations in other enzymes (especially alkaline phosphatase) come from the liver or a nonhepatic source such as the bones or placenta.[3] Only if alkaline phosphatase and GGT are both elevated—but the other liver enzymes are not—does the GGT provide important utility.[4] If both alkaline phosphatase and GGT are elevated, at least a portion of the alkaline phosphatase is of hepatobiliary origin. Conversely, if the GGT level is normal, the alkaline phosphatase elevation derives from nonhepatic disease (eg, bone disease). Even in this situation, however, comparable information can be obtained by measuring alkaline phosphatase isoenzymes.

Although GGT has been shown to rise with alcohol consumption and has been used as an indirect measure of compliance with alcohol abstinence, some experts doubt this correlation is sufficiently constant to permit GGT levels to serve as a surrogate marker for alcohol consumption.[5]

Most often, GGT measurement is included as part of a bundled panel of tests. Owing to the limitations of GGT as a test, the Cleveland Clinic has removed it from its "liver panel," as have many other major medical centers. Yet the test persists, and many clinicians receive GGT results whether they request them or not.

Do not get on a merry-go-round of testing

RECOMMENDATIONS

What, then, to do if the GGT is elevated but the AST (aspartate aminotransferase), ALT (alanine aminotransferase), alkaline phosphatase, bilirubin, and albumin levels are all normal? In deciding whether to evaluate the liver further, consider the patient's risk factors for liver disease, symptoms, and physical findings.

- Patients with risk factors for acquired liver diseases such as hepatitis B and C should have screening tests for these diseases. Alcohol con-

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sumption should be defined and, if excessive, modified.

- In men and postmenopausal women, screening for iron overload is always appropriate (serum ferritin, iron, iron-binding capacity, and percent transferrin saturation).
- Patients who are obese, diabetic, or have elevated blood lipids should have an ultrasound of the liver, which often reveals signals characteristic of fatty liver.
- Patients with hepatomegaly, splenomegaly, ascites, or other manifestations of liver disease require further study regardless of the GGT level.

If the patient has no risk factors or symptoms and the physical examination reveals nothing abnormal, an isolated GGT elevation does not require further investigation.[6] The test should not be repeated, and it should not trigger imaging studies or a liver biopsy. These patients rarely benefit from such add-on testing, nor do they benefit from referral to a gastroenterologist or hepatologist. They do not need to have their medications stopped.

Do discuss the abnormality with the patient, however. This might be a good time to inquire again about alcohol consumption, and to recommend moderation in its consumption. An obese patient may have fatty liver, currently only treatable with weight loss, and so in obese patients the need for weight reduction might be reinforced by pointing to the GGT elevation.

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