

## Practical Approach to Liver Testing in Managing Dyslipidemia

### *Liver Function Tests and Statin Therapy*

Elevations in liver function tests [alanine transferase (ALT) or aspartate transferase (AST)] are associated with statin therapy. Typically, these elevations are transient and return to baseline within two or three weeks. In large clinical trials, elevations in liver function tests greater than 3 times the upper limit of normal on more than two occasions that led to the withdrawal of therapy occurred in <1% of those treated with most statins. The exceptions were 80 mg of atorvastatin or when ezetimibe is combined with a statin which typically has a withdrawal rate of 2-3%. In most clinical studies, the incidence of elevations in ALT or AST is similar between patients taking a statin or placebo. This may reflect the fact that nearly 50% of the hyperlipidemic population has co-existing nonalcoholic fatty liver disease (1). However, it is important to remember that elevations in ALT or AST in the absence of elevations in bilirubin levels are not associated, either clinically or histologically, with liver injury (2, 3). These statin-induced elevations in ALT or AST may reflect reductions in hepatocyte cholesterol content or other co-morbidities. Hence, elevations in ALT or AST in the absence of other indications of hepatic injury appear to be clinically insignificant.

### *How often should liver function tests be monitored in patients taking statins?*

The general recommendation is that liver function tests should be performed at the initiation of statin therapy and periodically thereafter or after dose titration. However, clinical study data does not support this frequent monitoring. Statin-induced liver failure is rare and is estimated at approximately 1 per million person-years (4). Hence, routine clinical monitoring is not cost effective to identify this rare side effect.

### *How should patients with preexisting elevations in liver function tests be approached?*

The clinician should exclude other causes of increased ALT or AST including alcohol consumption, viral hepatitis, or other medication related causes (e.g. nonsteroidal anti-inflammatory agents). In patients with dyslipidemias and elevations in ALT or AST, nonalcoholic fatty liver disease should be excluded. This might include imaging tests to identify fatty liver. If nonalcoholic fatty liver disease is identified, then insulin resistance and/or type 2 diabetes needs to be excluded. Nonalcoholic fatty liver disease is the hepatic expression of the insulin resistance syndrome.

### *Can I start a statin in a patient with elevations in amino transferases?*

Once other etiologies are excluded, lipid lowering therapy can be started. Recent data demonstrates that the incidence of statin-induced elevations in AST or ALT are NOT increased in patients with preexisting elevations in liver function tests compared to patients with normal levels (3).

### **Should liver function tests ever be examined?**

A recent national liver expert panel recommends that it is prudent to measure amino transferase levels during routine medical evaluations or when it is clinically indicated (5). Since bilirubin and alkaline phosphatase levels are included in a comprehensive metabolic panel, this panel would be the preferred choice of diagnostic tests to test for liver damage. If liver enzymes are elevated, then other etiologies should be excluded as discussed above.

#### **SUMMARY**

- *Elevations in liver function tests (ALT/AST) infrequently occur with statin therapy*
- *In the absence of other liver abnormalities, elevations in ALT/AST are clinically insignificant*
- *Statin-induced liver failure is very rare and it is not cost effective to screen liver function tests for this side effect*
- *Liver function tests should be determined when clinically indicated or during routine medical evaluations*

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#### **REFERENCES**

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