

## STATINS AND LIVER TOXICITY

During Statins therapy monitoring of LFTs is essential.

Begin testing within 6 weeks of the onset of therapy and continue testing routinely, based on the patient's response and other therapies employed. The AST test is the most sensitive marker of the impact of statins and other dyslipidemic agents.

AST should not be elevated more than 2-3 times the ULN.

The ALT is less sensitive to statin impact, however, the ALT is excellent as an evaluation of "fatty liver." Fatty liver, or steatohepatitis, is a build-up of fat in the liver cells, usually related to medication, obesity, alcohol intake, starvation, diabetes, or high blood triglycerides.

The incidence of asymptomatic hepatocellular dysfunction (evaluated by AST and ALT) ranges from about 3% for any elevation to less than 1% for elevations greater than 3 times the ULN.

The most common cause of elevated LFTs in the dyslipidemic patient is a fatty liver. This results in an elevation of the ALT greater than the AST.

Elevation of the baseline AST, ALT, or CPK should prompt the practitioner to evaluate causation and consider treatment of the abnormality prior to initiation of medications that could further affect the liver. Should the cause be identified and the decision to initiate therapy be made, the practitioner should check the LFTs more frequently. The product information for selected dyslipidemic medications suggests checking of LFTs (not CPK) after 6 weeks of initiation of medication, and again 6 weeks after dosage adjustment.

**Ali's recommendation: checking AST within 2-4 weeks of statins initiation**

Table 4. Change in Transaminases Within 6 Months After Starting a Statin Stratified by Type of Statin Prescribed

	Atorvastatin (n = 819)	Simvastatin (n = 904)	Other statins <sup>a</sup> (n = 56)	P value
Median dose per day	10 mg	20 mg	20 mg	
Mean dose per day	14 ± 22	17 ± 41	23 ± 9	
Baseline AST (IU/L)	28 ± 21	29 ± 23	24 ± 8	0.3
Baseline ALT (IU/L)	26 ± 18	25 ± 17	32 ± 28	0.2
Proportion with elevated AST and/or ALT at baseline	18%	21%	13%	0.2
Incidence of liver biochemistries elevations <sup>b</sup>	2%	3.1%	4.3%	0.4
Change in AST (IU/L)	8 ± 60	34 ± 628	19 ± 86	0.5
Change in ALT (IU/L)	22 ± 98	42 ± 329	26 ± 80	0.4
Proportion that discontinued statin during follow-up (%)	10%	11.5%	8.5%	0.5

NOTE. Table represents cohorts 1 and 2 combined.

<sup>a</sup>Other statins include fluvastatin in 49 patients and pravastatin in 7 patients.

<sup>b</sup>This represents the combination of mild-moderate and severe elevations in liver biochemistries.

Conclusions:

Their study consisted of the following 3 cohorts. Cohort 1: 342 hyperlipidemic patients with elevated baseline enzymes (AST >40 IU/L or ALT >35 IU/L) who were prescribed a statin; cohort 2: 1437 hyperlipidemic patients with normal transaminases who were prescribed a statin; and cohort 3: 2245 patients with elevated liver enzymes but who were not prescribed a statin. The effect of statins on liver biochemistries was assessed over a 6-month period after statins were prescribed. Elevations in liver biochemistries during follow-up were categorized into mild-moderate or severe based on predefined criteria. The incidence of mild-moderate elevations and severe elevations in liver biochemistries in cohort 1 were 4.7% and 0.6%, respectively. Compared with cohort 1, individuals in cohort 2 had lower incidence of mild-moderate elevations (1.9%, P = 0.002) but not severe elevations (0.2%, P = 0.2). However, between cohorts 1 and 3, there were no differences in the incidence of mild-moderate elevations (4.7% vs. 6.4%, respectively, P = 0.2) or severe elevations (0.6% vs. 0.4%, respectively, P = 0.6). Statin discontinuation during the follow-up was similar between cohorts 1 and 2 (11.1% vs. 10.7%, respectively, P = 0.8). These data suggest that individuals with elevated baseline liver enzymes do not have higher risk for hepatotoxicity from statins. (**Gastroenterology. 2004 May;126(5):1287-92., Pharmacotherapy. 2004 May;24(5):584-91**)