

Statins and Liver Function Tests

Monitoring LFTs has become common practice during treatment with statins even though there is little evidence to support systematic hepatotoxicity due to statin therapy. Moreover, LFT monitoring is actively recommended by NICE who propose taking baseline LFTs and repeating at 3 and 12 months.¹

There are some drawbacks to this practice.

- Firstly, statins induce AST and ALT and cause a rise in all subjects during the first few weeks of therapy and it would therefore be prudent to wait several months before testing.
- It should be borne in mind that some patients do develop drug-induced toxicity (as with most drugs) and prescribers should be aware of the possibility of this in someone who becomes unwell, jaundiced or develops pruritus.
- A further complication is the effect of central obesity. Abdominal obesity is part of the metabolic syndrome and the associated fatty liver may cause an elevation in ALT. If a baseline measurement has not been taken, this elevation might incorrectly be blamed on the statin.
- There is no evidence to suggest that statins have an adverse effect on liver function in patients with chronic liver disease.

Baseline LFTs

Raised ALT is present in many patients often due to fatty liver or non-alcoholic steatohepatitis (NASH). In patients with ALT less than 3 times normal statins may improve the values.²

If baseline LFTs are abnormal a history for liver disease risk factors including drugs (prescribed, illegal and OTC) should be taken with a physical examination for liver disease and further investigations (such as a non invasive liver screen).

Since statins appear to be safe in chronic liver disease, there would appear to be no reason why they should not be prescribed whilst further investigations are being performed.

Raised LFTs whilst on statins

If ALT or AST are elevated but are less than 3 times the upper limit of normal then:

- Continue the statin and repeat in a month
- If they remain elevated but are less than 3 times the upper limit of normal then continue statin and repeat again in 6 months

If ALT or AST are greater than 3 times the upper limit of normal then:

- Discontinue statin and repeat LFTs in a month
- Take a history and examination
- Discontinue any other hepatotoxic drugs
- Give lifestyle modification such as losing weight, reducing alcohol intake and improving diabetic control.
- If ALT or AST continue to rise then consider referral to secondary care or undertake a non invasive liver screen

If the ALT or AST normalizes or returns to pre treatment levels when the statin is stopped

- If the indication was primary prevention the discuss intolerance to statins with the patient and look at other lifestyle measures
- If the indication was secondary prevention in cardiovascular disease, maximize the other secondary preventive measures
- If the indication was Familial Hyperlipidaemia then specialist advice should be sought

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Contraindications to statin prescribing

1. Hypersensitivity to the product
2. Active liver disease including unexplained, persistent elevations of serum transaminases or serum transaminase elevation > 3 x the upper limit of normal
3. Severe renal impairment
4. Myopathy
5. Concomitant cyclosporin
6. Existing polymyositis or dermatomyositis
7. Pre-disposing factors for myopathy/rhabdomyolysis, including: moderate renal impairment, hypothyroidism, personal or family history of muscle disorders, alcohol abuse, other drug therapy that raises plasma statin levels

Drugs which should be avoided or prescribed with care with statins

Amiodarone
Azole antifungals
Diltiazem
Cyclosporin
Erythromycin
Fibrates
Gemfibrozil
Nefazodone.
Nicotinic acid
Protease inhibitors
Macrolide antibiotics
Verapamil
Warfarin

None Invasive Liver Screen

Hepatitis A, B, C, Autoantibodies (ANA, AMA, ASA, AntiLKM), Immunoglobulins, Ferritin, AST (or ALT depending on lab) AAT (alpha 1 antitrypsin), AFP and ceruloplasmin

References

1. NICE Clinical Guideline 67 (May 2008). Lipid Modification- Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease.
2. Athyros VG et al. Lancet 2010: published online Nov24. DOI:10.1016/S0140-6736(10)61272-x

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