PHARMACOTHERAPY

Statins are safe in NAFLD

Statins are a potentially useful therapy in patients with the metabolic syndrome, since these individuals often have dyslipidemia and are at high risk of cardiovascular disease (CVD). However, nonalcoholic fatty acid liver disease (NAFLD) is a common component of the metabolic syndrome and, to date, many clinicians have been hesitant to prescribe statins in the presence of liver-enzyme abnormalities, owing to the reported adverse effects of these drugs on the liver. *Post-hoc* analysis of the prospective, intention-to-treat Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) study has now demonstrated that use of statins in patients with NAFLD is safe and effective.

Unlike many clinicians, Dr Vasilios Athyros and colleagues have been prescribing statins to patients with mild-to-moderately abnormal liver tests, because their personal clinical experience and data from other clinicians' small studies lead them to conclude that statins are safe and contribute to reduction of disease burden in these patients. In an attempt to validate or refute their conclusions, and since a formal investigation of the effect of statins on hard clinical end points in patients with mild-to-moderately abnormal liver function had not previously been undertaken, Athyros *et al.* set out to evaluate data from the GREACE study.

All 1,600 GREACE trial participants had coronary artery disease. Liver-enzyme levels were measured at baseline, at the 6-week timepoint, and at regular 6-month intervals over the 3-year follow-up period. Overall, a low rate of adverse liver effects (1.1%) was attributed to statin therapy.

At baseline, liver-enzyme levels were mildly-to-moderately elevated (up to three times the upper limit of normal) in 437 of the enrolled patients. After performing ultrasonography, and after excluding the possibilities of alcohol misuse, chronic hepatitis B and C, autoimmune hepatitis, and Wilson's disease, the investigators attributed the abnormal liver-test results to NAFLD. In this group of patients, statin therapy was associated with a 68% relative reduction in risk of cardiovascular events and significant reductions in levels of total cholesterol, LDL cholesterol, and triglycerides over the 3-year follow-up. Of note, the statin-associated relative risk reduction in the patients considered to have normal liver function at baseline was lower than that for patients with mild-to-moderately abnormal liver tests (39% versus 68%). In addition to conferring cardiovascular benefit to patients with mild-to-moderately abnormal liver function at baseline, statin therapy was associated with reductions in the levels of liver enzymes and an increase in the estimated glomerular filtration rate by the end of the study. By contrast, liver function was found to have worsened in those who did not receive statins.

When asked to comment on the recent analysis of GREACE, Dr Peter Jones (Baylor College of Medicine in Houston, TX, USA), who was not involved in the study, highlighted that "for the past 20 years, the FDA has required the adverse liver effects of statins [to be detailed] in their package inserts, and that has made many physicians wary of using them when liver tests are already elevated at baseline". He went on to state that "the results [of this *post-hoc* analysis] should make clinicians more comfortable with the initiation and continuation of statins in high risk patients with probable NAFLD".

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Original article Athyros, V. G. *et al.* Safety and efficacy of long-term statin treatment for cardiovascular events in patients with coronary heart disease and abnormal liver tests in the Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) Study: a *post-hoc* analysis. *Lancet* 376, 1916–1922 (2010)