Newer Epilepsy Drugs Cut Cholesterol, CRP Levels

BY MITCHEL L. ZOLER
Philadelphia Bureau

PHILADELPHIA — Switching from an enzyme-inducing to noninducing antiepileptic drug led to a significant fall in serum levels of cholesterol and C-reactive protein in a review of 38 patients.

The relatively high levels of serum cholesterol and C-reactive protein (CRP) in patients treated with either carbamazepine or phenytoin seemed large enough to have a significant clinical impact, Dr. Scott Mintzer said at the annual meeting of the American Epilepsy Society.

When those levels were compared with the lower serum levels of cholesterol and CRP patients achieved after switching to treatment with either levetiracetam or lamotrigine, Dr. Mintzer estimated treatment with one of the older drugs was linked with a roughly 50% increased risk for a cardiovascular event, based on rates noted in the cardiovascular literature. The rate includes an increased risk for stroke or a myocardial infarction.

The average total cholesterol level fell from 217 mg/dL on treatment with an older drug to an average of 191 mg/dL on treatment with a newer drug.

This is additional evidence that drugs such as carbamazepine and phenytoin, which induce hepatic cytochrome P450 enzymes, are not good for patients, said Dr. Mintzer, director of the epilepsy monitoring unit at the Jefferson Medical College, Philadelphia. Established adverse effects of enzyme-inducing antiepileptic drugs include reductions in serum level of vitamin D and testosterone, reduced sexual function in men, and interactions with other drugs. There are probably additional effects that have not yet been identified, he said in an interview.

The study examined changes in blood drawn from 38 patients with epilepsy treated at Jefferson who were switched from monotherapy with either carbamazepine or phenytoin to monotherapy with either levetiracetam or lamotrigine. The second blood specimen was drawn 6 weeks after switching to allow serum levels to stabilize.

The study excluded patients who were taking a statin or any other type of lipid-lowering medication. Results from prior studies by other investigators documented that the hepatic enzymes induced by the older antiepilepsy drugs speed the metabolism of statins and blunt their effect. This mechanism was not at work in this study because no patients were on a statin.

The average total cholesterol level fell from 217 mg/dL on treatment with an older drug to an average of 191 mg/dL on treatment with a newer drug, a 26-mg/dL difference that was statistically significant and was also large enough to be clinically significant. The total cholesterol level fell in almost all of the patients, but in some patients the drop was large. One patient's level fell by about 90 mg/dL. This marked interindividual variation suggests a pharmacogenetic effect, Dr. Mintzer said.

Most of the drop was in non–high density lipoprotein cholesterol, which fell by an average of 20 mg/dL (from 155 mg/dL to 135 mg/dL). High-density lipoprotein cholesterol decreased by an average of 6 mg/dL (from 62 mg/dL to 56 mg/dL).

Serum levels of high-sensitivity CRP were measured before and after switching in 35 patients. The average level on treatment with an enzyme-inducing drug was 4.2 mg/L, which fell to an average of 2.4 mg/L after patients were stable on a noninducing drug, a statistically significant decline and a potentially clinically significant difference, Dr. Mintzer said. The impact of antiepileptic drugs on CRP levels has not been previously reported, he added.

Three other serum markers linked to cardiovascular risk also fell following drug switching. The average serum level of lipoprotein (a) fell, but only in the patients switched off of carbamazepine. The average level of homocysteine and the number of particles of low-density lipoprotein cholesterol also fell after switching, but only in patients taken off of phenytoin.

The finding must be confirmed in a larger number of patients, Dr. Mintzer said. And because the magnitude of the effect of antiepileptic drug switching seems to vary widely among patients, the interaction must be examined in individual patients rather than in cross-sectional studies that sample large numbers of patients. The study did not have any commercial funding. ■