SHOULD ENZYME- INDUCING ANTIEPILEPTIC DRUGS BE AVOIDED? YES

Michael R. Sperling
Thomas Jefferson University, Philadelphia, PA, USA

Many antiepileptic drugs (AED) alter hepatic microsomal enzymes, either inducing or inhibiting enzymes within the cytochrome P450 complex (CYP). Many of the earliest developed and most commonly used agents, including phenobarbital, phenytoin and carbamazepine induce various enzymes, particularly CYP3A but others as well. Newer agents such as oxcarbazepine and topiramate also induce CYP though to a lesser extent. This property has the potential to cause problems.

Alteration of function of CYP leads to changes in metabolism of endogenous hormones, cholesterol metabolism, bone, and may affect other medications. Steroid hormones are all derived from cholesterol, including the sex hormones (estrogens, progesterone, testosterone, etc.), vitamin D, aldosterone, and cortisone. CYP induction can lead to alterations in the levels of these steroid hormones with the potential for detrimental effects. For example, vitamin D levels are reduced by phenytoin, and bone turnover and osteoporosis are more common in individuals who take enzyme inducing drugs than a non-inducer such as lamotrigine. LDL and lipoprotein a levels are raised by enzyme inducing AEDs. In addition, C-reactive protein is elevated by enzyme inducing agents. These effects have the potential to increase the risk for cardiovascular disease in people treated with these agents.

In addition, enzyme-inducing AEDs shorten the half-life and reduce the effectiveness of many of drugs, including oral contraceptives, anticoagulants, analgesics, glucocorticoids, antihypertensives, statins, psychoactive drugs, antiretrovirals, immunosuppressants, cytotoxics, and AEDs. Practically speaking, this means that oral contraceptives are less effective, survival is reduced in cancer patients and HIV patients, antihypertensive therapy and lipid-lowering therapy are less effective, and maintaining therapeutic levels of other AEDs becomes more difficult or, at times, impossible.

There are many AEDs that do not alter CYP function. These agents consequently have a more favorable profile and pose less health risk. They do not diminish the effectiveness of other drugs, lead to osteoporosis, and have the potential for increasing cardiovascular risk. For these reasons, enzyme-inducing AEDs should generally be avoided for first or second line therapy for epilepsy and be reserved for those individuals who fail or cannot tolerate therapy with more benign agents.