

Fibrates-Part 2

In part one, we began talking about Fibrate therapy and their role in lipid modulation. I want to start out by talking about fibrates and interactions with the kidneys. When the National Lipid Association's Safety Task Force published their recommendations to healthcare professionals in the March 2007 edition of *The American Journal of Cardiology*, they began by stating that before the initiation of fibrate therapy, the status of one's kidney function should be known. If significantly impaired renal function is present, the patient should be prescribed Lopid (gemfibrozil), unless taking a statin, or a lower starting dose of Tricor (fenofibrate-48 mg is the most common available dose) should be considered. With impaired kidney function, the periodic monitoring of kidney function is recommended. I am sure you asking why one should not take gemfibrozil while taking a statin? Gemfibrozil increases the likelihood of myopathy (see my posting titled *Statins and Muscle*) when combined with a statin. Due to pharmacokinetic interactions, gemfibrozil can increase the concentrations of simvastatin, lovastatin, pravastatin, atorvastatin, and rosuvastatin. It has the least effect on the statin called fluvastatin, which is sold under the brand name Lescol. The evidence shows that if gemfibrozil is necessary, fluvastatin is the appropriate statin option to consider. It baffles me that on a daily basis I see many patients on gemfibrozil combined with all the statins except fluvastatin. Many physicians do not know this fact. Most insurance company and medicare drug plans are also uninformed because each time I write a prescription for fenofibrate with a statin, it gets denied and it is recommended that I use gemfibrozil. It seems like I spend an hour a couple of days each week writing authorization letters to get my patients on the appropriate drugs. It should be noted that in patients with diabetes, fenofibrate is the safest and most appropriate choice. After the WHO and HHS trials, there was a concern about a possible increase in cancer-related deaths. Ultimately after significant observation, it was deemed to have occurred by chance.

In 2000, a joint ACC/AHA/NHLBI advisory committee on the use and safety of statins reviewed 8 controlled clinical trials of statin-fibrate therapy involving almost 600 patients. This review found that 1% of patients experienced CK levels >3 times the upper limit of normal without muscle symptoms, and 1% withdrew from therapy because of muscle discomfort. No cases rhabdomyolysis were reported. The task force concluded that the combination of a moderately dosed statin with a fibrate "appears to have a relatively low incidence of myopathy, especially when used in persons without multiple-system disease or multiple medications." In conclusion they said that fenofibrate is the preferred option when combined with a statin.

I want to say something about the studies done to support the use of fibrates in lipid management and the reduction of cardiovascular disease and death. One in particular, called the VA-HIT, gemfibrozil was associated with a 22% reduction in death from CAD and a 11% reduction in overall mortality. As I stated in my previous fibrate post, fibrates are recommended and are optimal therapy for patients with high triglycerides and low HDL and the VA-HIT remains the sole trial among other larger fibrate outcome trials to

actually study this population group. In conclusion, the use of gemfibrozil and fenofibrate in patients with abnormal lipids characterized by high triglycerides and low HDL cholesterol in clinical trials demonstrates an improved cardiovascular benefit.