

Niacin

I want to be back to discussing lipid modulating drugs. I have been getting many questions regarding niacin on my message board and what it exactly does. I know there is a lot of information out there that it is some kind of wonder drug that raises one HDL-C (good cholesterol) and keeps them from having heart attacks. This is only partly true. As I have said many times before, there is no way to measure how well HDL particles function. We only measure a number. In other words there is no qualitative test to measure how well the HDL particles work in our bodies, but only a quantitative test. Apart from the VA-HIT trial where gemfibrozil induced HDL-C rise was very small, there has never been a prospective randomized study done to correlate and HDL-C level with an outcome. Post-hoc analysis of that trial later revealed that gemfibrozil only worked in those patients with insulin resistance. In that group, there was no relationship between endpoints and change in HDL-C.

Although niacin is a member of the B-vitamin family and is sometimes referred to as vitamin B3, it is used in large pharmacological doses to treat lipid disorders and should no longer be thought of as vitamin therapy. It is a soluble B vitamin that impacts all lipid subfractions but is not widely used because of the associated side effects. Niacin-induced flushing, which is the result of vasodilatation of the blood vessels, is the most common side effect and usually occurs within 20 minutes following ingestion and may last for up to 60 minutes. There are three different types of niacin: 1) immediate release which needs to be taken in very high doses multiple times a day and which is associated with the highest incidence of flushing. 2) slow-release niacin which is the best tolerated with respect to flushing but has the highest incidence of liver irritation and 3) FDA approved intermediate release niacin which has an in-between degree of flushing but almost no liver toxicity.

The way niacin works is rather complicated, but in addition to its antiatherogenic activity, the primary use of niacin is to lower triglyceride levels. Niacin reduces the mobilization of free fatty acids from fatty tissue resulting in reduced secretion of VLDL-P from the liver which is a precursor of LDL-P. While it does lower LDL-C, LDL-P, apoB, this occurs through its triglyceride lowering abilities. Niacin also increases HDL-C and almost certainly improves HDL particle functionality. It induces HDL mediated removal of cholesterol from plaque in a process termed macrophage reverse cholesterol transport. Although niacin does lower Lp(a), in my previous posting I stated that the goal is to lower LDL-P and statins are the primary to drug to perform this function.

Niacin has been associated with abnormal liver tests and cause significant liver toxicity. This has only been seen with slow acting niacin and virtually never with immediate or extended release niacin. It should be discontinued if the liver enzymes (ALT/AST) exceed 3X the upper limit of normal. The use of over-the-counter niacin should be discouraged. It is recommended that the FDA approved product Niaspan be used to treat lipid disorders. Many of these preparations are not labeled as sustained release and when combined with a fiber (an example would be oat bran) can become sustained release and adversely affect the liver enzymes. Inositol is sold over the counter as flushless niacin,

but it has no ability to affect lipids and should never be used. Food maximizes the availability of niacin. It can raise uric acid levels and should be used cautiously in patients with gout. As I stated earlier, the most common complaint is flushing and this occurs in many patients treated with therapeutic doses of niacin and this is also the most common reason patients stop using the medication. This can be minimized by pretreatment with aspirin or motrin. Flushing increases when taken with hot beverages. Gastritis and peptic ulcer disease occurs in about 3% of patients on the medication and is another reason for inability to tolerate niacin. Hyperglycemia occurs in patients taking niacin. Patients who are borderline diabetics can become overtly diabetic although data from the ADMIT trial indicate that it can be used safely in diabetics.

Although we still await serious outcome data with niacin, there is good data from very small trials that adding niacin to a statin lessens the thickness of the carotid arteries (CIMT), improves findings on angiograms, and reduces clinical events (the FATS and HATS trials). We await confirmation of this in the much larger AIM HIGH trial which is currently underway. They are not seeing the 90% reduction in clinical events in the AIM HIGH trial that occurred in HATS or the trial would have been stopped for ethical reasons.

In conclusion, while niacin is a drug that should be kept in the armamentarium of a physician that practices lipidology, it should not be used as a first line drug to lower LDL-C or LDL-P. I primarily use it in combination with a statin in nondiabetic patients with known CAD who have low HDL-C and elevated LDL-P. As I write about in every posting, the name of the game to ensure cardioprotection is to lower LDL-P or apoB and this is now recommended by the American Diabetic Association and American College of Cardiology as a standard of care in patients with moderately high, high, or very high cardiometabolic risk. This consensus statement recommends that niacin is the preferred drug to add to statins to further reduce apoB in the hope of reducing clinical events.