An Overview of Statins and Alternative Treatments

By Mark Crawford, Contributing Writer

Cholesterol, a soft, waxy substance found in every human cell, is critical for vital functions such as the production of hormones, vitamin D, and digestive enzymes. The liver and cells make about 75% of blood cholesterol. The rest comes from the food we eat.

Since the 1950s, the medical community has strongly believed cholesterol is atherogenic—that too much cholesterol in the bloodstream (hypercholesterolemia) leads to plaque buildup, atherosclerosis, heart attacks, and stroke. Many studies have confirmed this idea, at least to some degree.

There are two main types of cholesterol: low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL transports cholesterol and triglycerides from the liver to peripheral tissues. Because high LDL levels are often associated with cardiovascular disease, it's often called "bad" cholesterol. HDL is known as "good" cholesterol because it seems to protect against heart disease. Some researchers believe HDL carries cholesterol away from the arteries and back to the liver or strips excess cholesterol from arterial plaque along the way.

Fighting Cholesterol with Statins

Statins are the most widely prescribed class of cholesterol-lowering drugs. Top sellers include atorvastatin (Lipitor), simvastatin (Zocor), and pravastatin (Pravachol). Other statins are fluvastatin (Lescol), lovastatin (Mevacor), and rosuvastatin (Crestor). Statins work by inhibiting the production of HMG-CoA reductase in the liver, an enzyme that helps synthesize cholesterol. A tremendous amount of scientific literature shows statins typically lower LDL cholesterol by 25% to 50%, usually with minimal side effects. These drugs also lower triglycerides, raise HDL cholesterol, and sometimes lower blood pressure, thereby reducing the risk of heart attack or stroke. According to the American Heart Association, high cholesterol is defined as having a total cholesterol count (HDL and LDL) of 200 mg/dL or higher.

Because of this vast body of research, most medical professionals accept that statins are safe and well-tolerated, and that they do a good job of fighting cardiovascular disease. This was recently reinforced by Dr. Jane Armitage's review of statin research from 1985 to 2006, as published in *The Lancet*.[1] "Since statins were first approved in 1987," she writes, "their ability to reduce the risks of vascular death, nonfatal myocardial infarction, stroke, and the need for arterial revascularization has been shown by several large, high-quality randomized trials." She indicates the side effects of muscle pain and weakness, serious muscle damage, and liver problems are rare at standard doses, with myopathy occurring in fewer than one in 10,000 patients. "Their proven impact on cardiovascular disease risk has been driving their widespread use," she adds.

The Agency for Healthcare Research and Quality reports that spending on statins increased 156% between 2000 and 2005, with the total number of prescriptions jumping from 90 million to 174 million. About 13 million Americans use statins.

A study published in the *New England Journal of Medicine*[2] tested statins on subjects with high C-reactive protein (CRP) (indicating inflammation) and healthy cholesterol numbers. Half of the subjects received 20 mg of rosuvastatin; the others received a placebo. Those taking the statin showed dramatic decreases in LDL cholesterol and CRP levels and recorded 50% fewer heart attacks and strokes. These results may encourage millions of people to take

statins as a long-term preventive measure, even though they would not normally be considered candidates for the drug.

Other Benefits

Research continues to show far-reaching benefits of statin therapy. A 2007 study[3] indicates statins may be beneficial in preventing glaucoma progression. They also appear to slow lung decline in the elderly (even smokers), possibly because of their anti-inflammatory properties.[4] The *Archives of Internal Medicine*[5] reported that people who were hospitalized with pneumonia were less likely to die within 90 days if they took statins before hospitalization. "Our study adds to the accumulating evidence that statin use is associated with improved prognosis after severe infections," says lead researcher Reimar Thomsen, MD.

Other studies show statins seem to provide some protection against dementia. A long-term study in the Netherlands[6] concluded statins substantially reduce the risk of Alzheimer's disease. New research at the University of Rochester Medical Center[7] revealed that simvastatin and pravastatin spur glial progenitor cells in the brain to become oligodendrocytes—up to five times the normal amount. These cells produce myelin, improve brain function, and could possibly fight MS (the long-term effects of having fewer glial progenitor cells for other functions, however, are unknown).

Risks of Statin Use

The Statin Effects Study at the University of California-San Diego (www.statineffects.com) lists statin side effects as "swelling, shortness of breath, vision changes, changes in temperature regulation, weight change, hunger, breast enlargement, blood sugar changes, dry skin, rashes, blood pressure changes, nausea"—typically in the mild category. Changes in liver function can occur for some patients, but are easily reversed by stopping the medication.

Muscle pain and weakness are fairly common with statin drugs. Myopathy is very rare, but when it does occur, it may result in habdomyolysis, a sometimes fatal condition. Peripheral neuropathy has also been reported.

Recent research[8] shows that statins at higher dosages impair the ability of skeletal muscles to heal themselves. When primary cell lines derived from quadriceps muscles were exposed to simvastatin, the viability of the proliferating cells was reduced by 50%. "The results indicate serious adverse effects of statins that may alter the ability of muscles to repair and regenerate due to the anti-proliferative effects of statins," writes lead researcher Dr. Anna Thalacker-Mercer.

Some patients report changes in memory, attention, or concentration while on statins. In a randomized controlled study published in the *American Journal of Medicine*,[9] Dr. Matthew Muldoon, at the University of Pittsburgh, demonstrated statins reduce cognition as determined by thinking and memory ability tests. (This may be due in part to lower levels of CoQ10, which is depleted in the presence of statins.)[10]

Beatrice Golomb, MD, director of the Statin Effects Study at the University of California-San Diego, has shown that simvastatin can cause disrupted sleep patterns, nightmares, and mood changes.[11] "This double-blind study also showed a significant adverse change in aggression scores compared to others," she reports. Antibiotics and antifungal drugs can interact with the statin drugs. Grapefruit juice affects metabolism of most statins (but not pravastatin) and should not be consumed during statin therapy (other juices, however, are acceptable). Myopathy and rhabdomyolysis occur more frequently in people who take statins with other cholesterol-lowering drugs at the same time, especially niacin.

"Previous studies have demonstrated statins can reduce heart disease risk between 25% and 50%," says Dr. David Jenkins, professor of nutritional science at the University of Toronto. "We don't, however, know the long-term effects of these drugs when used on a large section of the broader population that are at low risk in primary prevention. Taking a pill may give people the false impression that they have nothing further to do to protect their health, and [it may] prevent them from making serious lifestyle changes."

Are Statins Worth the Risk?

"There is no question that blood cholesterol is a risk factor," writes Dr. Martin Hadler, professor of medicine and microbiology/immunology at UNC-Chapel Hill, in his book, *Worried Sick: A Prescription for Health in an Overtreated America,*[12] "but it's not much of a risk factor. If you have no extraordinary family history, yet have extraordinarily high LDL cholesterol and low HDL cholesterol, it will cost you a year or two of life expectancy. Nearly all who are labeled 'high cholesterol' are far from the extreme and have minimal risk. These people are contending with a reduction in life expectancy of months. Is this meaningful, or even measurable?"

Hadler cites the milestone West of Scotland Study that was published in the *New England Journal of Medicine* in 1995,[13] which studied cholesterol levels in 6,595 healthy men who agreed to a five-year, randomized, placebo-controlled trial of pravastatin. The difference between the numbers of those who suffered a fatal myocardial infarction on placebo vs. those on Pravachol was only 0.6 percent, which Hadler claims is not statistically or clinically significant.

Thomas O'Bryan, DC, believes a far more telling statistic is the "number needed to treat (NNT)," which is a measure of the overall effectiveness of a particular medication. "For Lipitor, the NNT is 100," says Dr. O'Bryan. "That means 100 people need to take Lipitor for more than three years for one less heart attack to occur in that group. Compare that to the NNT for the antibiotic that knocks out the bacteria that creates ulcers—1.1. That means for every 11 people who receive the drug, 10 will benefit. That's the kind of result patients expect from their medications."

Therefore, he says, 99 out of 100 people who take statins are assuming health risks for no measurable benefit. Dr. Dana Lawrence says, however, that doctors should be aware that NNTs are more complex than it would appear, and that medications should be evaluated on a case-by-case basis. "NNTs really cannot be compared between different drugs with different mechanisms. You need to factor in all sorts of things: side effects, cost, etc." He adds that the NNT of 100 for Lipitor is important—to the one person who avoids a heart attack.

"The standard cholesterol test is over 30 years old," says Dr. O'Bryan. "For 50% of people with cardiovascular disease, the very first sign is death—we need to pay attention to more key indicators than just HDL and LDL. For example, there are small dense LDLs that are very atherogenic; the larger buoyant LDLs are not dangerous. It's quite possible to have high levels of atherogenic LDLs that will put you at risk, even though your total cholesterol is below 200. These risk markers, as well as CRP and homocystine levels, can be easily determined with a $200 VAP blood test."

Alternative Therapies

"More people will likely be taking statin drugs as the medical indications for these drugs keep expanding," says Dr. Daniel Richardson, division director of the Department of Nutrition and Biochemical Therapeutics at the National University of Health Sciences in Lombard, Illinois. "Fortunately, there are a number of very effective dietary, supplemental, and botanical agents available to treat patients with high cholesterol. We have seen good results

utilizing fiber-rich plant foods, omega-3 fatty acids, niacin, vitamin B6 and folic acid, Co-Q10, antioxidants of plant flavonoids, and botanicals."

A 2006 study in the *American Journal of Clinical Nutrition*[14] reported that a combination of key foods, such as soy protein, almonds, plant sterols, oats, and barley can reduce LDL levels as effectively as a first-generation statin (those who adhered to the diet lowered cholesterol levels by more than 20%). In a similar vein, Mayo Clinic researchers[15] compared the lipid-lowering effects of a 12-week alternative regimen (lifestyle changes, red rice yeast, and fish oil) with a standard dose of statin. The results showed that the alternative lifestyle reduced LDL as much as the statin therapy.

James J. Cerda, MD, a former professor at University of Florida College of Medicine, conducted considerable research on the cholesterol-lowering effects of grapefruit pectin. His research[16-18] indicated up to a 40% reduction in cholesterol over six weeks using a protein-pectin-guar gum product (now the main ingredient in ProFibe, a dietary supplement).

Niacin is well known to raise HDL by 15% to 35%, "which makes it one of the most effective drugs available for controlling cholesterol," says Gerald Gau, MD, a Mayo Clinic preventive cardiologist. "Niacin also decreases LDL and triglyceride levels."[19] Possible side effects include upset stomach, flushing, headache, and, rarely, liver damage. Niacin can also affect blood sugar, so diabetics may not be able to use it.

Dr. O'Bryan has had considerable success lowering cholesterol levels with niacin. "Time-release niacin (1.5-2.0 grams) will lower total cholesterol by 16%, LDL by 20%, and increase HDL by 11% after about six months," he says.

Red rice yeast extract is a common dietary staple from Asia that contains monacolin, a substance known to inhibit cholesterol synthesis. Red rice yeast extract also contains a naturally occurring statin (lovastatin). Side effects may include slight headache, stomach ache, bloating, and muscle pain. A UCLA School of Medicine study tested red rice yeast on subjects with high cholesterol levels.[20,21] Those who received red rice yeast over a 12-week period experienced significantly lower levels of total cholesterol, LDL, and triglycerides, compared to those taking placebo. The researchers concluded "red rice yeast provides a new, novel, food-based approach to lowering cholesterol in the general population."

Steven Zaeske, DC, president of the ACA Council on Diagnosis and Internal Disorders and a chiropractic internist in Orland Park, Illinois, recommends red rice yeast extract for patients who have very high (300 or above) cholesterol levels, or who show signs of inflammation (such as elevated CRP) in addition to elevated cholesterol, or patients who insist on taking something to reduce cholesterol. "Otherwise, I prescribe diet modification and exercise, and I investigate possible causes for their cholesterol elevation, such as insulin resistance, hypothyroidism, or liver dysfunction," says Dr. Zaeske.

For those high-cholesterol patients who do take red rice yeast extract, "Within three to six months we usually see a reduction of 20 to 30 points with none of the side effects typically seen with statins," he says. Because red rice yeast extract contains lovastatin, avoiding grapefruit is advised as a precaution. He also points out that it's necessary to supplement red rice yeast extract with Co-Q10.

"Chiropractors need to take the lead in educating their patients about nutrition and cardiovascular health," says Dr. O'Bryan. "There are a number of alternatives to statins that work just as well without the potentially dangerous side effects. Once the key risk markers are identified, it is a matter of dietary changes, eliminating allergy-causing foods, and then using other

remedies to control cholesterol if it is still high. People like to think they can solve health problems by taking a pill. What we need to do is build awareness that even just a few lifestyle changes can have a long-term, positive impact on our health—with far fewer risks."

Daniel Redwood, DC, points out that patients who have high cholesterol counts or other heart disease risk factors should be made aware that their primary focus should be on major lifestyle changes, particularly with regard to "research showing that cardiovascular disease drops substantially when meats and other saturated fat sources are sharply limited." In his opinion, a doctor of chiropractic should emphasize "holistic, integrative, cost-effective, lifestyle-based approaches [that] have been validated by solid research" before suggesting "specific nutrients whose value outside a context of major lifestyle changes is questionable at best." ■

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