



Cholesterol and Lipid Lowering Drugs

These drugs are used to treat abnormally high levels of one or more types of fats such as cholesterol or triglycerides. These drugs are given to reduce the risk of atherosclerosis (hardening of the arteries) usually when dietary and other measures have not worked. In patients with coronary disease, cerebro-vascular disease (strokes or TIA's), peripheral vascular disease, abdominal aortic aneurysm and diabetes, aggressive lowering of total cholesterol and LDL cholesterol (the "bad") cholesterol have been shown to reduce the risk of heart attack and stroke by as much as 30-50%.

In general cholesterol lowering agents are started early in patients with CAD. Modern medications are very effective in lowering cholesterol with minimal side effects. When initiated in patients with CAD and other manifestations of atherosclerosis, they should be continued indefinitely.

Classes of Lipid Lowering Medications:

Statins

Fibric Acid Derivatives

Niacin

Cholesterol Binding Resins

Cholesterol Absorption Inhibitors

These drugs differ with respect to mechanism of action and degree and type of lipid lowering. In general, cholesterol can only be lowered about 10-15% by diet alone and it is difficult to adhere to a diet consistently. All patients should adhere to a low cholesterol diet. In many cases additional lipid lowering with medication will be required. If required, these medications are best initiated early to attain maximum benefit as soon as possible. If diet alone is sufficient in the long term, the dose of lipid altering medication may be reduced or the medication discontinued entirely. Most often patients on lipid lowering medications for CAD will have to remain on these medications forever. This will ensure that the coronary disease will progress as little as possible and may even regress (get better).

The choice of agent depends on the lipid abnormality:

Lipid Profile	1 st Line Therapy	2 nd Line Therapy
LDL ↑	Statin	Resin
LDL ↑↑ & TG ↑	Statin	Niacin or Fibrate
LDL ↑ & TG ↑↑	Fibrate or Niacin	Combination Therapy
TG ↑ & HDL ↓	Fibrate or Niacin	Combination Therapy

Statins

Statins are a group of medications, which block the internal production of cholesterol in the liver by blocking the enzyme HMG CoA reductase, an essential step in cholesterol production. They also increase the rate of LDL (bad cholesterol) receptor turnover in the liver. These medications may lower the LDL cholesterol by anywhere from 20% to as much as 60% depending on medication and dose. They also have a modest effect on raising HDL (good cholesterol) and lowering triglycerides.

There have been many large scale studies of the benefits of STATINS in patients after a heart attack. These show significant reductions in the risk of death, cardiac events, strokes, and the need for angioplasty and bypass surgery in patients with CAD. The benefit is in the range of 25-40%. As well aggressive cholesterol lowering with statins in post-bypass patients has been shown to reduce the rate of coronary disease developing in the bypass grafts.



Currently available **STATINS** include:

Lovastatin (Mevacor)
Pravastatin (Pravachol)
Simvastatin (Zocor)
Fluvastatin (Lescol)
Atorvastatin (Lipitor)
Rosuvastatin (Crestor)

These medications are generally well tolerated with infrequent side effects. Side effects to monitor include the development of muscle pains and liver abnormalities. While on these medications, liver function tests and the cardiac muscle enzyme CPK should be checked periodically (at 2-3 months after starting the medication and then every 6-12 months. If you develop muscle pains on these medications, report your symptoms to your physician.

If your cholesterol improves on these medications, it means the medication is working. It does not mean you no longer need the medication. **Unless you are experiencing side effects do not stop your medications without checking with your doctor.**

Fibric Acid Derivatives

The fibric acid derivatives or **Fibrates** include:

Gemfibrozil (Lopid)
Fenofibrate (Lipidil micro, Lipidil Supra, Lipidil EZ)
Bezafibrate (Bezalip)

These agents act via a variety of mechanisms to lower triglycerides (35-50%) levels and raise HDL levels (15-25%). They may also reduce Lp (a) and fibrinogen, which have been identified as newer, non-traditional risk factors. Fibrates are particularly useful in diabetic patients whose characteristic lipid abnormality is high triglycerides and low HDL. In some patients who have combined lipid abnormalities, Fibrates are combined with statins to lower both triglycerides and LDL and to raise HDL. When combined it is best to take the Fibrate in the morning and the Statin in the evening. This minimizes the overlap of medication and the side effects. The fibrate prevents the rise of triglycerides that occurs after eating and the statin prevents the overnight production of cholesterol by the liver.

When combined fibrates and statins may cause inflammation of skeletal muscles resulting in muscle pain and weakness. This side effect is uncommon, but serious and any generalized muscle pain symptoms should be reported to your physician immediately.

Bile Acid Sequestrants (RESINS)

Bile acids are the breakdown products of cholesterol. They are excreted by the liver via the bile. They are 90% reabsorbed from the intestine and used to re-manufacture cholesterol in the liver. Bile Acid Sequestrants (RESINS) interfere with this intestinal reabsorption, by binding the bile acids in the gut and thus promoting their excretion from the body. These agents are not absorbed and hence have no systemic effects. They may lower the LDL cholesterol by 10-30% depending on the dose. The use of these agents is often limited by GI side effects such as nausea, bloating, cramping and abnormal liver function.

Cholesterol Absorption Inhibitors

Cholesterol absorption inhibitors are a new class of cholesterol lowering drugs which block absorption of cholesterol at the brush border of the intestine without affecting absorption of triglycerides or fat soluble vitamins. These drugs have the advantage of not being systemically absorbed and can lower cholesterol by about 20% on their own. When used in addition to statins they may provide an additional 15% cholesterol lowering. It is recommended to monitor liver function tests when using a cholesterol absorption inhibitor and a statin together. Side effects including fatigue, abdominal pain, diarrhea, muscle and joint pains and coughing are infrequent.

The only currently available cholesterol absorption inhibitors is Ezetimibe (Ezetrol).



Niacin

Niacin is a B-vitamin (no relationship to nicotine) and is one of the best medication available for patients with *elevated levels of both triglycerides and cholesterol and low levels of HDL cholesterol*. In well-controlled studies, niacin has been shown to reduce heart attacks and death from heart disease. It has also been shown to be effective in reducing the size of cholesterol deposits in the arteries of the heart.

Niacin is also available as a long acting preparation Niaspan®. Niaspan® is an extended release form of niacin intended for once daily dosing. Niaspan® may have less side effects and be better tolerated than short acting niacin. The starting dose is 500 mg and the dosing is not directly interchangeable with short acting niacin. Dose adjustments should be made at four weekly intervals. The maximum dose is 2000mg. Take Niaspan® only as directed. Do not chew the tablet. Take in the evening with a fatty snack.

Side-effects

Niacin is quite a safe medication. There is a risk of an increase in blood sugar levels in patients with diabetes but this can usually be controlled with diet. Uric acid levels in the blood tend to rise and, rarely, this may result in gout. In a few patients, small changes may occur in liver function tests. Patients with a history of duodenal ulcers may experience an increase in ulcer symptoms and should avoid this medication until the ulcer is well healed. You will be checked each time that you have a blood test for each of these possible complications and if you do experience any side-effects, they tend to resolve quickly once the niacin is stopped.

The most common side-effects with niacin are not serious ones but can make it difficult to adjust to the medication. When patients first start to take niacin, they will experience symptoms such as flushing, itching or tingling of the skin and slight lightheadedness. These side-effects are due to opening up of small blood vessels in the skin. Fortunately these symptoms tend to disappear as the body adjusts to the medication and are not usually a significant problem after the first month or two of treatment.

One to three coated aspirin per day will help to reduce flushing during the first few weeks of treatment. Take the coated aspirin approximately 1 hour before each meal or just before breakfast and take the niacin after your meal.

Start therapy as follows: 500 mg tablets

- 1/4 tablet after each meal for 2 weeks-then
- 1/2 tablet after each meal for 2-4 weeks-then
- 1 tablet after each meal for 2-4 weeks-then, if directed
- 2 tablets after each meal thereafter

Maintaining tolerance

If you experience excessiveness of flushing, increase the dose more slowly. Avoid taking niacin with a hot beverage or on an empty stomach. It is important to follow a regular pattern and take the niacin 2 or 3 times per day after meals. Usually, in a few weeks, flushing and itching disappear. However, if you miss taking the medication for even a day or two, these symptoms tend to return.

