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A Review on Anti-Cholesterol Drugs and Statins

Priyanka Patel*¹, Harnish Patel², Akshay Patel³, Taher Patel⁴

¹Managing Editor, IJPRBS, Gujarat, India

²Editor-In-Chief, IJPRBS, Gujarat, India

^{3,4}Assistant Professor, L.B Rao Institute of Pharmaceutical Education & Research,
B.D Rao Collage Campus, Khambhat, India

*E-mail: editorijprbs@gmail.com

ABSTRACT

An in-depth report on the diagnosis, treatment, and prevention of unhealthy cholesterol levels. The statins (or HMG-CoA reductase inhibitors) along with other drugs, such as cholestyramine (Questran), comprise the class of hypolipidemic drugs. Hypolipidemic drugs are prescribed - sometimes aggressively so - to lower cholesterol levels in people with or at risk of cardiovascular disease and certain inflammatory diseases such as sarcoidosis. Statins are prescribed even though their full mechanisms of action remain unclear. One strong possibility is that statins exert their effects via the body's nuclear receptors, which are intricately connected to innate immune function. Statins may have benefits other than just lowering your cholesterol. One promising benefit of statins appears to be their anti-inflammatory properties, which help stabilize the lining of blood vessels. This has potentially far-reaching effects, from the brain and heart to blood vessels and organs throughout the body. In the heart, stabilizing the blood vessel linings would make plaques less likely to rupture, thereby reducing the chance of a heart attack.

Key words: Hypercholesterolemia, LDL, HDL, Triglycerides

Introduction

Statins are the most effective drugs for the treatment of high cholesterol, particularly for lowering LDL levels. They also have modest effects in lowering triglycerides and increasing HDL levels. Statins inhibit the liver enzyme HMG-CoA reductase, which the body uses to manufacture cholesterol.

These drugs effectively reduce the risk of major coronary events, including first and second heart attacks and stroke, in adults with unhealthy cholesterol levels. Brands and Statins approved in the U.S. include: Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol), Atorvastatin (Lipitor), Rosuvastatin (Crestor)

Types of cholesterol drugs:

Statins: The following is a list of common cholesterol-lowering drugs known as statins: Lovastatin, Pravastatin, Simvastatin, Fluvastatin, Atorvastatin, Rosuvastatin, Atrovastatin, and Ezetimibe

Other cholesterol drugs:

The following is a list of common non-statin cholesterol-lowering drugs:

cholestyramine (Questran) – Part of another treatment protocol, cholestyramine is touted to relieve symptoms supposedly caused by the release of toxins as the Lyme spirochete is killed. However, cholestyramine is known to interfere with the action of tetracycline, an antibiotic in the same class – the tetracycline family of antibiotics – used by many of the MP antibiotics. Gemfibrozil (Lopid, Gemcor), Omacor, Pantethine.

Debatable mechanism of action for statins:

Large numbers of patients at risk for cardiovascular disease or stroke are prescribed statins – drugs that are marketed as improving health by lowering cholesterol. There's no question that statins can effectively lower cholesterol. But, does lowering cholesterol actually benefit patients with coronary artery disease and more importantly, are the effects of statins on patients with heart disease even related to their ability to lower cholesterol.

The fact that statin treatment lowers both total and cardiovascular mortality in high-risk individuals is taken as evidence that cholesterol lowering is effective. However, statins are just as effective whether cholesterol is lowered by a small amount (as in the unsuccessful non-statin trials) or by more than 40%. In addition, statin treatment is effective whether the initial LDL-C is high or low.^{3 4} If high LDL-C were causal, the greatest effect should have been seen in patients with the highest LDL-C, and in patients whose LDL-C was lowered the most, but this is not the case. Lack of dose-response cannot be attributed to the knowledge that the statins have other effects on plaque stabilization, as this would not have masked the effect of cholesterol-lowering, considering the pronounced lowering that was achieved.

Ravnskov compares two separate trials of a single statin, simvastatin: a 2002 trial (nicknamed HPS)⁶ and a 1994 study (nicknamed 4S)⁷. The 4S research team reported a three times greater risk of coronary death in the HPS trial, even though patients' total cholesterol in the 4S trial was decreased to a much lower extent. A seminal study called the ENHANCE trial was published in 2008. The trial tested the effects of a new cholesterol-lowering medication called Zetia (which, as opposed to the statins, works by decreasing cholesterol absorption in the intestine) on patients with cardiovascular disease. It found that Vytorin, a combination pill containing both Zetia and the statin Zocor (simvastatin), proved better than the statin alone at reducing levels of cholesterol. However, ENHANCE collaborators reported that Vytorin resulted in *growth* of plaque.

All together, this evidence suggests statins' ability to (slightly) improve health outcomes is independent of their ability to lower cholesterol. Contraindications of statins: In particular, the following drugs seem to make the statins more likely to cause problems: prenisolone and steroid inhalers, Methotrexate and Imuran, antimalarials such as Cloroquin and Plaquenil, thyroid preparations

Benefits of Statins:

Statins may have benefits other than just lowering your cholesterol. One promising benefit of statins appears to be their anti-inflammatory properties, which help stabilize the lining of blood vessels. This has potentially far-reaching effects, from the brain and heart to blood vessels and organs throughout the body. In the heart, stabilizing the blood vessel linings would make plaques less likely to rupture, thereby reducing the chance of a heart attack. Statins also help relax blood vessels, lowering blood pressure. In addition, statins could reduce your risk of blood clots. For these reasons, doctors are now beginning to prescribe statins before and after coronary artery bypass surgery or angioplasty, and following certain types of strokes. Statins could also have benefits that help prevent diseases that aren't related to your heart health, although more research is necessary. Other benefits of statins could include a reduced risk of Arthritis and bone fractures, Some forms of cancer, Dementia and Alzheimer's disease, Kidney disease, Statins may also be helpful in controlling the body's immune system response after an organ transplant.

Anti Cholesterol Drugs:**Lovastatin**

Lovastatin belongs to a class of medications called as HMG-CoA reductase inhibitors (statins). These anti cholesterol drugs are used in conjunction with lifestyle changes (diet, weight-loss, exercise) to reduce cholesterol and fatty substances in blood.

Lovastatin strength: 10mg/20mg

Common brand name: Mevacor

How to Use

It comes in tablet form and an extended-release tablet for oral intake. Regular tablets are taken about once or twice a day along with meals. Extended-release tablets are taken once a day during evening at bedtime. Follow label directions carefully, and consult doctor or pharmacist for further information. Take exactly as directed and not in any quantity variable to that prescribed by doctor. Extended-release tablets should be swallowed whole. Continue intake even on relief from symptoms and do not stop without consulting your doctor.

Side Effects

Lovastatin may cause certain side effects such as constipation. Consult doctor if symptom is severe and persists. Certain side effects can be serious. On occurrence of any side effects consult your doctor immediately. Some uncommon side effects are: Muscle pain, Lack of energy, Fever, Yellowish skin or eyes, Fatigue, Loss of appetite, Unusual bleeding

Precautions

Before taking lovastatin, inform doctor or pharmacist about any allergy to lovastatin or other medications. Consult doctor about any planned intake of prescription and nonprescription medications, nutritional supplements, vitamins, and herbal products. Inform doctor about your alcohol habits and medical history, especially any existing liver disease.

Avoid breastfeeding during this medication. ? In case of any surgery, including dental surgery, tell surgeon or dentist about lovastatin medication.

Over Dose

In case of overdose, call emergency services immediately.

Missed Dose

Take missed dose as soon as you remember. If its time for next dose, skip missed dose and continue regular dosing. Avoid double doses for compensating missed ones.

Storage

Keep medication in container, tightly closed, and out of reach of children. Store at room temperatures and away from excess heat & moisture. Throw away medication after consulting with pharmacist about proper disposal methods.

Simvastatin

Simvastatin belongs to a class of medication referred to as HMG-CoA reductase inhibitors. When used in conjunction with changes in lifestyle in terms of diet, weight-loss, exercise, etc, it reduces the amount of cholesterol and other fatty substances in blood. Simvastatin works by slowing cholesterol production in the body.

Simvastatin strength: 20mg

Common brand name: Zocor

How to Use

Simvastatin is available in tablet form for intake through mouth and usually taken once or thrice a day at around the same time. Follow the exact direction of your prescription or label and also consult your doctor or pharmacist for explanation about details. Take simvastatin exactly as directed by doctor and in quantities as prescribed by the doctor. Your doctor may begin Simvastatin on a low dosage and gradually increase it, to no more than once every 4 weeks. Persist with the medication even if there is relief and do not stop it without consulting with your doctor

Side Effects

Simvastatin may cause certain side effects. Inform your doctor if any of these symptoms are severe and do not go away: Constipation, Headache, Swelling, Loss of appetite, Nausea, Fever

Precautions

Before taking Simvastatin, Inform doctor & pharmacist about any allergies to Simvastatin or other medications. Inform doctor and pharmacist about any intake - existing or planned - of medications, nutritional supplements, vitamins, as well as herbal products. Consult your doctor about any history of liver disease, kidney disease, or other medical conditions. Inform doctor about your drinking habits. Inform your doctor about any pregnancy - planned or unplanned. If you do become pregnant while on Simvastatin, stop taking Simvastatin and inform doctor immediately. Do not breast-feed infants while on this medication. In case of any planned surgery, including that of dental surgery, inform doctor or the dentist about intake of Simvastatin. Consult doctor about the usage of alcoholic beverages, ask your doctor about the safe use of alcoholic beverages while you are taking simvastatin. Alcohol can increase the risk of serious side effects.

Over Dose

If case of an overdose, or incapacitation of the victim, breathing problems, etc., inform doctor or call local emergency services.

Missed Dose

Take missed dose on remembering it. If the next dosage is due, shortly, then skip the missed dose and take the next. Compensating for missed doses by double dosage is not safe.

Storage

Keep in the container, closed tightly, and out of the reach of children. Store at room temperatures and away from excess heat and moisture.

Pravastatin

Pravastatin is a HMG-CoA reductase inhibitor (statin) that is used in conjunction with lifestyle changes (diet, exercise, weight-loss) to reduce cholesterol content and other fatty substances in blood. It works by slowing cholesterol production in the body.

Pravastatin strength: 10mg/20mg

Common brand name: Pravachol

How to Use

Pravastatin comes in tablet format for oral intake. It is taken once a day independent of food intake. Take Pravastatin at the same time every day. Follow prescription directions carefully, and consult your doctor or pharmacist to explain details. Take Pravastatin exactly as directed and do not deviate from labelled prescription amounts. Your doctor may start with low dosage of Pravastatin and gradually increased dosage, not exceeding once every 4 weeks. Persist with Pravastatin even if there is relief.

Side Effects

Pravastatin may cause certain side effects. Consult your doctor if any of these symptoms occur and persist: Flu-like symptoms, Muscle pain, weakness, Nausea, Headache, Loss of appetite, Heartburn, Swelling

Precautions

Before taking Pravastatin: Consult doctor and pharmacist about any existing allergies. Consult doctor and pharmacist about any medications or supplements you might be under. If you are under cholestyramine or colestipol medication, take them 4 hours before or after Pravastatin. Antacids are to be taken an hour before Pravastatin. Inform doctor about alcohol intake and medical history, especially about any liver disease? Consult your doctor about pregnancy either existing or planned. Breastfeeding should be avoided. If you are to undergo surgery, including dental, inform the doctor or dentist about Pravastatin usage.

Over Dose

If there is overdose, or the victim is incapacitated, or has breathing problems, inform doctor or call local emergency services.

Missed Dose

In case of missed dose, take the missed dose on remembering it. However, if the next dose is due, then skip the missed dose and continue with regular schedule of dosage. Do not take double doses to compensate for the missed ones.

Storage

Keep medication in container, tightly closed, and out of the reach of children. Store at room temperatures and keep away from heat and moisture. Do consult pharmacist or doctor about proper disposal of outdated drugs.

Cholesterol medications:

Drug class and drug names	Benefits	Possible side effects and cautions
Statins Altprev(lovastatin)Crestor (rosuvastatin) Lescol (fluvastatin) Lipitor (atorvastatin) Mevacor(lovastatin)Pravachol(pravastatin) Zocor (simvastatin)	Decrease LDL and triglycerides; slightly increase HDL	Constipation, nausea, diarrhea, stomach pain, cramps, muscle soreness, pain and weakness; possible interaction with grapefruit juice
Bile acid binding resins Colestid (colestipol) Questran (cholestyramine/ sucrose) Welchol (colesevelam)	Decrease LDL	Constipation, bloating, nausea, gas; may increase triglycerides
Cholesterol absorption inhibitor Zetia (ezetimibe)	Decreases LDL; slightly decrease triglycerides; slightly increase HDL	Stomach pain, fatigue, muscle soreness
Combination cholesterol absorption inhibitor and statin Vytorin (ezetimibe-simvastatin)	Decreases LDL and triglycerides; increases HDL	Stomach pain, fatigue, gas, constipation, abdominal pain, cramps, muscle soreness, pain and weakness; possible interaction with grapefruit juice
Fibrates Lofibra(fenofibrate) Lopid(gemfibrozil) TriCor (fenofibrate)	Decrease triglycerides; increase HDL	Nausea, stomach pain, gallstones
Niacin Niaspan (prescription niacin)	Decreases LDL and triglycerides; increases HDL	Facial and neck flushing, nausea, vomiting, diarrhea, gout, high blood sugar, peptic ulcers
Combination statin and niacin Advicor (niacin-lovastatin)	Decreases LDL and triglycerides; increases HDL	Facial and neck flushing, dizziness, heart palpitations, shortness of breath, sweating, chills; possible interaction with grapefruit juice
Omega-3 fatty acids Lovaza (prescription omega-3 fatty acid supplement) Vascepa (Icosapent ethyl)	Decrease triglycerides	Belching, fishy taste, increased infection risk

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References

1. Kastelein JJ, Akdim F, Stroes ES, Zwinderman AH, Bots ML, Stalenhoef AF, Visseren FL, Sijbrands EJ, Trip MD, Stein EA, Gaudet D, Duivenvoorden R, Veltri EP, Marais AD, de Groot E Simvastatin with or without ezetimibe in familial hypercholesterolemia. *N Engl J Med.* 2008; 358:1431-43.
2. Ravnskov U High cholesterol may protect against infections and atherosclerosis. *QJM.* 2003;96:927-34.
3. Sacks FM, Moyé LA, Davis BR, Cole TG, Rouleau JL, Nash DT, Pfeffer MA, Braunwald E Relationship between plasma LDL concentrations during treatment with pravastatin and recurrent coronary events in the Cholesterol and Recurrent Events trial. *Circulation.* 1998; 97:1446-52.
4. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA.* 2001; 285:1711-8.
5. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet.* 2002;360:7-22.
6. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S) *Lancet.* 1994; 344:1383-9.
7. Ruland S, Gorelick PB Are cholesterol-lowering medications and antihypertensive agents preventing stroke in ways other than by controlling the risk factor? *Curr Atheroscler Rep.* 2003; 5:38-43.
8. Willrich MA, Hirata MH, Hirata RD Statin regulation of CYP3A4 and CYP3A5 expression. *Pharmacogenomics.* 2009; 10:1017-24.
9. Marzoa-Rivas R, Crespo-Leiro MG, Paniagua-Marin MJ, Llinares-García D, Muñoz-García J, Aldama-López G, Piñón-Esteban P, Campo-Pérez R, Castro-Beiras A Safety of statins when response is carefully monitored: a study of 336 heart recipients. *Transplant Proc.* 2005; 37:4071-3.
10. Langsjoen PH, Langsjoen JO, Langsjoen AM, Lucas LA Treatment of statin adverse effects with supplemental Coenzyme Q10 and statin drug discontinuation. *Biofactors.* 2005;25:147-52.
11. Ravnskov U, Rosch PJ, Sutter MC, Houston MC Should we lower cholesterol as much as possible? *BMJ.* 2006; 332:1330-2.
12. Lantuejoul S, Brambilla E, Brambilla C, Devouassoux G Statin-induced fibrotic nonspecific interstitial pneumonia. *Eur Respir J.* 2002; 19:577-80.
13. Geddes R Minocycline-induced lupus in adolescents: clinical implications for physical therapists. *J Orthop Sports Phys Ther.* 2007; 37:65-71.
14. Ballantyne CM, Corsini A, Davidson MH, Holdaas H, Jacobson TA, Leitersdorf E, März W, Reckless JP, Stein EA Risk for myopathy with statin therapy in high-risk patients. *Arch Intern Med.* 2003;163:553-64.
15. Rosenson RS Current overview of statin-induced myopathy. *Am J Med.* 2004; 116:408-16.
16. Sidaway JE, Davidson RG, McTaggart F, Orton TC, Scott RC, Smith GJ, Brunskill NJ Inhibitors of 3-hydroxy-3-methylglutaryl-CoA reductase reduce receptor-mediated endocytosis in opossum kidney cells. *J Am Soc Nephrol.* 2004; 15:2258-65.
17. Vidt DG, Cressman MD, Harris S, Pears JS, Hutchinson HG Rosuvastatin-induced arrest in progression of renal disease. *Cardiology.* 2004; 102:52-60.
18. Pullatt RC, Gadarla MR, Karas RH, Alsheikh-Ali AA, Thompson PD Tendon rupture associated with simvastatin/ezetimibe therapy. *Am J Cardiol.* 2007;100:152-
19. Armitage J. The safety of statins in clinical practice. *Lancet.* 2007 Nov 24; 370(9601):1781-90.
20. Barter P, Gotto AM, LaRosa JC, Maroni J, Szarek M, Grundy SM, et al. HDL cholesterol, very low levels of LDL cholesterol, and cardiovascular events. *N Engl J Med.* 2007 Sep 27; 357(13):1301-10.