

Review (Narrative)

Atorvastatin and Kidney

The Pros and Cons of the Cholesterol Killer

Abel Hawkes, PharmD; Karen Lynn Kristoff, PhD

SUMMARY

Atorvastatin, one of the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, takes effect on regulating the level of cholesterol. It is beneficial in most of the cases like preventing stroke and coronary heart disease. Whereas it has been noted that atorvastatin can the breakdown of the tissues in the skeletal muscle thus leading to the kidney failure. Atorvastatin itself or in combination with other drugs can result in toxin effect on non-targeted organs. We should be cautious when prescribe this drug with thorough evaluation and careful consideration. Individualized or personalized usage of atorvastatin should be an evidence-based manner. Kidneys, as the outlet of the wastes from cellular metabolism, have been shown that function as the causing aspect of many other diseases due to the problem of its blood vessels narrowing which eventually results in piling up of the disease-causing wastes. The fact that the kidney is not able to function normally and extract the waste in the body like cholesterol means that the cholesterol in the body blood vessel will be deposited on the wall. Even atorvastatin functions as the killer of cholesterol, it still should be cautious when prescribe this drug to patients with reduced renal function, especially to those with chronic kidney disease, because of its nephritic toxic effect.■

KEYWORDS HMG-CoA reductase inhibitor; Atorvastatin; Cholesterol; Kidney; Toxicity

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Author Affiliations: Author affiliations are listed at the end of this article.

Correspondence to: Dr. Karen Lynn Kristoff, PhD, Cardiovascular Institute, Department of Medicine, The Sages Pharmaceuticals, Grahamstown, 6139, South Africa
Email: k.l.kristoff@africa-11.com

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Atorvastatin is a drug that exists in a group of drugs by the name HMG-CoA reductase inhibitors or statins. The drug mainly serves the purpose of reducing levels of bad cholesterol in low-density lipoprotein or LDL and also triglycerides in the blood (1). It achieves this by increasing levels of good cholesterol in high-density lipoprotein or HDL. Atorvastatin is significant in the treatment of Kidney conditions resulting from high cholesterol as well as in the lowering of the risks of stroke, heart complications and other complications in persons with diabetes, coronary heart disease, and other significant risk factors (2). Atorvastatin has also been found important in decreasing the amount of cholesterol and other substances in the blood in children with familial heterozygous hypercholesterolemia, a condition common in children and teenagers between the ages of 10 to 17 years (3). The heterozygous hypercholesterolemia is a condition that is usually inherited whereby cholesterol cannot be removed from the body. It has been noted in rare cases that atorvastatin can cause a condition that can result in the breakdown of the tissues in the skeletal muscle thus leading to the kidney failure. Atorvastatin is marketed under the Lipitor trade name among many others. Atorvastatin only serves as the part of the treatment program that includes checking your diet, exercising and controlling your weight (4). This paper seeks to review the impact of Atorvastatin in the management of the kidney disorders by showing the way forward.

CAUTIONS NEEDED FOR ATORVASTATIN IN PRESCRIPTION

The atorvastatin medication is highly prescribed for use not only in the treatment of the kidney disorders but also in the reduction of the risk of a heart attack and stroke. It decreases the chances that a kidney or heart surgery will be needed in persons with the risks of developing kidney and heart diseases. Atorvastatin reduces the number of fatty acids, for example, the Low-density lipoprotein (LDL) cholesterol well known as the bad cholesterol as well as the triglycerides in the blood. It also increases the high-density lipoprotein (HDL) cholesterol well known as the good cholesterol in the blood. Atorvastatin works by lowering the rate of cholesterol production in the body thus decreasing the amount of cholesterol on the walls of arteries and blocks the blood

flowing to the heart, brain, kidney and other body parts (5).

The usage of the Atorvastatin comes in a pure tablet form that is taken orally by mouth. The usage time is usually once a day at around the same time every day accompanied by either food or without food. It is paramount to follow the prescriptions and directions as labeled and indicated by your doctor or pharmacist. Any deviation from those orders can lead to serious complications. In taking atorvastatin prescriptions, you should follow the various precautions as required by your doctor. You should tell your doctor and pharmacist if you have any allergies to atorvastatin, any ingredients of atorvastatin tablets or any other medications (4). The other aspect is that your doctor should be aware of the prescriptions and nonprescription medications, nutritional supplements, herbal products and vitamins you are currently taking or planning to take. You should mention medications including antifungal drugs such as Itraconazole, ketoconazole, boceprevir, and cimetidine; cobicistat-containing medications and other cholesterol-lowering medications (6). This way, the doctor will be able to change the drug doses if required or monitor any side effects that might come as a result.

The other precautions that should be considered when administering atorvastatin include; assessing whether you have liver diseases. Your doctor will have to take laboratory tests to see the workability of your liver. In cases where you have a liver disease, you will be required not to take atorvastatin. Information about pregnancy should also be produced as you are not supposed to be pregnant as you take the atorvastatin drugs (4). You are not supposed to take atorvastatin while you are pregnant as this will harm the fetus. In case you get pregnant while using the drugs, you should stop using them and contact your doctor immediately. Some other information that you should disclose to your doctor concerns the alcoholic content you consume each day especially if it is more than two bottles.

While taking the atorvastatin drugs, you are also required to follow special dietary instructions. You should eat a low fat and low cholesterol diet as well as follow all the exercises and dietary recommendations made by your doctor or your dietitian. In cases where you might forget to take your atorvastatin dose, you should take the missed dose as soon as you remember to do so. In the event where your dose is less than 12 hours until you take your next scheduled dose, you need to

skip the missed dose and go on to the normal dosing schedule (1).

Atorvastatin has various side effects despite the fact that it is significant in the prevention of the kidney disorders. Atorvastatin can lead to severe symptoms of diarrhea, joint pain, heartburn, gas, confusion, and memory loss and once such conditions are experienced, you should consult your doctor immediately. Some side effects of atorvastatin can be severe and thus requiring urgent medical care. Such effects include; increased muscle pain with tenderness and weakness, lack of energy, high fever, chest pains, nausea and increased tiredness (2). You can also experience unusual bleeding or bruising, loss of appetite, pain in the stomach's upper right part, having dark-colored urine, flu-like symptoms, yellowing of the skin or the eyes and itching pains. Other severe symptoms that also require urgent medical support include; difficulties in breathing or swallowing, the swelling of the face, lips, eyes, tongue, feet, ankles and the lower legs.

The storage and disposal of atorvastatin medication are an important factor to consider. The medication should be stored in the container it came in, and it should be tightly closed and out of children's reach. It should be kept at the room temperature and away from excess moisture and heat. Unrequired medications should be properly disposed of away from pets, children and other people who might consume (6). The best way to dispose of the atorvastatin medication is through a medicine take-back program in your community.

MECHANISMS OF ATORVASTATIN AND ITS IMPACT ON RENAL FUNCTION

The mechanism of action for Atorvastatin in the treatment of the kidney disorders is by a competitive inhibitor of HMG-CoA reductase. This reductase catalyzes the reduction of 3-hydroxy-3-methylglutaryl-coenzyme A to mevalonate which acts as the rate-limiting step in hepatic cholesterol biosynthesis. The inhibition of the enzyme helps to decrease cholesterol synthesis thus increasing the expression of the LDL receptors on hepatocytes. The absorption of atorvastatin usually undergoes an approximate time to maximum plasma concentration of 1 to 2 hours. Atorvastatin goes through a high intestinal clearance and metabolism which cause a low systemic availability (7). The liver is deemed as the primary site of atorvastatin action as it is the site of both LDL

clearance and cholesterol synthesis. It acts as the dosage of atorvastatin and not systemic drug concentration which correlates with the LDL-C reduction.

Atorvastatin is a prescribed drug that is recommended for reducing the level of Cholesterol in human blood through the reduction of the cholesterol produced in the liver. The scientists have proven that people with high level of cholesterol in their body a condition known as Hypercholesterolemia; have a high risk of suffering from cardiovascular disease. The cardiovascular disease is very dangerous since it can lead to the heart attack, chest pain, stroke and even peripheral vascular disease (8). The deposition of the cholesterol is very dangerous since it can cause blockage of blood in the heart or even in the brain. In this kind of condition, the doctor recommends the patient atorvastatin drug that helps in controlling the situation. The atorvastatin works by blocking the entire enzyme that is responsible or used in making cholesterol. The enzyme that is targeted by the atorvastatin is known as HMG-CoA reductase. In fact, the atorvastatin is sometimes referred as the HMG-CoA reductase inhibitors. Through the process of blocking the enzyme, the atorvastatin reduces the amount of plaques formed in the body as well as reducing already existing plaques that formed in blood vessels (9). The atorvastatin also controls the already existing plaques not to rupture and form clots. Consequently, the new studies show that the atorvastatin reduces the inflammation developed in arteries walls something that is more important to the people with lupus since they are more likely to suffer from the clogged arteries as a result of inflammation.

According to studies, the persons taking high doses of atorvastatin and more specifically statins have been deemed as more likely to develop kidney problems. There is no exact evidence of whether statins cause kidney injuries but the elevated risk in patients using high-potency statins is said to relate to an increased likelihood of damage to the muscles. The statins have also been found to block the production of the Q10 coenzyme that helps break down food in the body thus leading to kidney injury (10). The various signs and symptoms of kidney injury include darkened urine, difficulty in urinating and reduced frequency of urination. In cases where you are on a higher dose of statin and such issues with urination arise, you should consult your doctor.

Kidney is one of the most vital organs that require a lot of care and protection. The kidney is known for its



role in removing any waste from the blood. As we all know, the blood constituents many wastes of which some are useful in the body while others are toxic and require to be removed from the body. The kidney requires regular diagnosing and treatment to prevent any possible disease that may affect it. However, on the normal functions of the kidney are affected, it becomes a severe health problem that can easily result in death. Chronic kidney disease is one of the common diseases that put the life of human being in danger (3, 5). The disease tends to slow down the normal kidney functions over time something that endangers the human health. Once the organ has been affected it means that, it won't perform its role of extracting waste material from the blood and removal of excess water from the body. If not immediately prevented or treated at the early stage, the chronic kidney disease (CKD) gradually gets worse and may not be able to notice the symptoms at the beginning of days. The effect of kidney function may take place at a slow pace that, you may not realize until when the kidney stops working entirely. The final and severe stage of the CKD is known as the end-stage renal disease (ESRD). At this point, the condition is too painful and cruel to the person since the kidney is no longer able to remove the excess fluid and waste from the blood and that means that, the blood is contaminated by toxic substances in the body (8). The only treatment that can be done at this point is dialysis or a kidney transplant. Some common severe diseases that may affect the kidney include High blood pressure especially to the aged people and Diabetes. Some of the symptoms associated with the CKD include; trouble in sleeping,

not feeling hungry, itching, muscles cramps, and difficulty in catching your breath. Consequently, the person may start swelling feet and ankles, nausea, and vomit as well as too much or not enough urine. If the kidney stops working suddenly, the incident is known as acute kidney failure.

Studies show that most kidney diseases are caused by the problem blood vessels narrowing. The fact that, the kidney is not able to function normally and extract the waste in the body like cholesterol means that the cholesterol in the body blood vessel will be deposited on the wall. The process of depositing cholesterol continues and with time, the blood vessel narrows making it unable to transport enough blood to supply all the body tissues. At that time, it is when you encounter oxygen shortage in the body cells. Cholesterol is referred to as a fatty substance found in the blood vessels that is very useful in the body and is carried around the body in the blood. Once the blood vessels and the kidney have been damaged, the cholesterol can't be transported efficiently hence end up being deposited on the walls of the vessels eventually causing narrowing (8). Although cholesterol is useful for normal body and cell functions, a high level is toxic in the body and can result in Atherosclerosis. Atherosclerosis is a critical and severe condition where the cholesterol builds up in the arteries blocking smooth blood flow. Under that condition, the patient is advised to take drugs that can lower the high level of the Cholesterol in the body.

However, only the doctor who should recommend a person to use atorvastatin especially after the change of lifestyle does not sufficiently control the condition of

high levels of the low-density lipoprotein or in other words is known as “bad cholesterol.” The atorvastatin drugs should only be taken on prescription since they can be dangerous to the health of the user if overdosed. If you are not suffering from any kidney disease then you take the atorvastatin dose, you are at higher risk of suffering the acute kidney disease according to the new research was done in the America (9). As per the statistics, about 1,700 people annually suffers the kidney disease due to the act of taking atorvastatin while are not suffering from ant kidney disease (9). Consequently, the atorvastatin is also useful in the body due to its ability to raise the levels of high-density lipoproteins (HDL) or in other words “good cholesterol” something that protects the body from the heart attack. Moreover, the researchers indicate that the HDL can as well be used to carry the already formed plaque away from arteries. That would protect the blood vessels from the danger of blockage.

CONCLUDING REMARKS

From the facts analyzed about the usefulness of the atorvastatin in the prevention of the kidney, it can be concluded that the proper function of the organ depends on the atorvastatin drugs. The kidney is a very sensitive body organ that requires the high degree of protection for any infection. The atorvastatin is well known for its power and ability to control any abnormality condition in the kidney. However, the drug needs a lot of precautions when you are taking it since it can be so dangerous to your health. Moreover, there are a particular group of people who are not advised to take the atorvastatin like pregnant mothers. Nevertheless, atorvastatin is of great importance for a better condition of the human kidney. It indeed, protects the kidney from some severe diseases that can disrupt the normal functions of the kidney.■

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Author Affiliations: Cardiovascular Institute, Department of Medicine, The Sages Pharmaceuticals, Grahamstown, 6139, South Africa (Hawkes, Kristoff).

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REFERENCES

1. Fassett RG, Robertson IK, Ball MJ, Geraghty DP, Coombes JS. Effect of atorvastatin on kidney function in chronic kidney disease: A randomised double-blind placebo-controlled trial. *Atherosclerosis* 2010; 213:218-224.
2. Goicoechea M, de Vinuesa SG, Lahera V, Cachofeiro V, Gómez-Camperá F, Vega A, Luño J. Effects of atorvastatin on inflammatory and fibrinolytic parameters in patients with chronic kidney disease. *J Am Soc Nephrol* 2006; 17:S231-S235.
3. Shepherd J, Kastelein JJ, Bittner V, Deedwania P, Breazna A, Dobson S, Wenger NK. Intensive lipid lowering with atorvastatin in patients with coronary heart disease and chronic kidney disease: the TNT (Treating to New Targets) study. *J Am Coll Cardiol* 2008; 51:1448-1454.
4. Eknayan G, Hostetter T, Bakris GL, Hebert L, Levey AS, Parving HH, Toto R. Proteinuria and other markers of chronic kidney disease: A position statement of the national kidney foundation (NKF) and the national institute of diabetes and digestive and kidney diseases (NIDDK). *Am J Kidney Dis* 2003; 42:617-622.
5. Shepherd J, Kastelein JJ, Bittner VA, Carmena R, Deedwania PC, Breazna A, Wenger NK. Intensive lipid lowering with atorvastatin in patients with coronary artery disease, diabetes, and chronic kidney disease. *Mayo Clin Proceedings* 2008; 83:870-879.
6. Trialists CT. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. *Lancet* 2005; 366:1267-1278.
7. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, Mehlsen J. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): A multicentre randomised controlled trial. *Lancet* 2003; 361:1149-1158.
8. Bianchi S, Bigazzi R, Caiazza A, Campese VM. A controlled, prospective study of the effects of atorvastatin on proteinuria and progression of kidney disease. *Am J Kidney Dis* 2003; 41:565-570.
9. Takagi H, Umemoto T. A meta-analysis of randomized trials for ef-

fects of atorvastatin on renal function in chronic kidney disease. *Int J Cardiol* 2011; 152:242-244.

10. Lipitor – Statin & cholesterol drug could cause diabetes. (2016). Drug Watch. Retrieved 10 March 2016, from

<http://www.drugwatch.com/lipitor/> ("Lipitor – Statin & Cholesterol Drug Could Cause Diabetes", 2016).■