Original Article

# Impact of Lipid-Lowering Drugs on Lipid Profile in Hyperlipidemia Patients

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## Abstract

**Background:** Hyperlipidemia is an umbrella term for any of the genetic or acquired disorders that result in an elevated level of lipids circulating in the blood. These lipids can enter the walls of arteries and increase the risk of developing hardening of the arteries, which can lead to atherosclerosis, stroke, and heart attack. **Objectives:** The present study tries to investigate the impact of lipid-lowering drugs on lipid profile in patients with hyperlipidemia and to determine the best drug of choice in such patients. **Materials and Methods:** Sixty hyperlipidemia patients with the mean age of 45.52 ± 13.24 years admitted to a private clinic in Hilla city, Iraq, during a period extant from October 2022 to November 2022 were subjected to the present cross-sectional study. Patients were categorized according to the type of drug used and gender. Group 1 (G1) patients treated with rosuvastatin, group 2 (G2) patients treated with atorvastatin, group 3 (G3) patients treated with ezetimibe, and group 4 (G4) patients treated with combination of ezetimibe + simvastatin. Lipid profile was determined using enzymatic method. **Results:** The combination of ezetimibe + simvastatin has a better effect to lower the body mass index. Ezetimibe alone reduces total cholesterol (TC), whereas combination of ezetimibe + simvastatin was found to reduce TC, low-density lipoprotein cholesterol (LDL-C) and triacylglycerol (TG). Rosuvastatin raises the high-density lipoprotein cholesterol (HDL-C). **Conclusions:** The combination of ezetimibe and simvastatin gives a good result in reducing the level of TC in the body, and this leads to a better reduction of LDL-cholesterol than using atorvastatin alone.

**Keywords:** Atherosclerosis, atorvastatin, ezetimibe, hyperlipidemia, rosuvastatin

## Introduction

Hyperlipidemia also known as dyslipidemia is a condition associated with an increase of lipids in the blood. Lipids in the blood incorporated with vehicles to overcome the solubility problem; such vehicles are known as lipoproteins. The proportion of the proteins to lipids determines the density of these vehicles they contain.[1]

Hyperlipidemia is subdivided according to lipids elevated to hypercholesterolemia and hypertriglyceridemia or both combined.[2] Hyperlipidemia can be divided into two: primary (familial) with genetic cause and secondary (acquired) that result from other disease conditions. The abnormalities in the lipid and lipoprotein are widespread in all people of world wide, and they may consider as modifiable risk factors to cardiovascular disease because of their association with atherosclerosis and in some case with acute pancreatitis.[3,4]

The principle pharmacological strategies for atherogenic dyslipidemia treatment are based upon the role of statin to inhibit 3-OH-methylglutaryl Co-A (HMG-CoA) reductase. This enzyme is the rate-limiting step in the cholesterol synthesis in the cells. There is an accumulating evidence based on clinical trials indicating that the use of statins in the treatment of dyslipidemia by lowering low-density lipoprotein cholesterol (LDL-C) the predominant atherogenic lipoprotein.[5]

Statin's treatment alone is not available in all cases of atherogenic dyslipidemia because of their poor ability to decrease serum triacylglycerol (TG) and increase serum

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**Submission:** 20-Nov-2022 **Accepted:** 06-Dec-2022 **Published:** 02-Aug-2023



**How to cite this article:** Shemran KA, Edin SH, Alta'ee AH. Impact of lipid-lowering drugs on lipid profile in hyperlipidemia patients. Med J Babylon 2023;20:274-7.

Access this article online

Quick Response Code:

Website: www.medjbabylon.org

DOI: 10.4103/MJBL.MJBL_282_22

high-density lipoprotein cholesterol (HDL-C), but when they use in combination with other lipid lowering drug like omega-3 fatty acids, niacin, and fibrates, they give a good result by decreasing mortality and morbidity result from atherogenic dyslipidemia.[6]

Statin drugs are major prescribed lipid-lowering drugs in the United States. They in general are effective and supported in studies because they showed good results and may have little side effects. In many studies, they helped establish a practice standard for treating elevated levels of LDL-C to reduce the risk of coronary heat diseases (CHD). The seven most currently available statin agents are rosuvastatin (Crestor), cerivastatin (Baycol), fluvastatin (Lescol, Lescol XL), atorvastatin (Lipitor, Ator), simvastatin (Zocor, Lipex), lovastatin (Mevacor), and pravastatin (Pravachol).[7]

The present study aims to investigate the effect of lipid-lowering drugs on lipid profile in patients with hyperlipidemia and to determine the best drug of choice in such patients.

## Materials and Methods

This study was designed as a cross-sectional study. Patients were categorized according to the type of drug used and gender. Group 1 (G1) patients treated with rosuvastatin, group 2 (G2) patients treated with atorvastatin, group 3 (G3) patients treated with ezetimibe, and group 4 (G4) patients treated with a combination of ezetimibe + simvastatin.

Sixty hyperlipidemia patients with the mean age of 45.52 ± 13.24 years were participated in the present study. All patients admitted to a private clinic in Hilla city, Iraq, during a period extant from October 2022 to November 2022 were selected.

The body mass index (BMI) was calculated for all individuals participating in this study using the following specific formula that requires a body weight in kg and body height in $m^2$. BMI is a simple weight-for-height index commonly used to classify people as underweight, overweight, or obese. It measures by dividing the weight in kilograms by the square of the height in meters ($kg/m^2$).[4]

### Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It carries out with patients verbal and analytical approval before sample takes. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number S-27 (including the number and the date in 08/11/2022) to get this approval.

The determination of blood total cholesterol (TC), TG, and HDL-C was done using commercially available kits (Biomagreb kit, Morocco). Very-low-density lipoprotein - Cholesterol (VLDL-C) was determined using the following formula[8]:

VLDL-C=TG/5.

LDL-C was determined using the following equation[9]:

TC=HDL-C+VLDL-C+LDL-C in the fasting state.

### Statistical analysis

Mean ± standard deviation (SD) was used to express the results and student's t-test to compare between groups with *P* value of 0.05 limits.

## Results

BMI of males' participants in the present study was found to be obese for males treated with rosuvastatin and ezetimibe and overweight for males treated with atorvastatin and a combination of ezetimibe + simvastatin as shown in Table 1.

TC for patients was found to be elevated except those patients treated with ezetimibe and a combination of ezetimibe + simvastatin, as shown in Table 2.

TG for patients was found to be elevated in patients treated with atorvastatin, and the remaining groups were in the upper level of normal values, as shown in Table 2.

Results of HDL-C for patients participated in the present study were found to be within the normal values except those of patients treated with ezetimibe and a combination of ezetimibe + simvastatin. The highest elevation in good cholesterol was noticed in the patients treated with rosuvastatin in males and rosuvastatin and atorvastatin in patients, as shown in Table 2.

Very low-density lipoprotein cholesterol for patients was elevated except those patients treated with a combination of ezetimibe + simvastatin, whereas TG were elevated

**Table 1: Weight, height, and BMI for patients with hyperlipidemia**

| Drug | Weight (kg) (mean ± SD) | Height (m) (mean ± SD) | BMI ($kg/m^2$) (mean ± SD) |
|---|---|---|---|
| Rosuvastatin | 89.00 ± 5.7 | 162.00 ± 9.9 | 33.30 ± 4.2 |
| Atorvastatin | 80.00 ± 6.84 | 169.50 ± 6.8 | 28.53 ± 4.2 |
| Ezetimibe | 85.50 ± 3.5 | 164.00 ± 4 | 32.03 ± 2.1 |
| Ezetimibe + simvastatin | 87.00 ± 4.9 | 168.00 ± 11.5 | 30.82 ± 5.2 |

**Table 2: Lipid profile of patients with hyperlipidemia**

| Drug | TC (mg/dL) (mean ± SD) | TG (mg/dL) (mean ± SD) | HDL-C (mg/dL) (mean ± SD) | LDL-C (mg/dL) (mean ± SD) | VLDL-C (mg/dL) (mean ± SD) |
|---|---|---|---|---|---|
| Rosuvastatin | 242.00 ± 67.12 | 193.00 ± 42.94 | 56.00 ± 27 | 156.10 ± 42.8 | 38.60 ± 8.58 |
| Atorvastatin | 206.50 ± 74.6 | 177.00 ± 28 | 44.00 ± 22.34 | 126.00 ± 55.4 | 35.40 ± 5.6 |
| Ezetimibe | 179.00 ± 35.5 | 156.00 ± 21.6 | 23.00 ± 3.46 | 125.10 ± 34.6 | 31.20 ± 4.3 |
| Ezetimibe + simvastatin | 187.00 ± 60.18 | 127.00 ± 131.7 | 21.00 ± 20.4 | 114.60 ± 39 | 25.40 ± 26.3 |

HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TC: total cholesterol, TG: triacylglycerol, VLDL- C: Very-low-density lipoprotein - Cholesterol.



in patients treated with atorvastatin and the remaining groups were in the high level of normal vales, as shown in Table 2.

## Discussion

The effects of rosuvastatin on bad lipids, which are low-density lipoprotein LDL-cholesterol, are directly related to the dose taken. Whereas the higher doses have been more effective for rosuvastatin drug in patients suffering from hypercholesterolemia when compared with doses equivalent to the milligram for other types such as atorvastatin. At doses equivalent to milligrams or higher doses of simvastatin and pravastatin.[10]

A meta-analysis also showed that rosuvastatin could increase levels of the "good" lipid (HDL-cholesterol), as is the case with other statins.[11]

A 2014 Cochrane study provided good evidence of the importance and action of rosuvastatin in reducing levels of lipoproteins other than HDL-cholesterol linearly with dose. The level of HDL-cholesterol was found to be around 7% without any effect of the dose being observed.[12]

The combination of ezetimibe/simvastatin is usually used to treat high blood lipids. It consists of ezetimibe; this is known as Zetia, and another drug is simvastatin; this is known as Zocor, and these are common names used in the United States.[13]

The effect of ezetimibe in reducing the level of cholesterol in the blood can be attributed to its effect on the brush boundaries of the small intestine and thus prevents the absorption of cholesterol in food, which leads to a decrease in the concentration of intestinal cholesterol that reaches the liver.[14] Although simvastatin directly inhibits the activity of the enzyme HMG-CoA reductase, this enzyme is responsible for the limited step of the synthesis of cholesterol in the blood, as it was approved in 2017.[15]

This compound is produced and marketed by Merck and Co under different names depending on the country of production; in Europe, it is called Inegy, whereas in the United States, it is called Vytorin.[16]

The process of combining the two drugs ezetimibe and simvastatin is the best solution to give good results in reducing the level of cholesterol in the body, as it is the best treatment for both sources of cholesterol, whether intestinal cholesterol that we get from food (exogenous) or cholesterol that is made inside the body (endogenous). Thus, this leads to a decrease in the level of LDL-cholesterol, because it contains the highest percentage of cholesterol.[17]

The current study shows that the combination of ezetimibe and simvastatin gives a good result in reducing the level of cholesterol in the body, and this leads to a better reduction of LDL-cholesterol than using atorvastatin alone.

### Acknowledgments

The authors would like to thank all participants of this study.

### Financial support and sponsorship

Nil.

### Conflicts of interests

There are no conflicts of interest.

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