

# Comparative study of the effect of atorvastatin and fenofibrate on high-density lipoprotein cholesterol levels in patients with type 2 diabetes

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## ABSTRACT

Diabetes is the most common metabolic disease. Type 2 diabetes is a variable combination of insulin resistance and disorder in insulin secretion, leading to disorder of lipids and plasma lipoproteins. The most common pattern of dyslipidemia in diabetic is high triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C). This study was conducted to find a more effective drug to increase HDL-C. In this study, 80 patients (26 males and 54 females) with type 2 diabetes received fenofibrate in cross-sectional way for 2 months, and they did not take antilipid drugs for 2 month. Then, they underwent atorvastatin for 2 months and HDL-C was measured before and after taking drugs. Patients did not change their diet during this study. Effect of atorvastatin and fenofibrate on HDL-C levels in patients with type 2 diabetes was evaluated. The mean HDL-C and total cholesterol (TC) before and after taking drugs were 36.5 mg/dL and 174.56 mg/dL, respectively. After atorvastatin, the mean HDL-C and TC were 43.30 and 150.144 mg/dL, respectively, and after fenofibrate, 43.40 were mg/dL and 146.36 mg/dL, respectively. Atorvastatin caused increase in HDL-C by 18.44% and reduction in TC by 13.82% and fenofibrate increase in HDL-C by 18.62% and reduction in TC by 16.05%. No difference was seen between atorvastatin and fenofibrate in terms of effect on the HDL-C excess ( $P = 0.449$ ). In addition, no difference was seen between atorvastatin and fenofibrate in terms of effect on TC reduction ( $P = 0.992$ ). In conclusion various factors are involved in increasing the HDL, such as race, sex, nutrition, physical activity and, of course, medications. The effect of medications is also different on races and genetics. The value of increase in HDL-C after Fenofibrate and Atorvastatin was associated with gender so that it caused more increase of HDL-C in females.

**Key words:** Atorvastatin, fenofibrate, high-density lipoprotein cholesterol, type 2 diabetes

## INTRODUCTION

Type 2 diabetes is the most common type of diabetes.<sup>[1]</sup> Cardiovascular disease is one of the

macrovascular complications of diabetes and is very common in type 2 diabetic patients. It is also the most common cause of death in these patients.<sup>[2,3]</sup> One of the cardiovascular risk factors in diabetic patients is dyslipidemia. The most common form of dyslipidemia in diabetic patients is an increase in triglyceride (TG) and reduction in high-density lipoprotein cholesterol (HDL-C).<sup>[4,5]</sup> HDL-C is a lipoprotein with high

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density, and unlike other atherogenic lipoproteins, HDL-C has anti-atherogenic properties and plays a protective role in cardiovascular disease.<sup>[6,7]</sup>

HDL-C takes the cholesterol from foam cells in atherosclerotic lesions and protects low-density lipoprotein-cholesterol (LDL-C) against oxidative changes.<sup>[6]</sup> Atorvastatin is a lipid-lowering agent from  $\beta$ -Hydroxy  $\beta$ -methyl glutaryl-CoA inhibitors group. This drug with its usual dose reduces total cholesterol (TC) level by 20%–30%, reduces LDL-C level by 21%–60%, and reduces TG level by 7%–37% and increases HDL-C level by about 5%–10%.<sup>[7,8]</sup> Fenofibrate is a lipid-lowering drug of fibrates group. This group of drugs reduces very LDL-C through environmental effects.<sup>[9,10]</sup> Treatment with this drug reduces TG level by 30%–50% and increases serum HDL-C level by about 5%–15%.<sup>[11]</sup> However, it cannot reduce the LDL-C level as much as statins; however, it can be useful in diabetic patients because it transforms high-atherogenic LDL-C particles into floating particles, which have less atherogenic properties.<sup>[12,13]</sup> As reducing serum HDL-C level is one of the risk factors for cardiovascular diseases, to increase serum level of HDL-C, in addition to dietary measures, stop of smoking, exercise, and blood glucose control, drug therapy also seems to be essential.<sup>[6,14]</sup> This study was conducted to determine a more effective drug for increasing serum HDL-C levels.

## METHODOLOGY

This study was a prospective, clinical cross-sectional study. The study population included 80 patients with type 2 diabetes. This study compared the effect of atorvastatin and fenofibrate on HDL-C level. HDL-C and TC levels were measured before and after the study and fenofibrate was prescribed to these patients for 2 months and HDL-C and TC levels were measured. Anti-lipid drug was not used for 1 month. Atorvastatin was started for patients for 2 months and HDL-C and TC were measured. The obtained data were analyzed using IBM SPSS Statistics for Windows, Version 21 (IBM Corp., Armonk, NY: USA) statistical tests of paired *t*-test ANOVA and *t*-test. The significance level in this study was considered  $P < 0.05$ .

## RESULTS

The subjects were 80 patients (32.5% male and 67.5% female). The mean HDL-C and TC are shown in Table 1.

The mean serum HDL-C levels before and after fenofibrate and atorvastatin are shown in Table 2 ( $P = 0.035$ ).

Generally, without considering the gender, atorvastatin and fenofibrate did not differ significantly in reducing TC ( $P = 0.99$ ) and increasing the serum of HDL-C ( $P = 0.449$ ). Mean TC after fenofibrate was 146.3 mg/dL and after taking fenofibrate was 147.1 mg/dL in males and 147.3 mg/dL in females. The TC level did not show a significant relationship with gender after taking fenofibrate. Atorvastatin increased HDL-C level by 18.54% and decreased TC level by 13.82%. Atorvastatin increased serum HDL-C by 12.2% in males and 21% in females. Fenofibrate increased serum HDL-C level by 14% in males and 20% in females.

The mean fasting blood glucose (FBS) before and after treatment was 105 mg/dL and 110 mg/dL, respectively, and the mean glycated hemoglobin (HbA1c) before and after treatment was 6.5% and 6.7%, respectively. The mean TG before and after treatment with fenofibrate was 215 and 180 mg/dL, respectively, and before and after treatment with atorvastatin was 195 and 205 mg/dL, respectively.

## DISCUSSION

The effect of the medicine cannot be limited to studies in other countries.<sup>[15,16]</sup> Various factors are involved in increasing the HDL, such as race, sex, nutrition, physical activity, and of course, medications.<sup>[16]</sup> The effect of medications is also different on races and genetics.<sup>[17,18]</sup> Today, in modern therapy, the patient's genetic predisposition is determined for the best medicine.<sup>[19,20]</sup> Genetic variants can effect drug metabolism, drug transport, or drug targets.<sup>[21,22]</sup> Genetic variation likely contributes substantially to the variation in drug response observed across human populations.<sup>[23]</sup> The field of pharmacogenomics, which seeks to relate genetic variability to variability in human drug response, has evolved considerably from candidate gene studies to studies of variation across whole genomes of human populations containing individuals who exhibit a range of responses to different drugs.<sup>[24,25]</sup> The present study compared the effect of atorvastatin and fenofibrate on the increase of serum HDL-C in 80 diabetic patients. This study is important for two reasons. First, all intervening factors were completely eliminated, and second, atorvastatin and fenofibrate were prescribed only to increase HDL-C and other indices such as TG, TC, FBS, and HbA1c were normal. This study showed

**Table 1: Levels of high-density lipoprotein cholesterol and total cholesterol before and after antilipid therapy**

Parameters	Before drug	Fenofibrate	P	Before drug	Atorvastatin	P	P*
HDL (mg/dl)	36.55±4.91	43.33±91	<0.001	36.55±4.91	43.30±853	<0.001	0.449
TC (mg/dl)	174.56±31.97	146.46±21.36	<0.001	174.56±31.97	150.44±24.65	<0.001	0.995

Mean±SD, First P is about Fenobarbate before and after treatment, The second P is about before and after treatment with Atorvastatin, \*P value between atorvastatin and fenofibrate, SD: Standard deviation, TC: Total cholesterol, HDL: High-density lipoprotein

**Table 2: Levels of high-density lipoprotein cholesterol in male and female before and after antilipid therapy**

Parameters	Before drug	Fenofibrate	Atorvastatin
HDL-C (mg/dl)			
Female	37.78±4.92	45.41±9.41	45.78±7.68
Male	34±3.96	31±6.88	38.15±8.14
P	0.021	0.035	0.006

Mean±SD. SD: Standard deviation, HDL-C: High-density lipoprotein cholesterol

that atorvastatin increased the serum HDL-C by 18.54% and decreased the TC by 13.82%. However, in other studies, atorvastatin increased serum HDL-C level by 5%–10% and reduced TC by 20%–30%. However, in some studies, the level of TC decreased by 40% and level of HDL-C increased by 5%–10%.<sup>[14]</sup> No study has used atorvastatin as the first line of treatment to increase HDL-C, but proper blood glucose control and use of fibrates have been used as the first line of treatment to increase HDL-C.<sup>[4,9,26]</sup> The important result of this study was a significant relationship between increase in HDL-C after atorvastatin and gender ( $P = 0.006$ ), while other studies did not examine the relationship between gender and the effect of these drugs.<sup>[3,27]</sup> In this study, atorvastatin increased HDL-C by 21% in females and by 12.2% in males, reflecting the greater effect of atorvastatin on serum HDL-C in females. In this study, fenofibrate increased serum HDL-C level by 18.54% and decreased the TC by 16.05%. Other studies have reported different level of increase in HDL-C (6%–19%, 10%–25%–10%–15%).<sup>[27,28]</sup> The level of reduction in TC was also reported 10%.<sup>[12,29,30]</sup> The increase in serum HDL-C level in this study was consistent with results of previous studies, but the effect of fenofibrate on TC was higher than that of previous studies. It could be due to the low sample size, specific conditions of patients, and the difference in the duration of treatment. In this study, a significant correlation was found between serum HDL-C levels after fenofibrate and gender ( $P = 0.035$ ). Thus, fenofibrate increased serum HDL-C levels by 14% in males and by 20% in females. In this study, unlike previous studies, no difference was found between atorvastatin and fenofibrate in terms of their effect on HDL-C ( $P = 0.449$ ). Atorvastatin and fenofibrate also did not differ significantly in terms of effect on TC ( $P = 0.099$ ). Considering the significant relationship between gender and atorvastatin and fenofibrate, more extensive studies are needed in this regard and conducting more extensive studies is recommended to determine the effect of these drugs on Iranian patients.

## CONCLUSION

Various factors are involved in increasing the HDL, such as race, sex, nutrition, physical activity, and of course, medications. The effect of medications is also different on races and genetics. The value of increase in HDL-C after

Fenofibrate and Atorvastatin was associated with gender so that it caused more increase of HDL-C in females.

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## Conflicts of interest

There are no conflicts of interest.

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