

# Effect of Atorvastatin in Patients with Type 2 Diabetes Mellitus

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## Abstract

**Background:** Dyslipidemia is an important factor in causation of cardiovascular disease in type 2 diabetics. Type 2 diabetes is associated with a substantially increased risk of cardiovascular disease, but the role of lipid-lowering therapy with statins for the primary prevention of cardiovascular disease in diabetes is inadequately defined.

**Aim of the Study:** The study was planned to compare the effect of atorvastatin in patients with type 2 diabetes mellitus and dyslipidemia, in reaching target levels of various lipids as suggested by ADA (2001).

**Material and methods:** 100 patients with type 2 diabetes mellitus were carried out in this study. The criteria for diagnosis of diabetes mellitus and dyslipidemia were based on those laid down by ADA (2001), Patients with type 2 diabetes mellitus with a serum level of LDL-c >100 mg/dl and/or HDL-c <45 mg/dl and/or TG >200 mg/dl were recruited for this study. Patients (n=100) were given atorvastatin in an initial dose of 10 mg per day. After 6 and 12 weeks of atorvastatin therapy, the lipid profile levels were tested. Total cholesterol, TG and HDL-c levels were measured enzymatically. Low-density lipoprotein cholesterol values were calculated using the Friedewald equation.

**Results:** After 12 weeks of atorvastatin therapy, Glycosylated Hb decreased from a mean of 9.1 % to 8.7%. Similarly, fasting plasma glucose decreased from 155.6 to 148 mg/dl and significantly reduced the levels of total cholesterol (31%), LDL-c (40.7%) and TG (27.3%), and increased the levels of HDL-c (-23.1%).

**Conclusion:** In our study, Type 2 Diabetes Mellitus did not achieve the target levels of various lipids in diabetic dyslipidemia as per the American Diabetes Association guidelines. Thus, atorvastatin is an effective lipid-lowering drug in achieving the goal for lipids, especially LDL-c.

## INTRODUCTION

Patients with type 2 diabetes mellitus have a twofold to fourfold excess risk of coronary artery disease (CAD) compared with nondiabetic patients. (1) Indeed, 70% to 85% of adult diabetic patients die of CAD, cerebrovascular disease, peripheral vascular disease, or a combination of these conditions. (2) In type 2 diabetes mellitus, dyslipidemia is usually present in the form of increased serum triglyceride (TG) levels, decreased high-density lipoprotein cholesterol (HDL-c) levels, normal or slightly higher low-density lipoprotein cholesterol (LDL-c) levels as compared to nondiabetics. (3) However, the qualitative abnormalities of LDL-c (denser, smaller, glycosylated and oxidised particles) increase their affinity towards the endothelium, making them more atherogenic. Thus, an elevated level of LDL-c is the primary risk and prognostic factor for coronary heart disease (CHD) in patients with type 2 diabetes mellitus. (4) The various statins (lovastatin, pravastatin, simvastatin,

fluvastatin, atorvastatin) not only lower the lipid levels but also stabilize vulnerable plaque, restore endothelial function, and have an antiplatelet, anti-inflammatory, and antioxidant action. (5) As per recent American Diabetes Association (ADA) criteria 2001 (6) the role of atorvastatin in the management of dyslipidemia in patients with type 2 diabetes mellitus is not very well elucidated.

This study was planned to compare the effect of atorvastatin in patients with type 2 diabetes mellitus and dyslipidemia, in reaching target levels of various lipids as suggested by ADA (2001).

## MATERIAL AND METHODS

### STUDY DESIGN AND PATIENTS

The study was carried out on 100 patients with type 2 diabetes mellitus. The criteria for diagnosis of diabetes mellitus and dyslipidemia were based on those lay down by ADA (2001). (6), Patients with type 2 diabetes mellitus with

a serum level of LDL-c >100 mg/dl and/or HDL-c <45 mg/dl and/or TG >200 mg/dl were recruited for this study.

All patients with type 2 diabetes mellitus had been under a fair or moderate glycemic control with a total glycosylated hemoglobin (GHb) <10%. Blood pressure was maintained at less than 140/90 mmHg and controlled with only calcium channel blockers.

Diabetic patients suffering from hypothyroidism, renal disease, including diabetic nephropathy, and cirrhosis of liver were not included in the present study.

Patients (n=100) were given atorvastatin in an initial dose of 10 mg per day. After 6 and 12 weeks of atorvastatin therapy, the lipid profile levels were tested. The patients were asked to report any side effects at every visit. The creatine phosphokinase (CPK) level was estimated if the patient had symptoms of myopathy.

**BIOCHEMICAL INVESTIGATION**

A detailed history was taken and a thorough physical examination, including calculation of anthropometric measurements, carried out in each patient. Total cholesterol, TG and HDL-c levels were measured enzymatically. (7,8) Low-density lipoprotein cholesterol values were calculated using the Friedewald equation. (9)

**STATISTICAL ANALYSIS**

Statistical analysis was carried out using Sigma stat version 3.0 software. The one-way ANOVA test was used. The <0.05 levels was used for statistical evaluation. Data were expressed as mean±standard deviation. The patients were asked to avoid various drugs like phenytoin, corticosteroids, vitamin C, vitamin A, β-blockers, etc., which could affect cholesterol and TG, levels during the estimation.

**RESULTS**

Demographic data are shown in Table 1. The average age was 50.2 years with average weight was 65.3 kg.

**Figure 1**

Table 1: Demographic Data in Patients with Type 2 Diabetes Mellitus

Variable	N =100
Age (Years)	50.2 ± 8.9
Sex (M: F)	55: 45
Weight (Kg)	65.3 ± 9.5
Waist: Hip Ratio	0.95 ± 0.12
Body Mass Index (kg/m <sup>2</sup> )	26.5 ± 6.5
Systolic BP (mmHg)	128.5 ± 8.2
Diastolic BP (mmHg)	81.2 ± 7.5

Values Expressed as Mean ± SD

Effect of Atorvastatin Therapy (10 mg/day) after 6 and 12 weeks in Patients with Type 2 Diabetes Mellitus are shown in Table 2. After 12 weeks of atorvastatin therapy, Glycosylated Hb decreased from a mean of 9.1 % to 8.7% Similarly, fasting plasma glucose decreased from 155.6 to 148 mg/dl thus; there was no significant alteration in glycemic control after the therapy.

**Figure 2**

Table 2: Effect of Atorvastatin Therapy (10 mg/day) after 6 and 12 weeks in Patients with Type 2 Diabetes Mellitus

Parameters	Base-Line Mean ± SD	After 6 Weeks		After 12 Weeks	
		Mean ± SD	% Change	Mean ± SD	% Change
Blood Glucose (mg/dl)	155.6 ± 10.2	151 ± 12.5 NS	---	148 ± 15.3 NS	---
Glycosylated Hb (%)	9.1 ± 0.91	8.85 ± 0.65 NS	---	8.73 ± 0.72 NS	---
TC (mg/dl)	260.2 ± 40.2	190.7 ± 35.6 *	26.7	179.3 ± 28.6 *	31.0
TG (mg/dl)	180.7 ± 45.2	145.3 ± 24.6 *	19.5	131.2 ± 30.2 *	27.3
LDL-C (mg/dl)	178.3 ± 42.3	113.5 ± 22.6 *	36.3	105.6 ± 25.6 *	40.7
HDL-C (mg/dl)	38 ± 5.6	45.2 ± 7.6 **	-18.9	46.8 ± 8.4 **	-23.1

\* P<0.001 as compared to Base-Line; \*\* P<0.05 as compared to Base-Line; NS = Non Significant  
TC - Total Cholesterol; TG - Triglyceride; LDL-C- LDL-Cholesterol; HDL-C- HDL-Cholesterol

After 12 weeks of atorvastatin therapy, TC, TG and LDL-C were significantly less (p<0.001) expect HDL-C was significantly high (P<0.05) as compared to Base line.

After 12 weeks treatment, significantly reduced the levels of total cholesterol (31%), LDL-c (40.7%) and TG (27.3%), and increased the levels of HDL-c (-23.1%)

**DISCUSSION**

The present study revealed that LDL dyslipidemia was the most prevalent while TG dyslipidemia was the least prevalent form of dyslipidemia when the ADA (2001) guidelines for diabetic dyslipidemia and CHD risk were

applied. TG levels were lowered by 19.5%, similar to the levels obtained by an atorvastatin therapy of 10 mg for 6 weeks. Regular exercise and diet has been shown to be consistently effective in lowering TG levels. (10) After 12 weeks of treatment, Low-density lipoprotein was lowered by only 40.7%, a finding that implies that even with strict dietary control and rigorous exercise, which may not be possible for diabetics. (11) The HDL-c was increased by 23.1%, a finding similar to the ADA's observation that most studies have failed to demonstrate a significant improvement in HDL-c levels.

Atorvastatin did not affect glycemic control in diabetics, as assessed by fasting plasma glucose and GHb, like most of the other studies except that of Daubresse et al. (1994). (12) Thus, atorvastatin is an effective lipid-lowering drug in achieving the goal for lipids, especially LDL-c (40.7%), as compared to base-line alone in patients with type 2 diabetes mellitus with dyslipidemia.

In the present study, it was found that in Type 2 diabetic dyslipidemia does not achieve lipid levels low enough to reach the target levels as per the ADA guidelines. The imitations of the present study include a short-term follow-up and a small number of subjects.

### CONCLUSION

In our study, Type 2 Diabetes Mellitus did not achieve the target levels of various lipids in diabetic dyslipidemia as per the American Diabetes Association guidelines. Thus, atorvastatin is an effective lipid-lowering drug in achieving the goal for lipids, especially LDL-c. However, more and long-term randomized follow-up studies are required to evaluate the efficacy of atorvastatin or other lipid-lowering drugs in Indians with type 2 diabetes.

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