Comparison the Effect of Niacin Treatment with and without Atorvastatin on Lipid Profile in Type 2 Diabetic Patients

Mohammad Afkhami-Ardekani[1], Mahmood Emami-Meibodi[2], Naimeh Mostafae[3], Arezoo Afkhami-Ardekani[4*], Boshra Najafi[5]

1. Professor of Endocrinology & Metabolism, Department of Internal Medicine, School of Medicine, Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
2. Assistant Professor of Cardiology, Department of Cardiology, School of Medicine, Afshar Heart Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
3. Obstetrics and Gynecology, Department of Obstetrics and Gynecology, School of Medicine, Shahid Sadoughi General Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
4. General Physician, Shahid Sadoughi University of Medical Science, Yazd, Iran.
5. Diabetes Research Center, Shahid Sadoughi University of Medical Science, Yazd, Iran.

***Correspondence:**
Arezoo Afkhami – Ardekani, Safaeeyah, Shhid Sadoughi Hospital, Yazd, Iran.
Tel: (98) 353 522 3999
Email: afkhamiam@yahoo.com

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Abstract

Objective: The risk of cardiovascular disease increased in diabetic patients due to lipoprotein metabolism disorder and insulin resistance. There is different type of dyslipidemia in diabetic patient. The nicotinic acid (niacin) is categorized as vitamin B family and decreases low-density lipoproteins (LDL) and triglyceride (TG) level and increases high-density lipoproteins (HDL). The aim of this study was to compare the effect of niacin treatment with and without atorvastatin on lipid profile on diabetic patient.

Materials and Methods: This study is cross over clinical trial on 30 diabetic patients (9 men, 21women) referred to diabetes research center of Yazd (IRAN). At initiation of study administered atorvastatin alone (20 mg/day) for 6 weeks (protocol A), and after 3 weeks washout period, started atorvastatin (20 mg/day) with niacin (50 mg/day) for 6 weeks (protocol B). Statistical analysis was accomplished by using SPSS for windows, version 11.50 and kappa and paired T-test.

Results: Patients on protocol B had statistically significant more increase of HDL-C (*P*-value= 0.08) and decrease of TG than profile A (*P*-value= 0.024). Also, 2 hours post prandial blood sugar and HbA1c changes in two groups were not significant A (*P*-value= 0.226), B (*P*-value= 0.918). Patient in group B had statistically significant decrease in systolic blood pressure and diastolic blood pressure than group A (*P*-value= 0.010, *P*-value= 0.015).

Conclusion: This study showed decrease of TG, LDL-C and total cholesterol and increase of HDL in both groups. There are significant changes in HDL-C and TG in group B that used niacin with atorvastatin than group A.

Keywords: Niacin, Atorvastatin, Type 2 diabetes mellitus, Lipid profile

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) over 30 years is about 14.2% in Yazd (1). Nicotinic acid (niacin) is one of the vitamin B groups that decreases low - density lipoproteins (LDL-C) and triglyceride (TG) level and increases high-

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density lipoproteins (HDL-C) (2-10). It is the effective drug to increase or HDL-C level and the best drug to decrease of lipid that effect on plasma lipoprotein a (LP-a) level. The niacin is useful for the patient with mixed hyperlipidemia and low LDL-C level (11-14). ''The Arterial Disease Multiple Intervention Trial (ADMIT) was a prospective, placebo-controlled study''. ADMIT evaluated the healthy and effect of a combination of HDL-C elevating, antioxidant vitamin, and low-dose warfarin therapy on atherosclerotic vascular disease risk factors in patients with peripheral arterial disease and diabetes. Niacin can increase HDL levels due to increasing HDL-cholesterol and decreased TG (15-18). The high risk of cardiovascular disease in diabetic patients depended to lipoprotein metabolism disorder or resistance of insulin (13-20). Lipid metabolism disorder and plasma lipoprotein are the risk factors of atherosclerosis (20-33). Decrease of HDL-C is the risk factor of cardiovascular disease. HDL-C decrease of 1mg/dl causes increase of coronary arterial disease (34). The goal of this study was to compare the effect of niacin treatment with and without atorvastatin on lipid profile in T2DM patients.

Materials and Methods

This study is a clinical trial with cross-over method on thirty T2DM patients (9 men, 21 women) referred to Yazd diabetic research center with specific criteria. The inclusion criteria included: patient with dyslipidemia (total cholesterol > 200, LDL-C >100, TG >150, HDL-C>50 (woman) and HDL-C > 40 (men), HbA1c <10, no statin medication in past 1 month.

The exclusion criteria were patient who did not use drugs and did not come to center routinely. In according to cross-over method; at first atorvastatin (20 mg/day)medication was done in 6 weeks (protocol A) and after 3 weeks as wash out period then atorvastatin (20 mg/day) with niacin (50 mg/day) for 6 weeks (protocol B) were used. Data gathering was done with a check list included demographic subject, duration, complication (nephropathy, retinopathy, neuropathy, diabetic food) and controlling of diabetes, lipid profile (TG, total cholesterol , LDL , HDL) and lab test (HbA1c, 2HPP, FBS, ALT, AST) and drug complication (dyspepsia, headache, myalgia, sever myopathy, hepatitis, rhabdomyolysis, skin flashing) before and after treatment.

Statistical analysis

Statistical analysis was doing by using SPSS for Windows, version 11.50 and kappa and paired test. Data of continuous variables showed as mean ± standard deviation. Differences between groups were showed by the paired sample tests. Statistical significance was set at *P*-value< 0.05.

Ethical considerations

This study was approved by Azad Islamic University of Yazd as the doctor of medicine (MD) (Code: IR.10510101852023).

Results

Thirty (30) T2DM patients finished the study. The mean age of patients was 52.3 (± 4.5) years old with mean weight 72.4 (± 12.2) kg, height 158.1 (± 9.4) cm, waist circumflex 103.7 (± 8.9) cm, hip circumflex 101.8 (± 5.6) cm, body mass index (BMI) 28.9 (± 4.5) kg/m2, waist/hip ratio1.01 (± 0.01) and duration of diabetes 6.1 (± 3.7) years. Seventeen (56.6%) of patients have neuropathy and 6 (20%) of them have retinopathy and one (3.33%) of them has diabetic foot (Table 1).

Patients that treatment with protocol A and B have significant decrease in TG, total cholesterol, LDL-C and increase of HDL-C (*P*-value= 0.009). Patient who were treated with protocol A (only atorvastatin) were statistically significant for decrease total cholesterol (*P*-value= 0.009) and LDL (*P*-value= 0.016) than profile B (niacin with atorvastatin).Subjects who were treated with profile B were statistically significant in increase of HDL and decrease of TG than

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profile A (*P*-value= 0.08, *P*-value= 0.024) (Table 2,3).

This study analysis changes of lipid profile in according to BMI in two groups. Patients with normal weight (BMI< 25) and over weight (BMI= 25-30) in group A is statistically significant decrease in total cholesterol than group B (*P*-value= 0.046, *P*-value= 0.027) Obese patient (BMI> 30) in group B is statistically significant increase of HDL and decrease of TG than group A (*P*-value= 0.000, *P*-value= 0.010). Means of changes lab tests are FBS 13.3 (± 8) (5.3%), 2hpp 31 (± 4.7) (2.2%), HbA1c 0.7 (± 0.3) (3.5%) in profile A and FBS 12.8 (± 4.9) (3.3%), 2hpp 17.2 (± 4) (1.8%), HbA1c 1.0 (± 0.4) (1.2%) in profile B that statistically significant decrease of FBS in profile A (*P*-value= 0.000). 2hpp and HbA1c changes in two group is not significant A (*P*-value= 0.226), B (*P*-value= 0.918). Patient in group B is statistically significant decrease in SBP and DBP than group A (*P*-value= 0.010, *P*-value= 0.015) and the changes is less than 5 mmHg and not significant. Complication include sever myopathy, rhabdomyolysis, myalgia, arthralgia, increase of ALT and AST was not detected in any patient. Skin flashing (26.7%), dyspepsia (6.7%) and headache (3.3%) were detected.

Discussion

This study showed Patients treated only by atorvastatin were statistically significant for decrease total cholesterol (*P*-value= 0.009)

Table 1. Baseline characteristic and biochemical markers of patients

Variables	Mean (± SD)
BMI (Kg/m2)	28.9 (± 4.5)
FBS (mg/dl)	148 (± 20.3)
2hpp (mg/dl)	211 (± 38.3)
HbA1C %	8.4 (± 1.3)
TG (mg/dl)	94.6 (± 33.3)
Cholesterol (mg/dl)	299 (± 50.2)
LDL (mg/dl)	191.7 (± 44.1)
HDL (mg/dl)	39.6(± 12.3)
Systolic blood pressure (mm/Hg)	130.8 (± 16.6)
Diastolic blood pressure (mm/Hg)	75.8 (± 9.5)

Table 2. Biochemical parameters before and after atorvastatin consumption

Variables	Pre-trial Mean (± SD)	Post-trial Mean (± SD)	*P*-value*
FBS (mg/dl)	148.3 (± 20.3)	140.3 (± 19.1)	0.003
2hpp (mg/dl)	211.9 (± 38.3)	207.2 (± 37.6)	0.410
HbA1C %	8.4 (± 1.3)	8.1 (± 1.2)	0.032
TG (mg/dl)	330.3 (± 92.1)	235.8 (± 65.8)	0.0001
Cholesterol (mg/dl)	299.6 (± 50.2)	195.2 (± 25)	0.0001
LDL (mg/dl)	191.7 (± 44.1)	103.6 (± 21.4)	0.0001
HDL (mg/dl)	39.6 (±12.3)	44.8 (± 13.6)	0.0001
Systolic blood pressure (mm/Hg)	130.8 (±16.6)	128.1 (± 11.3)	0.016
Diastolic blood pressure (mm/Hg)	75.8 (± 9.5)	74.3 (± 8.5)	0.402

*-paired T-test

Table 3. Biochemical parameters before and after atorvastatin and niacin consumption

Variables	Pre-trial	Post-trial	*P*-value*
FBS (mg/dl)	145.5 (± 26.3)	150.4 (± 19.4)	0.044
2hpp (mg/dl)	213.5 (± 37.6)	209 (± 35.8)	0.214
HbA1C %	8.3 (± 1.2)	8.2 (± 1.1)	0.232
TG (mg/dl)	308.2 (± 78.8)	202 (± 49.9)	0.0001
Cholesterol (mg/dl)	275.7 (± 38.2)	181.1 ±(21.4)	0.0001
LDL (mg/dl)	173.7 (± 38.8)	92.5 (± 18.2)	0.0001
HDL (mg/dl)	41.7 (± 11.8)	48.6 (± 13.4)	0.0001
Systolic blood pressure (mm/Hg)	131.3 (± 15.5)	127.2 (± 14.9)	0.087
Diastolic blood pressure (mm/Hg)	78 (± 7.6)	74.8 (± 8.03)	0.049

*-paired T-test

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and LDL-C (*P*-value= 0.016) than patients treated with niacin and atorvastatin. Patients treated with atorvastatin plus niacin were statistically significant increase of HDL and decrease of TG than group give only atorvastatin (*P*-value= 0.08, *P*-value= 0.024).

Lipid lowering drug use is an essential method in both patients with peripheral arterial disease and diabetic patients to reduce the risk of atherosclerotic vascular disease (13,16). in spite of ability of Niacin to increase HDL-C and lower triglycerides, the use of niacin has been weaken in patients with diabetes,(10-13) due to increasing of glycemic control in patients with and without diabetes who were treated with niacin (3,17-19).

Many article reports of niacin-induced glucose intolerance are performing on uncontrolled diabetic patients (17-20). Many of these studies were performed on patients without diabetes (18-20) and some studies conducted on patients with diabetes (3,17,21,22).

One of another study showed niacin high withdrawal rates because poor glycemic control in patients with diabetes on slow-release niacin. These data may also present a difference between sustained release and crystalline (immediate release) (23).

Many studies showed decreased glucose tolerance and increased plasma insulin levels in person without diabetes after niacin administration (18,19,22-24). A study showed minimum effect of niacin administration on insulin levels and glucose in normal person (25).

For treatment of dyslipidemia in type 2 diabetes mellitus suggested offensive lipid lowering statin drugs or fibrates (12). Though LDL-C is suggested as the first goal of treatment, it is visible that hypertriglyceridemia and decreased HDL-C are very common in type 2 diabetes mellitus, and are with increased risk of atherosclerotic vascular disease (10,13). Niacin reduces plasma triglycerides by reducing hepatic production of VLDL, and increases HDL-C by up to 30%, by reducing hepatic removal of apolipoprotein A-1 (26-27). Niacin also reduces plasma LDL-C by 10% to 15% (28). Though the LDL-C lowering of niacin may be compared with that of statin drugs, niacin has a biggest effect on HDL-C, triglycerides, and lipoprotein (a) (4). In many patients with diabetes, treatment with gemfibrozil and niacin may be need to be lower triglycerides to goals (29).

There is bounded data about lipid-modifying interventions reduce benefit for patients with diabetes for lowering cardiovascular morbidity and mortality .The Scandinavian Simvastatin Survival Study referred that patients with diabetes may be reduce coronary artery disease with simvastatin (30). In the Helsinki Heart study, patients with diabetes experienced a 60% reduction in coronary artery disease with gemfibrozil (31). In the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT), patients with diabetes may be reduce coronary artery disease with gemfibrozil (32).

In spite presence of some information about disagreeing use of niacin in diabetes (10,12) the present study suggested lipid lowering doses of immediate-release niacin can be used safely in patients with type 2 diabetes mellitus. Niacin therapy may be supplanted as recurring to statin or fibrates in patients with diabetes fail to enough effect on hypertriglyceridemia or HDL-C increasing. Remarkably in cases of lack of effect of statin and fibrates drugs, Niacin may be considered first drug for treatment of diabetic dyslipidemia.

There are many drugs used for control of lipid and the best of them is most effective in decrease of cholesterol and LDL-C and increase of HDL-C. The combination therapy is used for patient with both hypertriglyceridemia and hypercholesterolemia that not control with one drug or high LDL-C and low HDL-C. The use of niacin and statin are very helpful for patient with LDL-C that not controlled by statin and HDL-C is below 40 mg/dl. Patient with hyperlipidemia (hypertriglyceridemia and hypercholesterolemia) that treated by fibrate do not reach normal LDL-C level and this patients are candidate for statin added to their treatment that can slightly increase HDL-C

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level (5 -10%), although fibrate effect on HDL-C (increase 5 – 10%) but niacin is more effective for increase of HDL-C (30%) (33).

Conclusions

There were statistical significance decrease of TG, LDL-C and total cholesterol and increase of HDL-C in both groups. There were significant changes in HDL and TG in group B than group A. There were no any drug complication in two groups.

Conflict of Interest

The authors declared that they have no conflict of interests.

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