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Post-Prandial Lipid Levels for Assessing Target Goal Achievement in Type 2 Diabetic Patients Taking Statin

It is inconvenient to perform serum lipid analysis in fasting state in diabetic patients with drug treatment. In patients with statin treatment and Asian diet, it has not been clearly known whether non-fasting values could be used for the clinical decision making in diabetic patients. In this study, fasting and post-prandial plasma lipid profiles of hospitalized type 2 diabetic patients taking statin, were measured in whom standard diabetic breakfast in traditional Korean style were provided. In repeated-measures ANOVA, there were no significant differences among fasting, post-prandial 2 and 4 hr low-density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol values. When compared to fasting levels, both post-prandial 2 hr and 4 hr LDL cholesterol levels were misclassified as not achieved target goal only in 4% of patients. Post-prandial HDL cholesterol matched with fasting values in women, without exception. In conclusion, the fasting and post-prandial LDL and HDL cholesterol levels are not significantly different each other and can be used in the assessment of achieving target goal in type 2 diabetes taking statin after Korean diet.

Key Words : *Fasting; Postprandial Period; Lipid Goal; Diabetes Mellitus, Type 2; Korean Diet*

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INTRODUCTION

In type 2 diabetes mellitus (DM), lipid-lowering therapy is one of the most important cares together with blood glucose and blood pressure control (1). The Adult Treatment Panel III (ATP III) guidelines of the National Cholesterol Education Program (NCEP) extend the population that is believed to benefit from cholesterol reduction by adding patients with DM to the secondary prevention group (2). The target goal of lipid control in type 2 DM became stricter and the percentage of patients achieved the target goal got to be less satisfactory.

Guidelines recommended that lipid profiles would be best obtained in the fasting state. The American Diabetes Association (ADA) recommended to measure fasting lipid profile at least once a year for screening of dyslipidemia in most diabetics (1). However, only 50% of all patients have their lipid test result annually (3-5). The ATP III of NCEP guidelines mentioned about measuring cholesterol in the nonfasting state. The guideline states, "If the testing opportunity is nonfasting, only the values for total cholesterol (TC) and high density lipoprotein (HDL) cholesterol will be usable" (2). Most patients in medical offices are in the nonfasting state. Fasting is much uncomfortable in diabetics because of the fear of both hyperglycemia and hypoglycemia. This may limit lipid profile test, thus decrease the number of patients who were prescribed drug therapy. As a result, percentage of patients who arrived the goal levels of lipid was lowered. Instead of rescheduling the patient for fasting levels, testing nonfasting lipid might improve doctor and patient compliance with ATP III guidelines.

There are several studies showing that nonfasting total cholesterol, HDL cholesterol, and low-density lipoprotein (LDL) cholesterol levels can identify most of patients who did not meet the goal of cholesterol levels (6-9). However, other studies showed that nonfasting levels were significantly different from fasting levels (10). All of previous studies were performed for Western diet and some of them were not conducted with standardized meal. In addition, few reports studied fasting and post-prandial lipid profile with statin treatment in diabetes patients. In this study, we tried to compare the fasting and post-prandial lipid profiles in type 2 DM with statin treatment under traditional Korean diet.

MATERIALS AND METHODS

Subjects and methods

Our subjects were clinically stable type 2 diabetes patients

taking statins at least for previous 3 months and their other medications have not been changed during the last 3 months. Patients with a history of severe hypoglycemia, severe hyperglycemia, bleeding disorder, liver diseases, renal insufficiency (serum creatinine >1.5 mg/dL), malnutrition, and pregnant and lactating women were excluded.

Subjects were admitted to Maryknoll Medical Center. Following an overnight fast of at least 10 hr, fasting venous blood samples were obtained. Subjects were then provided with a standard diabetic diet. They finished their meal within 30 min. Venous blood was sampled at 2 hr and 4 hr following a standard breakfast. This study was approved by the Institutional Review Boards of Maryknoll Medical Center, and written informed consent was obtained from each patient.

Serum levels of total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were measured enzymatically with a Hitachi 7600-020 (Hitachi Co., Tokyo, Japan) automatic analyzer, with coefficients of variation of 1.2% for cholesterol and 1.9% for triglycerides.

Statistical analysis

Statistical analyses were performed with the SPSS software, version 15.0 (SPSS Inc., Chicago, IL, USA). Repeated measured t tests were used to determine if differences in fasting and nonfasting measurements for total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride were statistically significant.

We adopted the ATP III guideline for diabetes to assess if they meet the treatment goal. The target of LDL cholesterol for patients with diabetes was set at <100 mg/dL (2.59 mM/L) and the non- HDL cholesterol target was <130 mg/dL (3.36 mM/L). The HDL cholesterol goal for diabetic women and men were >50 mg/dL (1.3 mM/L) and >40 mg/dL (1.04 mM/L), respectively. The agreements between the fasting and post-prandial 2 hr or 4 hr values for each goal were assessed by sensitivity, specificity and McNemar test.

Table 1. Baseline characteristics and dietary intake of the study subjects

Characteristics	Mean values±SD
Gender: M/F (number)	14/21
Age (yr)	57.8±9.9
BMI (kg/m^2)	24.3±3.5
DM duration (yr)	10.1±7.4
HbA1c (%)	7.8±1.6
Energy of breakfast (kcal)	520±52
Carbohydrate (% of energy)	60
Total fat (% of energy)	20
Protein (% of energy)	20

BMI, body mass index; DM, diabetes mellitus.

RESULTS

Characteristics of subjects and diet

The number of participants was 35, and 60% of them were women. Their mean age was 57.8±9.9 yr and mean body mass index (BMI) was 24.3±3.5 kg/m^2. Mean known diabetic duration was 10.1±7.4 yr and their mean HbA1c was 7.8±1.6% (Table 1). Their standardized diabetic breakfast was provided by Korean traditional style including steamed rice and several side dishes. Their mean total calories were supposed to be 1,778.6±298.1 kcal and mean calories of breakfast was 520±52 kcal, composed by 20% of protein, 20% of fat and 60% of carbohydrate.

Fasting and post-prandial lipid values

The levels of total cholesterol after meal were increased compared to fasting total cholesterol values, and their changes were statistically significant (*P* value <0.05) (Fig. 1, Table 2). Post-prandial LDL cholesterol levels were slightly lower than fasting values but did not show any statistical significance. The significant changes in HDL cholesterol after standard breakfast were not observed in our study. The levels of triglyceride at post-prandial 2 hr and post-prandial 4 hr were significantly higher than fasting tirglyceride value (*P* value <0.05). Triglyceride levels were highest at post-prandial 4 hr, 23.4% higher than the fasting levels (Fig. 1, Table 2).

Attainment of target lipid values

We adopted the ATP III guideline to compare the number and the percentages of patients who achieve their target goal between fasting and post-prandial lipid levels. The target of LDL cholesterol for patients with diabetes is less than 100 mg/dL (2.59 mM/L). Twenty seven out of 35 patients met the LDL cholesterol treatment goal in post-prandial 2 hr LDL cholesterol level (Table 3). Among them, 96% had LDL cholesterol level less than 100 mg/dL in fasting state. In terms of post-prandial 4 hr values, our study showed the same results. Both post-prandial 2 hr and 4 hr LDL cholesterol values were 87.5% sensitive and 96.3% specific. We set a goal in HDL

Table 2. Mean values of fasting and post-prandial (PP) lipoproteins

Lipoproteins	Fasting	PP2 hr	PP4 hr
Total cholesterol* (mg/dL)	150.1±37.4	152.8±36.1	154.23±39.1
LDL cholesterol (mg/dL)	83.6±28.1	82.8±26.0	82.9±27.1
HDL cholesterol (mg/dL)	40.5±12.8	40.3±11.8	40.6±12.9
Triglyceride (mg/dL)	122.7±54.1	137.0±74.1*	151.4±89.9*

Data are presented as mean value±SD.
*P<0.05 compared to fasting value by repeated measure test.
LDL, low-density lipoprotein; HDL, high density lipoprotein.

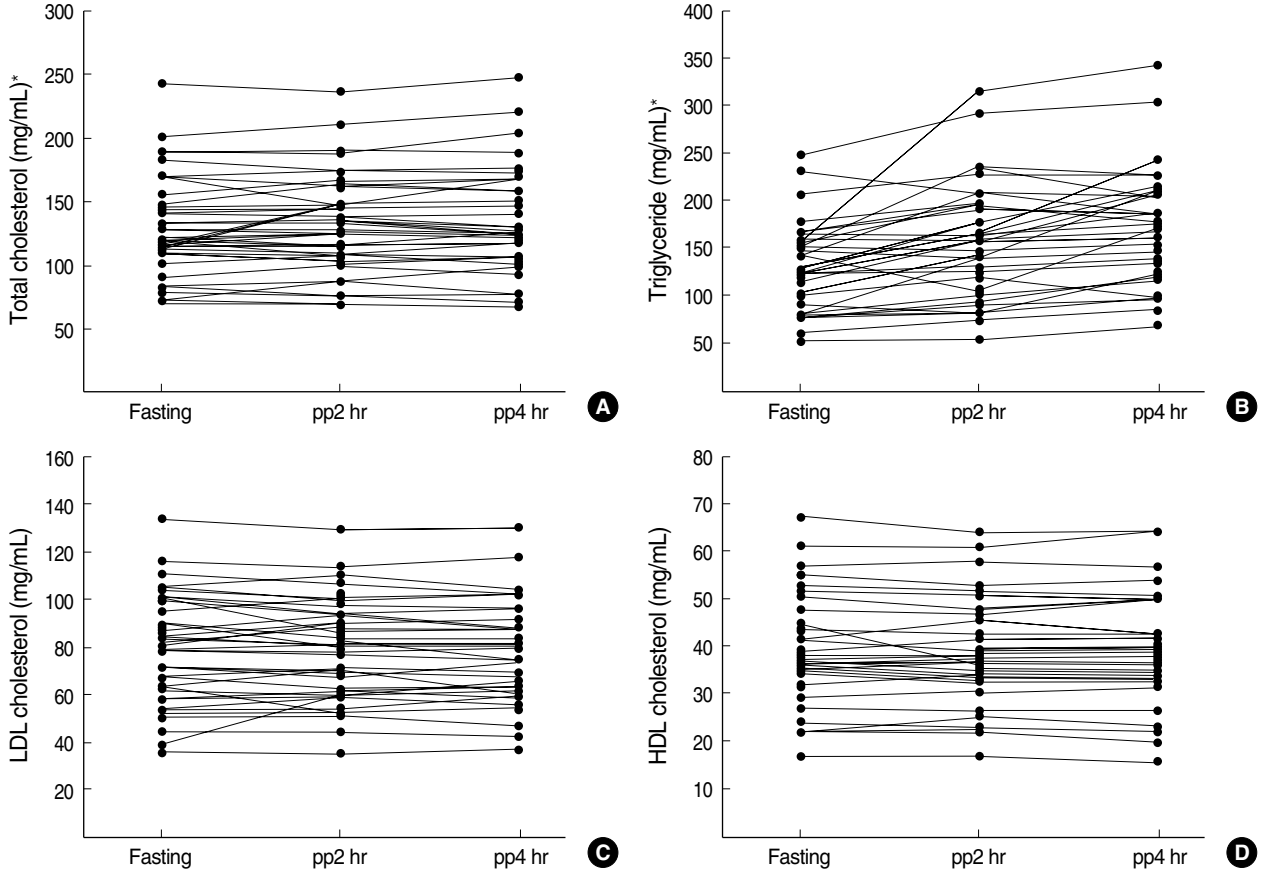

Fig. 1. Changes in fasting and post-prandial 2- and 4-hr lipid values. (A) total cholesterol, (B) triglyceride, (C) LDL cholesterol, (D) HDL cholesterol.
*P<0.05 compared to fasting value by repeated measure test.

Table 3. Comparison of achieving of target goal between fasting, post-prandial (PP) 2 and 4 hr LDL cholesterol (LDL-C)

Concentration of LDL-C	Number	Fasting		P value
		LDL-C <100 Number (%)	LDL-C ≥100 Number (%)	
PP 2 hr				
<100	27	26 (96)	1 (4)	
≥100	8	1 (12)	7 (88)	NS
PP 4 hr				
<100	27	26 (96)	1 (4)	
≥100	8	1 (12)	7 (88)	NS

The unit of LDL cholesterol is mg/dL. 100 mg/dL=2.6 mM/L.
P value was calculated by McNemar test.
LDL, low-density lipoprotein; NS, not significant.

cholesterol for women as >50 mg/dL (1.3 mM/L). In our study, the patients achieving goal at post-prandial 2 hr and 4 hr HDL cholesterol levels were perfectly matched to fasting (Table 4). Compared to fasting HDL cholesterol levels in men, pp 2 hr and 4 hr levels were misclassified as achieved target goal in 22% and 12%, respectively (Table 4). For identifying women with low fasting levels of HDL cholesterol, post-prandial 2 hr and 4 hr HDL cholesterol values were all 100% sensitive and specific. In men, the sensitivity and specificity of post-prandial 2 hr HDL cholesterol values were 77.8% and 87.5%, respectively. In case of post-prandial 4 hr HDL cholesterol, both sensitivity and specificity were 100%. Fourteen % of subjects with elevated non-HDL cholesterol levels would be false negative if post-prandial 2 hr non-HDL cholesterol estimates were used for assessing target goal. When we use 4 hr post-prandial non-HDL cholesterol, false negative was 7% of patients (Table 5).

DISCUSSION

The lowering LDL cholesterol levels in individuals with and without pre-existing coronary heart disease has been shown to reduce cardiovascular event and total mortality (11-15). However, despite the widespread use of statins during the last decade, recent studies have shown that about 60-70% of patients do not arrive the goal (16-20). The failure of achieving target has been related to a number of factors, including

Table 4. Comparison of achieving of target goal between fasting, post-prandial (PP) 2 and 4 hr HDL cholesterol by gender of the subjects

	Number	Fasting		*P* value		Number	Fasting		*P* value
		LDL-C >50 Number (%)	LDL-C ≤50 Number (%)				LDL-C >40 Number (%)	LDL-C ≤40 Number (%)	
Female					Male				
PP 2 hr					PP 2 hr				
HDL-C>50	4	4 (100)	0 (0)		HDL-C>40	5	5 (100)	0 (0)	
HDL-C≤50	17	0 (0)	17 (100)	NS	HDL-C≤40	9	2 (22)	7 (78)	NS
PP 4 hr					PP 4 hr				
HDL-C>50	4	4 (100)	0 (0)		HDL-C>40	6	6 (100)	0 (0)	
HDL-C≤50	17	0 (0)	17 (100)	NS	HDL-C≤40	8	1 (12)	7 (88)	NS

The unit of HDL cholesterol is mg/dL, 50 mg/dL=1.3 mM/L and 40 mg/dL=1.0 mM/L.
P value was calculated by McNemar test.
HDL, high density lipoprotein; LDL, low-density lipoprotein; NS, not significan.

Table 5. Comparison of achieving of target goal between fasting, post-prandial (PP) 2 and 4 hr non-HDL cholesterol (non-HDL-C)

Concentration of non-HDL-C	Number	Fasting		*P* value
		Non HDL-C<130 Number (%)	Non HDL-C≥130 Number (%)	
PP 2 hr				
<130	29	25 (86)	4 (14)	
≥130	6	0 (0)	6 (100)	0.125
PP 4 hr				
<130	27	25 (93)	2 (7)	
≥130	8	0 (0)	8 (100)	0.500

The unit of non HDL cholesterol is mg/dL, 130 mg/dL=3.36 mM/L.
P value was calculated by McNemar test.

insufficient pharmacological effect at the starting dose of a statin and a subsequent lack of willingness to escalate statin dose. One study reported that only 33% of patients had tested lipid levels (21). And the situation has not been improved over the years. Only 40% coronary disease patients knew current lipid values (22). They suggested that the fact they don't have recent lipid result might be another reason for not attainment of lipid goal. Most people visit their doctor in nonfasting state and if they are diabetic patients, it is not easy to keep them fasting because of hypoglycemic risk. In order to obtain fasting lipid results, we have to reschedule the patient to perform fasting level test and let them take a risk of hypoglycemia and hyperglycemia. If nonfasting lipid are tested, doctor and patient compliance with ATP III guidelines might be improved and more people may reach the goal.

The results of present study showed that nonfasting LDL and HDL cholesterol levels were not different from fasting levels in type 2 diabetes patients with Korean diet and taking statins. Other recent study showed that fasting and nonfasting LDL cholesterol levels were not significantly different in type 2 DM (10). Several reports showed nonfasting LDL cholesterol level were significantly different to fasting one (6-9). But their study protocol was different. They provided Western diet. They used a fat rich diet which was consisted of 880 calories and 57% of calories from fat (7, 10) or usual Western breakfast which was consisted of 500 calories, 40% from fat and 44% from carbohydrate (9). Compared to western diet, traditional Korean diet has lower fat percentage out of total calories. The amount of fat in diet can influence plasma LDL and HDL cholesterol level (23-25). Atorvastatin reduced mean changes in LDL and HDL cholesterol after meal (8). Those studies may be explanations why our study did not show any significant differences between fasting and nonfasting LDL and HDL cholesterol.

For detecting patients who attain target LDL and HDL cholesterol levels, the both post-prandial 2 hr and 4 hr LDL cholesterol levels misclassified only 4% of patients and none in case of post-prandial HDL cholesterol. We may suggest we can keep our treatment without further action if nonfasting LDL cholesterol and HDL cholesterol levels meet the goal. When we compared the patients who did not achieve goal in post-prandial 2 hr and 4 hr levels to fasting LDL cholesterol levels, 12% of patients were false positive. Even if we increase the dose of statin to attain target goal using post-prandial LDL cholesterol level, more patients meet the goal and have more benefit evidenced by previous large studies. Nonfasting HDL cholesterol levels were matched perfectly to fasting level in women and showed 12-22% false positive in men. In real clinical practice, checking post-prandial LDL and HLD cholesterol level may save our money and time and increase compliance of patients and doctor.

One study showed that lower fasting and post-prandial levels of plasma total, LDL and non-HDL cholesterol during metformin versus repaglinide treatment in type 2 DM (26). We did not compare the effect of oral hypoglycemic agents on cholesterol level because the number of our subjects was so small. In order to minimize the effect of various medications, we selected our subjects who had kept their treatment without any change at least for 3 months.

It is concluded that post-prandial LDL and HDL choles-

terol levels are not significantly different from fasting values in type 2 diabetes receiving statin treatment on Korean diet. For the assessment of achieving target goal in those patients, the fasting and post-prandial LDL and HDL cholesterol levels do not show significant differences.

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