International Journal of Computational and Experimental Science and ENgineering (IJCESEN)
Vol. 7-No.3 (2021) pp. 146-155
http://dergipark.org.tr/en/pub/ijcesen

ISSN: 2149-9144

Research Article

Effect of Rosuvastatin on Fasting and Postprandial Lipid Profile in Hypertriglyceridemia Patients

Abdulkadir ÇAKMAK*

Assistant Prof., Amasya University Sabuncuoğlu Şerefeddin Education and Research Hospital, Department of Cardiology

* **Corresponding Author -Email:** abdulkadir.cakmak@amasya.edu.tr **ORCID:** 0000-0001-7427-3368

Article Info:

DOI: 10.22399/ijcesen.827419
Received : 17 November 2020
Accepted : 28 November 2021

Keywords

Coronary heart disease
Hypertriglyceridemia
Rosuvastatin
Triglycerides

Abstract:

Coronary heart disease (CHD) is a main cause of mortality due to cardiovascular diseases. Hypertriglyceridemia (HTG) is a multifactorial condition implicated in the pathogenesis of CHD. Serum triglyceride (TG) levels were routinely obtained under fasting conditions; however, recent evidences implicate that postprandial triglyceride levels may be more important for CHD risk. Aim of this study was to investigate the effect of rosuvastatin on fasting and postprandial TG levels in the patients with borderline-high TG levels. 51 patients (18-75 years old; 26 female) with LDL-c between 100 and 160 mg/dL and triglyceride levels between 150 and 300 mg/dL were included in this study. Basal fasting and postprandial lipid profile and hsCRP levels of the patients were obtained and patients were requested to take 10 mg/day rosuvastatin for one month. At the end of one month, the measurements were repeated. Rosuvastatin significantly decreased both fasting and postprandial TG levels compared to basal levels ($p<0.001$). The decrease in the postprandial TG levels after rosuvastatin treatment were significantly higher than the decrease in fasting TG levels ($p<0.001$). No differences between genders were observed with regards to decrease in the fasting and postprandial TG levels. In patients with metabolic syndrome, rosuvastatin treatment decreased fasting and postprandial TG levels after one month, however, the change was not different from the patients without metabolic syndrome. In conclusion, the decrease in postprandial TG levels after rosuvastatin treatment that was shown may be clinically important in prevention of CHD in HTG patients.

1. Introduction

Cardiovascular diseases (CVDs) are the major cause of death worldwide and coronary heart disease (CHD) is indicated to be a main cause of the death due to CVDs [1]. Despite of the gradual decrease in the CHD-related deaths, almost 30 % of mortality older than Hypertriglyceridemia (HTG) is a multifactorial condition that is the consequence of interaction between both genetic and environmental factors and develops due to increased very low-density lipoprotein (VLDL) cholesterol (LDL-c) and chylomicron levels, as well as their remnants [2,3]. HTG has a strong association with the low levels of high-density lipoprotein (HDL) cholesterol (HDL-c) and high levels of LDL-c that are the risk of coronary heart disease (CHD) and has been suggested to have a relation with premature CHD [4,5]. Multifactorial analyses weakened association between HTG and CHD [6,7] as the triglyceride (TG) levels are affected by various factors such as obesity, severe alcohol consumption, diabetes mellitus (DM), insulin resistance, hypertension and smoking [8], however, various studies indicated HTG as an independent risk factor for CVD [9].

Increased TG levels are defined by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) as fasting TG levels are higher than 150 mg/dL in adults and levels spanning 150-199 mg/dL is defined as borderline-high TG levels, while TG levels equal or higher than 500 mg/dL is indicated as very high TG levels [10]. On the other hand, a following guidelines published by Endocrine Society focused on the connection between the pancreatitis risk in the

subjects with severely high TG levels and classified the TG levels higher than 2,000 mg/dL as very severe HTG resulting in pancreatitis [11, 12]. Both guidelines are prepared to help clinicians for the evaluation of the risk of both CVD and pancreatitis and to improve the treatment options [13].

Routine serum TG measurement has been conducted under fasting conditions to acquire more stable TG concentration measurement and calculate the LDL levels [14], however, recent suggestions are that the fasting is not required for the routine TG profile screening [15] and lipid measurements under fasting and postprandial conditions depends on the scenario that is questioned [16]. Fasting and postprandial TG levels may vary depending on the content and time of last meal [17] and postprandial HGT is associated with the CHD risk that is related to increased levels of chylomicron, as well as LDL-c and VLDL-c, have atherogenic activity as they potentiate the platelet activity and coagulation cascade [18]. In addition, evidences suggest that increased postprandial TG levels has been indicated to be a risk factor for CHD by several studies [19-21].

Statins that were firstly identified in 1976 [22] inhibits a rate limiting enzyme, hydroxymethyl glutaryl coenzyme A reductase (HMG-CoA), in cholesterol biosynthesis [23] exert their antiatherosclerosis activities by reducing the LDL-c [24] and decreasing thrombin formation [25]. Rosuvastatin exerts its beneficial cardiovascular activities by not only competitively inhibiting the HMG-CoA and improving the cholesterol profile but also acting as antioxidant, antithrombotic and anti-inflammatory [26]. Previous studies showed that 20 mg/day [27] rosuvastatin treatment led to 62 % decrease in the cardiovascular events in the patients with normal LDL-c levels and high levels of high-sensitivity C-reactive protein (hsCRP) and decreased fasting TG levels by 17 % [27]. Several studies also showed that statins lowered the fasting and postprandial plasma TG and apolipoprotein (apo)B-48 levels [28-33]. An 8-week treatment with 5 mg rosuvastatin was found to decrease fasting LDL-c, total cholesterol and TG levels significantly [34]. Therefore, in this study, we aimed to determine the effect of rosuvastatin on fasting and postprandial TG levels in the patients with TG levels between 150 and 300 mg/dL and LDL-c levels between 100 and 160 mg/dL

2. Patients and Methods

Patients admitted to and evaluated at Cardiology Department at Başkent University Faculty of Medicine between March 2009 and February 2010 were included in this study. Inclusion criteria of were determined being between 18 and 75 years old, having LDL-c levels between 100 and 160 mg/dL, indication of statin use according to the NCEP ATPIII [30], and having TG levels between 150 and 300 mg/dL, while the exclusion criteria were being younger than 18 and older than 75 years old, having medical history of DM, chronic liver disease, chronic kidney disease and chronic renal failure, connective tissue disease, gastrointestinal malabsorption disorders, enteropathies, acute myocardial infarction (MI), unstable angina pectoris, acute/chronic pancreatitis, hyperthyroidism and hypothyroidism, having TG levels below 150 mg/dL and above 300 mg/dL and LDL-c levels below 100 mg/dL and above 160 mg/dL. This study was approved by Başkent University Clinical Research Ethics Committee on 03/02/2009 (Approval no: B.30.2. BŞK.0.05.05.01/95).

A group of 51 patients who were evaluated in the cardiology department of our hospital, met the inclusion criteria and gave their consent were included in this study. Blood pressure, height, weight, CHD risk factors, alcohol consumption pattern of the patients, as well as the medications that they used, were recorded. Patients with body mass index (BMI) higher than 30 kg/m2 were classified as obese. Presence of three factors of that a waist circumference exceeding 102 cm in males and 88 cm in females, TG levels higher than 150 mg/dL, HDL-c below 40 mg/dL in males and 50 mg/dL in females, blood pressure equal or above 130/85 (systole/diastole) and blood glucose levels equal or higher than 100 mg/dL were considered as the diagnosis of metabolic syndrome in the patients. The activity level (sports, exercise) below 150 minutes per week was taken as the sedentary life criterion. If the patient was exercising at least five days a week for more than 30 min/day, patient was noted as exercising regularly. Patients who were consuming 2-3 days a week around 30 g alcohol per day and were identified as alcohol consumers. Patients with a history of anginal symptoms, ECG variations and elevated cardiac enzyme levels indicating the presence of coronary artery disease, if the coronary angiography of the patient showed at least one lesion with more than 50 % stenosis, if the patient underwent percutaneous coronary intervention at any time or underwent coronary artery bypass surgery, the patient was then included in the CHD group.

After a 12-hour fasting period, total cholesterol, LDL-c, TG, HDL-c and hsCRP levels of the patients were measured. The patient was then given a breakfast as described in the oral lipid loading test protocol below and measurements were repeated four hours later. Breakfast was prepared by the

Nutrition and Dietetics Unit in the cafeteria of our hospital and served as a breakfast plate.

Since the biochemical markers measured in our study are highly affected by diet, patients were requested not to make any dietary changes during the study period. Patients were recommended to take their medicines at the same time of day. The patients were questioned whether they were using their drugs properly or not at the first month follow-up.

In oral fat load tests conducted by administering fat-enriched enteral solutions or meals with high calorie and high fat content, the fat content ranges from 31% to 80% [35-38]. In our study, breakfast was preferred for fat loading because it was easier to tolerate and provide. All patients were given an average breakfast consisting of 60% fat, 16.8% protein and 23.2% carbohydrate with a total energy content of 891 kcal.

Complete blood count and blood biochemistry (TG, total cholesterol, LDL-c, HDL-c, hsCRP, blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), blood urea nitrogen (BUN), creatinine, sodium (Na+), potassium (K+) and thyroid stimulating hormone (TSH)) measurements were conducted on the admission day and one month after. TG, total cholesterol, LDL-c, HDL-c, blood glucose, AST, ALT, CK, BUN, creatinine, Na+ and K+ measurements were conducted by using a modular autoanalyzer (Roche Diagnostics GmbH, Germany), hsCRP measurements were conducted by using a CRP Ultra reagent Abbott® Architect C8000 Analyser (Sentinel Diagnostics, Italy), TSH measurements were conducted by using an Architect i2000 autoanalyzer (Abbott, Wiesbaden, Germany) and haematology measurements Abbott Cell-Dyne® 3700 System (Abbott Diagnostics, Santa Clara, USA)..

2.1. Statistical analyses

Shapiro-Wilk test was used to check the normal distribution of the continuous variables. The homogeneity of the variances was analysed by Levene test. Student's t-test was used to compare the gender differences in several variables. In case of the variables did not meet prerequisites of parametric tests, Mann-Whitney U test was used to compare the gender differences. The relation between the data were investigated by Pearson Chi-square, G-test and Fisher Exact test where applicable. Two-way repeated measures of analysis of variance by including sex factor was used to compare the pre- and post-treatment and fasting and postprandial values of the parameters by including sex factor. Before this analysis was performed, it was determined that the variables had a right skewed distribution, the logarithmic transformation was applied to the variables to provide the prerequisites for analysis of repeated measurements.

Statistical analysis results were expressed as n (%) for categorical variables and mean ± standard deviation (SD) and median for continuous variables. A p value lower than 0.05 was considered statistically significant. SPSS 16.0 statistical package program (Statistical Package for the Social Sciences, version 16.0, SSPS Inc., Chicago, IL, USA) was used to analyse the data set.

3. Results

This study included 51 patients (Table 1). The mean age of the patients was 54.3±11.6 and 26 of the patients were female (Table 1). Mean BMI of the patients were 28.1 ± 4.1 (mean body weight 77.4 ± 16.1 kg and mean height 165.8 ± 10.3 cm). Waist circumference was 108.4±9.4 cm and mean hip circumference was 108.9 ± 9.4 cm). A group of 12 patients (23.5 %) had CHD history and 5 out of them had MI, six of them had coronary artery bypass surgery and one patient percutaneous coronary intervention history. Forty patients (78.4 %) had metabolic syndrome. 19 patients were obese, and 36 patients had sedentary lifestyle (Table 1). 17 patients were smokers while 11 patients were exercising regularly. The results of basal laboratory examination for blood parameters and complete blood counts of patients are also summarized in Table 1.

The comparison between the genders with regards to the demographical and lifestyle characteristics, significant differences were found only in the CHD history and alcohol use and diet between the genders ($p<0.05$; Table 2). When the basal fasting and postprandial (after oral lipid load) lipid and hsCRP values were investigated it was found that TG and total cholesterol values were significantly higher ($p<0.001$, LDL-c and HDL-c were significantly lower ($p<0.01$ and $p<0.001$, respectively) in the patients after lipid load (under postprandial conditions), while hsCRP levels were found unaffected (Table 3). After oral lipid loading, patients received 10 mg/day rosuvastatin for one month, then patients fasting ALT, AST, CK and blood lipid profile, as well as the postprandial blood lipid profile after lipid load was investigated. There were no significant differences between the basal and post-treatment ALT (22.2±5.7 and 22.8±6.0, respectively), AST (24.1±9.2 and 24.7±7.1, respectively), and CK values (65.3±26.2 and 76.0±27.6, respectively). On the other hand, TG and total cholesterol levels were significantly

Table 1. *Demographical characteristics of the patients (n=51).*

	Female(n=26)	Male(n=25)	p-value
Age (years (mean ± SD)	55.2 ± 11.2	49.9 ± 12.1	0.588
Patient condition			
BMI (kg/m²)	27.9 ± 4.7	28.3 ± 3.4	0.758
Waist circumference (cm)	107.4±11.5	109.1±5.5	0.155
Metabolic syndrome, n (%)	19 (73.1 %)	21 (84.0 %)	0.499
CHD history, n (%)	2 (7.6 %)	10 (40 %)	**0.040***
Hypertension, n (%)	17 (65.4 %)	16 (64.0 %)	0.918
Obesity, n (%)	69 (34.6 %)	10 (40 %)	0.691
Lifestyle Sedentary lifestyle, n (%)	19 (73.1 %)	17 (68.0 %)	0.764
Smoking, n (%)	6 (23.1 %)	11 (44.0 %)	0.090
Alcohol use, n (%)	0	2 (8.0 %)	**0.034***
Exercise, n (%)	6 (23.1 %)	5 (20 %)	0.789
Diet, n (%)	7 (26.9 %)	1 (4.0)	**0.026***

Table 2. *Comparison between the female and male patients with regards to demographical characteristics *p<0.05*

Age (years (mean ± SD))	54.3 ± 11.6
Gender, n (%)	
Female	26 (50.9 %)
Male	25 (49.1 %)
Patient condition	
BMI (kg/m²)	28.1 ± 4.1
Waist circumference (cm)	108.4 ± 9.4
Metabolic syndrome, n (%)	40 (78.4 %)
CHD history, n (%)	12 (23.5 %)
Family history of CHD, n (%)	21 (41.2 %)
Hypertension, n (%)	33 (64.7 %)
Obesity, n (%)	19 (37.3 %)
Lifestyle	
Sedentary lifestyle, n (%)	36 (70.6 %)
Smoking, n (%)	17 (33.3 %)
Alcohol use, n (%)	3 (5.9 %)
Exercise	11 (21.6 %)
Laboratory parameter	
Fasting glucose (mg/dL)	93.9 ± 8.8
Sodium (mmol/L)	139.1 ± 2.5
Potassium (mmol/L)	4.2 ± 0.4
Haemoglobin (g/dL)	14.5 ± 1.3
Haematocrit (%)	42.7 ± 4.4
Leukocyte (10^3/mm³)	7,354 ± 1,620
Thrombocyte (10^3/mm³)	285,333 ± 51,690
AST (U/L)	22.2 ± 5.7
ALT (U/L)	24.1 ± 9.2
CK (U/L)	65.3±26.2
TSH (IU/mL)	2.1±1.0
BUN (mg/dL)	15.3±4.3
Creatinine (mg/dL)	0.8±0.2

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BMI, body mass index; BUN, Blood urea nitrogen; CHD, coronary heart disease; CK, Creatine kinase; TSH, Thyroid stimulating hormone.

Table 3. *Basal fasting and postprandial (after lipid load) lipid and hsCRP levels (n=51).*

	Fasting	Postprandial	p value
TG (mg/dL)	191.0 ± 41.4	337.4 ± 117.1	**<0.001***
Total cholesterol (mg/dL)	212.6 ± 23.7	237.0 ± 28.1	**<0.001***
LDL-c (mg/dL)	133.8 ± 19.6	129.8 ± 20.5	**<0.01***
HDL-c (mg/dL)	41.5 ± 8.4	39.4 ± 8.6	**<0.001***
hsCRP (mg/L)	5.5 ± 5.1	5.7 ± 5.0	0.168

HDL-c, high-density lipoprotein-cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-c, low-density lipoprotein-cholesterol; TG, triglyceride.

Table 4. *Post-treatment fasting and postprandial (after lipid load) lipid and hsCRP levels (n=51).*

	Fasting	Postprandial	p value
TG (mg/dL)	152.1±50.6	258.0±95.9	**<0.001***
Total cholesterol (mg/dL)	154.9±22.0	172.9±24.4	**<0.001***
LDL-c (mg/dL)	80.4±16.9	77.0±16.0	**<0.001***
HDL-c (mg/dL)	43.6±9.7	41.9±9.0	**<0.001***
hsCRP (mg/L)	4.9±4.8	4.8±4.6	0.474

HDL-c, high-density lipoprotein-cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-c, low-density lipoprotein-cholesterol; TG, triglyceride.

higher at the post-treatment period after lipid load (p<0.001; Table 4), while LDL-c and HDL-c levels were significantly lower (p<0.001; Table 4). On the other hand, there were no significant differences between the fasting and postprandial hsCRP levels (p=0.474; Table 4). When the fasting lipid parameters and hsCRP values were compared at the baseline and post-treatment, TG, total cholesterol and LDL-c levels were found to be significantly lower (p<0.001; Table 5). On the other hand, fasting HDL-c levels were found higher and hsCRP was found lower at post-treatment period, but these differences were not statistically significant (p=0.068 and p=0.091, respectively; Table 5). On the other hand, postprandial TG, total cholesterol, LDL-c and hsCRP levels were significantly lower after one-month rosuvastatin treatment when compared with basal values(p<0.001 for TG, total cholesterol and LDL-c and p<0.05 for hsCRP;

Table 5). In addition, postprandial HDL-c levels were found to be higher after rosuvastatin treatment compared to baseline ($p<0.05$; Table 5).

The differences between the pre-treatment fasting and postprandial TG levels (191.0±41.4 mg/dL and 337.4±117.1 mg/dL, respectively) and post-treatment fasting and postprandial TG levels (152.1±50.6 mg/dL and 258.0±95.9 mg/dL, respectively) were compared with Wilcoxon test. The differences between the fasting and postprandial TG levels at the baseline and post-treatment period were found as 38.9±46.2 mg/dL and 79.4±96.8 mg/dL, respectively and the change in the decrease in TG levels (30.5±46.2 mg/dL) were found significant ($p<0.001$).

When the fasting and postprandial TG values of male and female subjects were compared at the baseline and after one-month rosuvastatin treatment, both fasting and postprandial TG levels were found to be decreased after rosuvastatin treatment ($p<0.001$; Table 6). On the other hand, there were no statistically significant differences in TG levels between the genders when the basal fasting ($p=0.47$), basal postprandial ($p=0.14$), post-treatment fasting ($p=0.57$) and post-treatment postprandial ($p=0.19$) levels were compared. In both males and females, the level of decrease in postprandial TG levels were higher than the decrease in fasting TG levels after one-month rosuvastatin administration ($p<0.001$). However, Wilcoxon test revealed that this decrease in the TG levels did not differ between the genders ($p=0.784$).

In the patients both with or without metabolic syndrome, TG levels were significantly higher after lipid load compared to fasting TG levels both at baseline and after one-month rosuvastatin treatment ($p<0.001$; Table 7). On the other hand, fasting TG levels were significantly lower after one-month rosuvastatin treatment in the patients with metabolic syndrome ($p<0.001$) while no difference was observed in the patients without metabolic syndrome ($p<0.112$; Table 7). Similarly, post-lower after rosuvastatin treatment in the patients with metabolic syndrome ($p<0.001$) but there was no significant effect of rosuvastatin level in postprandial TG levels patients without metabolic syndrome ($p<0.089$; Table 7). In addition basal fasting TG levels were significantly lower in the patients without metabolic syndrome compared to the patients with metabolic syndrome ($p<0.009$; Table 7), however, no significant differences were observed in basal postprandial, post-treatment fasting and post-treatment postprandial TG levels between the patients with metabolic syndrome and patients without metabolic syndrome (Table 7).

The analyses in the obese and non-obese patients revealed that the basal, as well as after one-month rosuvastatin treatment, postprandial TG levels were significantly higher than fasting levels in both patient groups ($p<0.001$; Table 8). On the other hand, fasting TG levels after rosuvastatin treatment were significantly lower than the baseline levels in both groups ($p\leq0.001$; Table 8). Similarly, postprandial TG levels after rosuvastatin treatment were significantly lower than the baseline levels ($p<0.01$; Table 8). However, there were no significant differences between the groups any of the parameters that were compared (Table 8).

Table 5. *Comparison of fasting and postprandial (after lipid load) lipid and hsCRP levels at the baseline and one-month rosuvastatin treatment (n=51; in the statistical analysis of postprandial measurements log-transformed values were used).*

	Fasting		
	Basal	**Post-treatment**	**p value**
TG (mg/dL)	191.0±41.4	152.1±50.6	**<0.001***
Total cholesterol (mg/dL)	212.6±23.7	154.9±22.0	**<0.001***
LDL-c (mg/dL)	133.8±19.6	80.4±16.9	**<0.001***
HDL-c (mg/dL)	41.5±8.4	43.6±9.7	0.068
hsCRP (mg/L)	5.5±5.1	4.9±4.8	0.091
	Postprandial		
	Basal	**Post-treatment**	**p value**
TG (mg/dL)	337.4±117.1	258.0±95.9	**<0.001***
Total cholesterol (mg/dL)	237.0±28.1	172.9±24.4	**<0.001***
LDL-c (mg/dL)	129.8±20.5	77.0±16.0	**<0.001***
HDL-c (mg/dL)	39.4±8.6	41.9±9.0	**<0.05***
hsCRP (mg/L)	5.7±5.0	4.8±4.6	**<0.05***

HDL-c, high-density lipoprotein-cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-c, low-density lipoprotein-cholesterol; TG, triglyceride.

4. Discussions

HTG is an independent risk factor for CHD [9]. TG levels are routinely measured under fasting conditions to obtain more stable TG levels and therefore to calculate LDL levels [14]. Nevertheless, it was recently suggested that fasting is not necessary for routine TG profiling [15]. In addition, previous studies indicated that postprandial TG levels are as important risk factor as fasting TG levels for CHD [39-41]. In our study, we investigated the effects of rosuvastatin, a statin that is used in the treatment of hyperlipidaemia, on fasting and postprandial TG and hsCRP levels. Rosuvastatin is known to decrease fasting TG levels between 17% and 25% [27]. Several other studies indicated significant reductions in fasting

Table 6. *Comparison of fasting and postprandial (after lipid load) TG levels at the baseline and one-month rosuvastatin treatment within the genders.*

	Basal		Post-treatment		^{a}p value	^{b}p value	^{c}p value	^{d}p value
	Fasting	Postprandial	Fasting	Postprandial				
Female (n=26)	186.8 ±36.5	313.8 ±88.5	148.5 ±46.1	240.7 ±88.0	**<0.001***	**<0.001***	**<0.001***	**<0.001***
Male (n=25)	195.3 ±46.3	362.0 ±138. 4	156.2 ±55.0	275.8 ±102. 2	**<0.001***	**<0.001***	**<0.001***	**<0.001***

*p<0.05

[a]p: Comparison of the basal fasting and postprandial TG levels within genders

[b]p: Comparison of the post-treatment fasting and postprandial TG levels within genders

[c]p: Comparison of the basal and post-treatment fasting TG levels within genders

[d]p: Comparison of the basal and post-treatment postprandial TG levels within genders

Table 7. *Comparison of fasting and postprandial (after lipid load) TG levels at the baseline and one-month rosuvastatin treatment within and between the patients with and without metabolic syndrome.*

	Basal		Post-treatment		^{a}p value	^{b}p value	^{c}p value	^{d}p value	^{e}p value	^{f}p value	^{g}p value	^{h}p value
	Fasting	Postprandial	Fasting	Postprandial								
α (n=40)	197.0±43.4	350.3±124.7	155.5±48.3	264.7±92.2	**<0.001***	**<0.001***	**<0.001***	**<0.001***	**0.009***	0.059	0.329	0.919
Ø (n=11)	169.3±23.3	290.3±69.2	139.1±58.7	234.2±109.7	**<0.001***	**0.003***	0.112	0.089				

α: patients with metabolic syndrome, Ø: patients without metabolic syndrome, *p<0.05

[a]p: Comparison of the basal fasting and postprandial TG levels within the groups

[b]p: Comparison of the post-treatment fasting and postprandial within the groups

[c]p: Comparison of the basal and post-treatment fasting TG levels within the groups

[d]p: Comparison of the basal and post-treatment postprandial TG levels within the groups

[e]p: Comparison of the basal fasting TG levels between the groups

[f]p: Comparison of the basal postprandial between the groups

[g]p: Comparison of the post-treatment fasting TG levels between the groups

[h]p: Comparison of the post-treatment postprandial TG levels between the groups

Table 8. *Comparison of fasting and postprandial (after lipid load) TG levels at the baseline and one-month rosuvastatin treatment within and between obese and non-obese patients.*

	Basal		Post-treatment		^{a}p value	^{b}p value	^{c}p value	^{d}p value	^{e}p value	^{f}p value	^{g}p value	^{h}p value
	Fasting	Postprandial	Fasting	Postprandial								
Obese (n=19)	197.0±43.7	325.3±130.7	160.6±37.3	264.7±92.2	**<0.001***	**<0.001***	**0.001***	**0.009***	0.721	0.623	0.231	0.424
Non-obese (n=32)	187.3±40.3	344.3±109.2	147.1±56.7	262.2±100.7	**<0.001***	**<0.001***	**<0.001***	**<0.001***				

*p<0.05

[a]p: Comparison of the basal fasting and postprandial TG levels within the groups

[b]p: Comparison of the post-treatment fasting and postprandial within the groups

[c]p: Comparison of the basal and post-treatment fasting TG levels within the groups

[d]p: Comparison of the basal and post-treatment postprandial TG levels within the groups

[e]p: Comparison of the basal fasting TG levels between the groups

[f]p: Comparison of the basal postprandial between the groups

[g]p: Comparison of the post-treatment fasting TG levels between the groups

[h]p: Comparison of the post-treatment postprandial TG levels between the groups

TG levels at different doses for different treatment periods [42,43]. In our study, 10 mg/day rosuvastatin treatment for one month resulted in a 20% decrease in fasting TG levels, similar to the results published previously. Atorvastatin, another statin, treatment led to significant reductions in the postprandial TG levels [30,44]. In our study, besides the decrease in postprandial TG level was significant, the decrease in postprandial TG value was more pronounced from the decrease in fasting TG level upon rosuvastatin treatment. This finding suggests that control of postprandial TG levels by rosuvastatin treatment, similar to the control of fasting TG levels, may be another aspect of the efficacy of rosuvastatin in the prevention of CHD.

In our study, when the hs-CRP levels were examined, the only significant change was seen between the baseline postprandial levels and postprandial levels after one-month rosuvastatin treatment. Several long-term (two to 33 months) studies revealed beneficial effects of rosuvastatin on decreasing hsCRP levels [27,42,45]. The fact that the significant difference appeared only at the levels of postprandial levels in our study may be related to the short length of the treatment period.

The frequency, occurrence, treatment process and outcomes of CHD show some differences between women and men. For example, CHD mortality and stroke risk are higher in women in the presence of DM, but the evaluation of women in studies is not as clear and detailed as men and besides cultural, behavioural, psychosocial and socioeconomic differences, gender-dependent factors and CHD outcomes in women are not as well explained as in men [46]. Lipoprotein risk factors that are important for CHD also differ in women. The risk prediction of HDL-c is stronger than that of men, oestrogen prevents the storage of LDL-c in arterial wall, and in postmenopausal women, TG is an independent risk factor (proatherogenic lipid profile) for CHD in women [47, 48]. In a 2-year study conducted revealed that BMI, HDL-c are most correlated risk factors with hsCRP for CHD for both genders and hsCRP levels were positively correlated with mean blood pressure and blood glucose in men while it was with TG levels in women [49]. Also, a recent meta-analysis revealed that statins have beneficial effects on both genders, they are more effective in improving lipid profile in women older than 70 years [50]. In our study, rosuvastatin treatment was found equally affecting TG levels in men and women.

The positive effects of statins on dyslipidaemia in the patients with metabolic syndrome was shown by various groups [51,52]. On the other hand, atherosclerosis was shown to progress in the obese patients although they receive statin treatment [53]. Another study suggested that the type of statin to be used should be chosen in obese patients with type 2 DM depending on their lipid profile and condition [54]. In our study, independent of condition of the patients with regards to metabolic syndrome, postprandial TG levels significantly higher than fasting TG levels both at baseline and after one-month rosuvastatin treatment. Similar results were obtained when obese patients were compared with non-obese patients. However, both fasting and postprandial TG levels were significantly lower after one-month rosuvastatin treatment compared to the baseline fasting and postprandial TG levels in the patients with metabolic syndrome but in the patients without metabolic syndrome. However, no significant differences in the TG levels between obese and non-obese patients were observed. These results suggest that one-month rosuvastatin treatment may improve TG levels in patients with metabolic syndrome. In our study, no side effects of rosuvastatin treatment were observed. In addition, liver function parameters were not significantly affected by rosuvastatin treatment. As treatment period was limited with one month, safety profile of short-term 10 mg/day rosuvastatin seems reliable.

In our study, we evaluated the effect of rosuvastatin treatment on laboratory parameters as the risk factors for CHD (Lipid profile and hsCRP), however, clinical endpoints were not determined. Nevertheless, the importance of postprandial lipid metabolism on the atherosclerotic pathogenesis has been implicated by several studies and postprandial TG levels may be more important indicators than fasting TG levels. Therefore, we believe that the significant decrease in the postprandial TG levels is clinically important. In order to investigate this clinically important effect, studies evaluating the clinical endpoints on larger cases are needed.

Author Statements:

- The authors declare that they have equal right on this paper.
- The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper
- The authors declare that they have nobody or no-company to acknowledge.

References

[1]. Shi A, Tao Z, Wei P, Zhao J. Epidemiological aspects of heart diseases. Experimental and

therapeutic medicine. 2016;12(3):1645-50. doi:10.3892/etm.2016.3541.

[2]. Johansen CT, Wang J, Lanktree MB, McIntyre AD, Ban MR, Martins RA et al. An increased burden of common and rare lipid-associated risk alleles contributes to the phenotypic spectrum of hypertriglyceridemia. Arteriosclerosis, thrombosis, and vascular biology. 2011;31(8):1916-26. doi:10.1161/ATVBAHA.111.226365.

[3]. Ariza M-J, Sánchez-Chaparro M-A, Barón F-J, Hornos A-M, Calvo-Bonacho E, Rioja J et al. Additive effects of LPL, APOA5 and APOE variant combinations on triglyceride levels and hypertriglyceridemia: results of the ICARIA genetic sub-study. BMC medical genetics. 2010;11:66-. doi:10.1186/1471-2350-11-66.

[4]. Berneis KK, Krauss RM. Metabolic origins and clinical significance of LDL heterogeneity. J Lipid Res. 2002;43(9):1363-79. doi:10.1194/jlr.r200004-jlr200.

[5]. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation. 1989;79(1):8-15. doi:10.1161/01.cir.79.1.8.

[6]. Hulley SB, Rosenman RH, Bawol RD, Brand RJ. Epidemiology as a guide to clinical decisions. The association between triglyceride and coronary heart disease. N Engl J Med. 1980;302(25):1383-9. doi:10.1056/nejm198006193022503.

[7]. Sarwar N, Danesh J, Eiriksdottir G, Sigurdsson G, Wareham N, Bingham S et al. Triglycerides and the risk of coronary heart disease: 10,158 incident cases among 262,525 participants in 29 Western prospective studies. Circulation. 2007;115(4):450-8. doi:10.1161/circulationaha.106.637793.

[8]. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. Am J Cardiol. 1998;81(4a):18b-25b. doi:10.1016/s0002-9149(98)00033-2.

[9]. Han SH, Nicholls SJ, Sakuma I, Zhao D, Koh KK. Hypertriglyceridemia and Cardiovascular Diseases: Revisited. Korean circulation journal. 2016;46(2):135-44. doi:10.4070/kcj.2016.46.2.135.

[10]. National C. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106(25):3143-421.

[11]. Brunzell JD, Schrott HG. The interaction of familial and secondary causes of hypertriglyceridemia: role in pancreatitis. J Clin Lipidol. 2012;6(5):409-12. doi:10.1016/j.jacl.2012.06.005.

[12]. Chait A, Brunzell JD. Severe hypertriglyceridemia: role of familial and acquired disorders. Metabolism. 1983;32(3):209-14. doi:10.1016/0026-0495(83)90184-1.

[13]. Rygiel K. Hypertriglyceridemia - Common Causes, Prevention and Treatment Strategies. Current cardiology reviews. 2018;14(1):67-76. doi:10.2174/1573403X14666180123165542.

[14]. Berglund L, Brunzell JD, Goldberg AC, Goldberg IJ, Sacks F, Murad MH et al. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. The Journal of clinical endocrinology and metabolism. 2012;97(9):2969-89. doi:10.1210/jc.2011-3213.

[15]. Nordestgaard BG, Langsted A, Mora S, Kolovou G, Baum H, Bruckert E et al. Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points-a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. European heart journal. 2016;37(25):1944-58. doi:10.1093/eurheartj/ehw152.

[16]. Driver SL, Martin SS, Gluckman TJ, Clary JM, Blumenthal RS, Stone NJ. Fasting or Nonfasting Lipid Measurements. Journal of the American College of Cardiology. 2016;67(10):1227. doi:10.1016/j.jacc.2015.12.047.

[17]. Langsted A, Freiberg Jacob J, Nordestgaard Børge G. Fasting and Nonfasting Lipid Levels. Circulation. 2008;118(20):2047-56. doi:10.1161/CIRCULATIONAHA.108.804146.

[18]. Masuda D, Yamashita S. Postprandial Hyperlipidemia and Remnant Lipoproteins. Journal of atherosclerosis and thrombosis. 2017;24(2):95-109. doi:10.5551/jat.RV16003.

[19]. Nordestgaard BG, Benn M, Schnohr P, Tybjærg-Hansen A. Nonfasting Triglycerides and Risk of Myocardial Infarction, Ischemic Heart Disease, and Death in Men and Women. JAMA. 2007;298(3):299-308. doi:10.1001/jama.298.3.299.

[20]. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. Jama. 2007;298(3):309-16. doi:10.1001/jama.298.3.309.

[21]. Egeland GM, Igland J, Sulo G, Nygard O, Ebbing M, Tell GS. Postprandial triglycerides predict incident acute myocardial infarction among those with favourable HDL-cholesterol: Cohort Norway. Eur J Prev Cardiol. 2015;22(7):872-81. doi:10.1177/2047487314535681.

[22]. Endo A, Kuroda M, Tsujita Y. ML-236A, ML-236B, and ML-236C, new inhibitors of cholesterogenesis produced by Penicillium citrinium. J Antibiot (Tokyo). 1976;29(12):1346-8. doi:10.7164/antibiotics.29.1346.

[23]. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2013(1):Cd004816. doi:10.1002/14651858.CD004816.pub5.

[24]. Stancu C, Sima A. Statins: mechanism of action and effects. J Cell Mol Med. 2001;5(4):378-87. doi:10.1111/j.1582-4934.2001.tb00172.x.

[25]. Tripodi A, Pellegatta F, Chantarangkul V, Grigore L, Garlaschelli K, Baragetti A et al. Statins decrease thrombin generation in patients with

hypercholesterolemia. Eur J Intern Med. 2014;25(5):449-51. doi:10.1016/j.ejim.2014.03.016.

[26]. Cortese F, Gesualdo M, Cortese A, Carbonara S, Devito F, Zito A et al. Rosuvastatin: Beyond the cholesterol-lowering effect. Pharmacological Research. 2016;107:1-18. doi:https://doi.org/10.1016/j.phrs.2016.02.012.

[27]. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, Jr., Kastelein JJ et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359(21):2195-207. doi:10.1056/NEJMoa0807646.

[28]. Otokozawa S, Ai M, Van Himbergen T, Asztalos BF, Tanaka A, Stein EA et al. Effects of intensive atorvastatin and rosuvastatin treatment on apolipoprotein B-48 and remnant lipoprotein cholesterol levels. Atherosclerosis. 2009;205(1):197-201. doi:10.1016/j.atherosclerosis.2008.11.001.

[29]. Battula SB, Fitzsimons O, Moreno S, Owens D, Collins P, Johnson A et al. Postprandial apolipoprotein B48-and B100-containing lipoproteins in type 2 diabetes: do statins have a specific effect on triglyceride metabolism? Metabolism. 2000;49(8):1049-54. doi:10.1053/meta.2000.7744.

[30]. Parhofer KG, Laubach E, Barrett PH. Effect of atorvastatin on postprandial lipoprotein metabolism in hypertriglyceridemic patients. J Lipid Res. 2003;44(6):1192-8. doi:10.1194/jlr.M300011-JLR200.

[31]. Parhofer KG, Barrett PH, Schwandt P. Atorvastatin improves postprandial lipoprotein metabolism in normolipidemlic subjects. J Clin Endocrinol Metab. 2000;85(11):4224-30. doi:10.1210/jcem.85.11.6978.

[32]. Ng TW, Watts GF, Stuckey BG, Ching HL, Chan DC, Uchida Y et al. Does pravastatin increase chylomicron remnant catabolism in postmenopausal women with type 2 diabetes mellitus? Clin Endocrinol (Oxf). 2005;63(6):650-6. doi:10.1111/j.1365-2265.2005.02396.x.

[33]. Chan DC, Watts GF, Barrett PH, Martins IJ, James AP, Mamo JC et al. Effect of atorvastatin on chylomicron remnant metabolism in visceral obesity: a study employing a new stable isotope breath test. J Lipid Res. 2002;43(5):706-12.

[34]. Tonu S, Dewan Z, Akhter N, Banerjee S. A comparative study of atorvastatin and rosuvastatin on lipid lowering efficacy in hyperlipidemic patients. Bangabandhu Sheikh Mujib Medical University Journal. 2018;11(1):17-0. doi:10.3329/bsmmuj.v11i1.35244.

[35]. Hadjadj S, Paul JL, Meyer L, Durlach V, Verges B, Ziegler O et al. Delayed changes in postprandial lipid in young normolipidemic men after a nocturnal vitamin A oral fat load test. J Nutr. 1999;129(9):1649-55. doi:10.1093/jn/129.9.1649.

[36]. Karpe F, Bell M, Bjorkegren J, Hamsten A. Quantification of postprandial triglyceride-rich lipoproteins in healthy men by retinyl ester labeling and simultaneous measurement of apolipoproteins B-48 and B-100. Arterioscler Thromb Vasc Biol. 1995;15(2):199-207.

[37]. Guerci B, Paul JL, Hadjadj S, Durlach V, Verges B, Attia N et al. Analysis of the postprandial lipid metabolism: use of a 3-point test. Diabetes Metab. 2001;27(4 Pt 1):449-57.

[38]. Atar A, Atar I, Gülmez Ö, Ertan Ç, Özgül AS, Yücel M et al. Postprandial triglyceride levels in patients with or without metabolic syndrome and their relationship with coronary artery disease. Turk Kardiyoloji Dernegi Arsivi. 2007;35:482-8.

[39]. Meyer E, Westerveld HT, de Ruyter-Meijstek FC, van Greevenbroek MM, Rienks R, van Rijn HJ et al. Abnormal postprandial apolipoprotein B-48 and triglyceride responses in normolipidemic women with greater than 70% stenotic coronary artery disease: a case-control study. Atherosclerosis. 1996;124(2):221-35. doi:10.1016/0021-9150(96)05832-7.

[40]. Karpe F, Steiner G, Uffelman K, Olivecrona T, Hamsten A. Postprandial lipoproteins and progression of coronary atherosclerosis. Atherosclerosis. 1994;106(1):83-97. doi:10.1016/0021-9150(94)90085-x.

[41]. Boccalandro F, Farias J, Boccalandro C, Vaisman D. Frequency of postprandial lipemia after a first acute coronary event (unstable angina pectoris or non-ST-segment elevation acute myocardial infarction) and the effects of atenolol on the lipemia. Am J Cardiol. 2002;90(2):153-6. doi:10.1016/s0002-9149(02)02440-2.

[42]. Saito Y, Yamada N, Shirai K, Sasaki J, Ebihara Y, Yanase T et al. Effect of rosuvastatin 5-20mg on triglycerides and other lipid parameters in Japanese patients with hypertriglyceridemia. Atherosclerosis. 2007;194(2):505-11. doi:10.1016/j.atherosclerosis.2006.11.028.

[43]. Hunninghake DB, Stein EA, Bays HE, Rader DJ, Chitra RR, Simonson SG et al. Rosuvastatin improves the atherogenic and atheroprotective lipid profiles in patients with hypertriglyceridemia. Coron Artery Dis. 2004;15(2):115-23.

[44]. Schaefer EJ, McNamara JR, Tayler T, Daly JA, Gleason JA, Seman LJ et al. Effects of atorvastatin on fasting and postprandial lipoprotein subclasses in coronary heart disease patients versus control subjects. Am J Cardiol. 2002;90(7):689-96. doi:10.1016/s0002-9149(02)02591-2.

[45]. Wedel H, McMurray JJ, Lindberg M, Wikstrand J, Cleland JG, Cornel JH et al. Predictors of fatal and non-fatal outcomes in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA): incremental value of apolipoprotein A-1, high-sensitivity C-reactive peptide and N-terminal pro B-type natriuretic peptide. Eur J Heart Fail. 2009;11(3):281-91. doi:10.1093/eurjhf/hfn046.

[46]. Pilote L, Dasgupta K, Guru V, Humphries KH, McGrath J, Norris C et al. A comprehensive view

of sex-specific issues related to cardiovascular disease. Cmaj. 2007;176(6):S1-44. doi:10.1503/cmaj.051455.

[47]. Regitz-Zagrosek V, Lehmkuhl E, Mahmoodzadeh S. Gender aspects of the role of the metabolic syndrome as a risk factor for cardiovascular disease. Gend Med. 2007;4 Suppl B:S162-77.

[48]. LaRosa JC. Women, lipoproteins, and cardiovascular disease risk. Int J Fertil. 1992;37 Suppl 2:63-71.

[49]. Nasermoaddeli A, Sekine M, Kagamimori S. Gender differences in associations of C-reactive protein with atherosclerotic risk factors and psychosocial characteristics in Japanese civil servants. Psychosom Med. 2006;68(1):58-63. doi:10.1097/01.psy.0000195882.00407.05.

[50]. Karlson BW, Palmer MK, Nicholls SJ, Barter PJ, Lundman P. Effects of age, gender and statin dose on lipid levels: Results from the VOYAGER meta-analysis database. Atherosclerosis. 2017;265:54-9. doi:10.1016/j.atherosclerosis.2017.08.014.

[51]. Pyorala K, Ballantyne CM, Gumbiner B, Lee MW, Shah A, Davies MJ et al. Reduction of cardiovascular events by simvastatin in nondiabetic coronary heart disease patients with and without the metabolic syndrome: subgroup analyses of the Scandinavian Simvastatin Survival Study (4S). Diabetes Care. 2004;27(7):1735-40. doi:10.2337/diacare.27.7.1735.

[52]. Deedwania PC, Hunninghake DB, Bays HE, Jones PH, Cain VA, Blasetto JW. Effects of rosuvastatin, atorvastatin, simvastatin, and pravastatin on atherogenic dyslipidemia in patients with characteristics of the metabolic syndrome. Am J Cardiol. 2005;95(3):360-6. doi:10.1016/j.amjcard.2004.09.034.

[53]. Sandfort V, Lai S, Ahlman MA, Mallek M, Liu S, Sibley CT et al. Obesity Is Associated With Progression of Atherosclerosis During Statin Treatment. J Am Heart Assoc. 2016;5(7):e003621. doi:10.1161/JAHA.116.003621.

[54]. Sindhu S, Singh HK, Salman MT, Fatima J, Verma VK. Effects of atorvastatin and rosuvastatin on high-sensitivity C-reactive protein and lipid profile in obese type 2 diabetes mellitus patients. J Pharmacol Pharmacother. 2011;2(4):261-5. doi:10.4103/0976-500X.85954.