■ Sun-056 ■

Combined use of rosuvastatin and ezetimibe improves hepatic steatosis in patients with dyslipidemia

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Background/Aims: Rosuvastatin plus ezetimibe are beneficial for the management of dyslipidemia. We investigated whether rosuvastatin plus ezetimibe improves hepatic steatosis (HS) in patients with dyslipidemia. **Methods:** Between January and August 2018, 114 patients with dyslipidemia treated for 6 months with rosuvastatin plus ezetimibe were analyzed in this retrospective cohort study. The degree of HS was assessed using the hepatic steatosis index (HSI). HS improvement and presence of fatty liver were defined as a ≥5% reduction in HSI score and HSI ≥36, respectively. **Results:** The mean age of the study population (50 males and 64 females; 49 non-diabetic and 65 diabetic) was 57.4 years. At baseline, the mean body mass index total cholesterol level, low-density lipoprotein (LDL) cholesterol level, high-density lipoprotein (HDL) cholesterol level, triglyceride level, and HSI were 25.1 kg/m², 207.4 mg/dL, 126.1 mg/dL, 52.9 mg/dL, 146.4 mg/dL, and 36.1, respectively. During the 6-month treatment, HS burden was constant (mean HSI=36.3 and 36.4 at 3 and 6 months, respectively). On multivariate analyses, ultrasonographic fatty liver and HSI ≥ 36 were selected as independent predictors of HS improvement. However, when 53 (46.5%) patients with fatty liver (HSI≥36) were selected, HS burden was significantly improved (mean HSI=40.8, 39.3, and 39.7 at baseline, 3 months, and 6 months, respectively). **Conclusions:** The use of rosuvastatin plus ezetimibe for the management of dyslipidemia did not improve HS burden in all patients with dyslipidemia, but it improved HS burden in the subgroup with fatty liver.

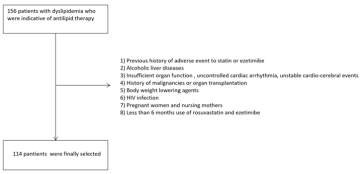

Figure 1. Flowchart of how the study population was selected.

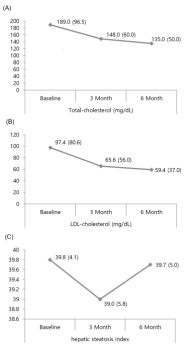

Figure 2. Changes in lipid profiles and hepatic steatosis index (HSI) during the 6 months of treatment. Total cholesterol (A), low-density lipoprotein cholesterol (LDL-C) (B), and HSI (C) significantly decreased at 6 months in the subgroups with HSI ≥ 36. Values are presented as median (interquartile range).

Table 1. Baseline characteristics of the study population (n=114).

Variables	All	Non-diabetes (n=49, 43.0%)	Diabetes (n=65, 57.0%)	*P* value
Demographic variables				
Age, years	57.4 ± 11.0	55.1 ± 12.3	59.0 ± 11.3	0.079
Male gender	50 (43.9)	24 (49.0)	26 (40.0)	0.351
Body mass index, kg/m²	25.1 ± 3.2	24.1 ± 3.1	25.9 ± 3.3	0.004
Diabetes	65 (57.0)	-	65 (100)	-
Hypertension	66 (57.9)	25 (50.9)	41 (66.2)	0.040
Viral hepatitis	17 (14.9)	8 (16.3)	9 (13.8)	0.715
Ultrasonographic fatty liver	58 (57.8)	9 (26.4)	9 (13.8)	0.762
Laboratory variables				
Platelet count, 10⁴/L	245.0 ± 70.0	240.4 ± 70.8	245.5 ± 70.5	0.778
Creatinine kinase, IU/L	128.0 ± 102.0	137.7 ± 89.0	121.7 ± 106.2	0.409
Alanine aminotransferase, IU/L	28.0 ± 25.9	31.2 ± 33.8	27.0 ± 18.7	0.390
Aspartate aminotransferase, IU/L	27.2 ± 12.6	27.0 ± 16.1	25.4 ± 8.8	0.101
Alkaline phosphatase, IU/L	82.1 ± 47.8	80.0 ± 55.0	76.2 ± 32.3	0.082
Total bilirubin, mg/dL	0.8 ± 0.4	0.8 ± 0.5	0.8 ± 0.2	0.240
Serum albumin, g/dL	4.1 ± 0.4	4.1 ± 0.4	4.0 ± 0.3	0.621
Serum creatinine, mg/dL	1.0 ± 1.1	1.0 ± 1.5	1.0 ± 1.7	0.525
Total cholesterol, mg/dL	207.4 ± 62.8	233.3 ± 60.4	187.0 ± 55.2	<0.001
LDL-cholesterol, mg/dL	126.1 ± 55.7	148.0 ± 57.9	109.0 ± 46.7	<0.001
HDL-cholesterol, mg/dL	52.9 ± 16.0	58.5 ± 18.1	49.0 ± 12.9	0.002
Triglyceride, mg/dL	146.4 ± 67.0	145.8 ± 67.2	146.8 ± 68.5	0.941
*HbA1c, mmol/mol	-	-	7.4 ± 1.5	-
*Fasting insulin, pIU/mL	-	-	8.2 ± 5.8	-
Prothrombin time, INR	0.97 ± 0.07	0.96 ± 0.06	0.98 ± 0.09	0.464
*HOMA-IR	-	-	2.9 ± 1.8	-
Hepatic steatosis index	36.1 ± 5.7	31.0 ± 5.4	37.8 ± 5.4	<0.001

Variables are expressed as mean ± SD or n (%).
*HbA1c, fasting insulin, and HOMA-IR are available in diabetic patients.
LDL, low-density lipoprotein; HDL, high-density lipoprotein; INR, international normalized ratio; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 2. Changes in laboratory profiles during the treatment period.

Variables	Baseline	At 3 months	At 6 months	*P* value[12]	*P* value[13]
Creatinine kinase, IU/L	128.0 ± 148.2	143.7 ± 114.7	135.2 ± 113.3	0.731	0.510
Fasting sugar, mg/dL	124.2 ± 55.3	120.0 ± 42.8	118.2 ± 36.7	0.471	0.230
Alanine aminotransferase, IU/L	28.8 ± 25.9	30.5 ± 23.7	31.0 ± 21.7	0.710	0.413
Aspartate aminotransferase, IU/L	27.2 ± 12.6	27.1 ± 15.4	26.7 ± 11.2	0.097	0.173
Total bilirubin, mg/dL	0.8 ± 0.4	0.7 ± 0.3	0.8 ± 0.4	0.094	0.482
Serum albumin, g/dL	4.1 ± 0.4	4.1 ± 0.4	4.0 ± 0.3	0.871	0.241
Serum creatinine, mg/dL	1.0 ± 1.2	1.0 ± 1.5	1.0 ± 1.7	0.588	0.470
Total cholesterol, mg/dL	207.4 ± 62.8	191.6 ± 57.9	190.3 ± 47.6	<0.001	<0.001
LDL-cholesterol, mg/dL	126.1 ± 55.7	74.5 ± 45.5	69.9 ± 36.7	<0.001	<0.001
HDL-cholesterol, mg/dL	52.9 ± 16.0	51.8 ± 18.4	52.4 ± 17.3	0.891	0.951
Triglyceride, mg/dL	146.4 ± 67.0	141.2 ± 70.3	132.6 ± 77.0	0.216	0.049
Prothrombin time, INR	0.97 ± 0.07	0.98 ± 0.07	0.98 ± 0.06	0.766	0.643
Hepatic steatosis index	36.1 ± 5.7	36.3 ± 5.0	36.4 ± 5.4	0.651	0.417

Variables are expressed as mean ± SD or n(%).
LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 3. Changes in laboratory profile during the treatment period in the subgroup with fatty liver by hepatic steatosis index (≥36 (n=53).

Variables	Baseline	At 3 months	At 6 months	*P* value[12]	*P* value[13]
Creatinine kinase, IU/L	128.0 ± 102.0	137.7 ± 89.0	131.7 ± 156.2	0.600	0.705
Fasting sugar, mg/dL	137.7 ± 94.7	131.1 ± 59.1	126.6 ± 48.9	0.461	0.216
Alanine aminotransferase, IU/L	30.0 ± 32.8	30.1 ± 17.2	31.0 ± 17.7	0.630	0.339
Aspartate aminotransferase, IU/L	26.3 ± 12.8	26.1 ± 18.4	27.4 ± 11.9	0.970	0.400
Total bilirubin, mg/dL	0.8 ± 0.4	0.7 ± 0.4	0.8 ± 0.3	0.902	0.302
Serum albumin, g/dL	4.1 ± 0.4	4.1 ± 0.4	4.0 ± 0.3	0.871	0.241
Serum creatinine, mg/dL	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.595	0.375
Total cholesterol, mg/dL	189.7 ± 60.5	170.0 ± 49.1	145.6 ± 47.8	<0.001	<0.001
LDL-cholesterol, mg/dL	108.5 ± 55.1	71.0 ± 39.7	48.6 ± 33.8	<0.001	<0.001
HDL-cholesterol, mg/dL	47.2 ± 12.0	46.3 ± 12.9	46.4 ± 11.1	0.379	0.291
Triglyceride, mg/dL	172.3 ± 85.5	162.9 ± 86.0	170.0 ± 88.2	0.520	0.600
Prothrombin time, INR	0.98 ± 0.06	1.00 ± 0.09	0.96 ± 0.03	0.890	0.590
Hepatic steatosis index	40.8 ± 4.1	39.3 ± 4.2	39.7 ± 5.0	0.004	0.046

Variables are expressed as mean ± SD or n(%).
LDL, low-density lipoprotein; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 4. Binary logistic regression to identify predictors of hepatic steatosis index improvement at 6 months.

Variables	Univariate	Multivariate		
	P value	OR	95% CI	*P* value
Demographic variables				
Age, years	0.235	-	-	-
Male gender	0.976	-	-	-
Body mass index, kg/m²	0.148	-	-	-
Diabetes	0.141	-	-	-
Hypertension	0.461	-	-	-
Ultrasonographic fatty liver	0.009	3.212	1.041-9.913	0.042
Laboratory variables				
Creatinine kinase, IU/L	0.071	-	-	-
Fasting sugar, mg/dL	0.181	-	-	-
Alanine aminotransferase, IU/L	0.003			
Aspartate aminotransferase, IU/L	0.075	-	-	-
Alkaline phosphatase, IU/L	0.770	-	-	-
Total bilirubin, mg/dL	0.257	-	-	-
Serum albumin, g/dL	0.621	-	-	-
Serum creatinine, mg/dL	0.202	-	-	-
Total cholesterol, mg/dL	0.585	-	-	-
LDL-cholesterol, mg/dL	0.893	-	-	-
HDL-cholesterol, mg/dL	0.736	-	-	-
Triglyceride, mg/dL	0.751	-	-	-
Prothrombin time, INR	0.227	-	-	-
HSI ≥ 36	0.006	3.501	1.220-10.001	0.019

HSI, hepatic steatosis index; OR, odds ratio; CI, confidence interval; LDL, low-density lipoprotein; HDL, high-density lipoprotein; INR, international normalized ratio.