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Research Article

Head to Head Comparison of Efficacy and Safety of Atorvastatin and Rosuvastatin

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Abstract

Background: Statins are the first-line anti-lipemic pharmacotherapy, having been shown to reduce both low-density lipoprotein cholesterol levels and cardiovascular events. Different statins demonstrate therapeutic equivalence in reducing total and LDL cholesterol

Objective: Analyzing high-intensity statin therapy with atorvastatin and rosuvastatin to define therapeutic equivalence.

Methods: Prospective, open-label, interventional, single-center study comparing four high-intensity treatment regimens: 40/80 mg atorvastatin and 20/40 mg rosuvastatin. Data was collected from patients records and blood sampling at entry and after six months, for: cholesterol (C), HDL-C, LDL-C, triglycerides, Apolipoprotein (Apo) A1 and Apo B, fasting blood glucose, myoglobin, creatine phosphokinase, aspartate and alanine aminotransferase, in order to measure lipid-lowering effects and potential side-effects. Statistical analysis: Chi2 test, t-test, ANOVA, Bonferroni analysis of variance, paired samples t-test and non-parametric tests. Significance determined at a level of < 0.05.

Results: 154 patients aged 60.5 ± 9.7y., 80 males/74 females were enrolled in the study. Mean LP values at study entry: C-6.31 mmol/L, LDL-C-4.41 mmol/L, HDL-C-1.13 mmol/L, TG-2.53 mmol/L, ApoA1-1.44 mg/L and ApoB-1.02 mg/L. Mean changes for 40/80 mg atorvastatin and 20/40 mg rosuvastatin were as follows: total C lowering: 22, 30, 29 and 40%; LDL-C: 30, 34, 49 and 51% and ApoB: 17, 8, 21 and 21%, respectively. Increase of HDL-C: 13, 22, 31 and 41%; and ApoA1: 6, 7, 16 and 19%, respectively.

Conclusion: Rosuvastatin is more effective than atorvastatin in total cholesterol lowering in 1:4 ratio. The effectiveness, regarding LDL-C and HDL-C, demonstrates linear progression, with rosuvastatin being more effective, compared to atorvastatin, at any dose. The effects on ApoA1, ApoB and TG were persistent across both dose-regiments, as opposite to atorvastatin. No major side-effects were observed.

Keywords: *Atorvastatin; Rosuvastatin; Hyperlipidemia; Lipoproteins; Prevention; Adverse Effects; Cholesterol, Dose-Regimens*

Abbreviations

ASCVD: Atherosclerotic Cardiovascular Disease; LDL-C: Low-Density Lipoprotein Cholesterol; MVE: Major Vascular Events; C: Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; TG: Triglycerides; Apo A1: Apolipoprotein A1; Apo B: Apolipoprotein; FBG: Fasting Blood Glucose; CPK: Creatine Phosphokinase; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ULN: Upper Limit of Normal; DAPT: Dual Antiplatelet Therapy; HMG-CoA: 3-Hydroxy-3-Methylglutaryl Coenzyme A; RCTs: Randomized Clinical Trials

Introduction

Dyslipidemia is one of the major risk factors for atherosclerotic cardiovascular disease (ASCVD), and statins are the treatment of choice for hyperlipidemia and ASCVD risk-reduction. In addition to their lipid-lowering effects, they significantly reduce ASCVD through their pleiotropic effects: antioxidant, anti-inflammatory and antithrombotic.

The Atherosclerosis Risk in Communities (ARIC) study, performed on 13,342 individuals, provided evidence that protection against ASCVD happens in a graded fashion with low-density lipoprotein cholesterol (LDL-C) levels [1]. The Cholesterol Treatment Trialists' (CTT) Collaboration meta-analyses detected about 25 000 major vascular events (MVE) (composite of coronary deaths or non-fatal myocardial infarctions, strokes of any type, and coronary revascularisation procedures). Comparing routine versus no routine statin treatment, there was a 20% proportional reduction in the MVE rate per mmol/L LDL-C reduction. Regarding the comparison of more versus less intensive statin regimens, the average 0.5 mmol/L further LDL-C reduction lead to an additional 15% proportional reduction in the MVE rate. By combining the findings from the two previously mentioned sets of trials, it can be concluded that a LDL-C concentration reduction by 2 mmol/L reduces MVE risk by about 45% [2,3].

Different statins have different potencies, with the newer agents (e.g. atorvastatin and rosuvastatin) able to produce larger reductions in LDL-C per mg of drug, compared to the older agents (e.g. simvastatin and pravastatin). Each dose doubling leads to an additional reduction of about 6 percentage points in LDL-C (e.g. 43% vs 49% reductions with atorvastatin 20 mg vs 40 mg daily), leading to an equivalent ASCVD risk-reduction [1].

The American College of Cardiology/American Heart Association 2013 Blood Cholesterol Guideline gives recommendations regarding statin therapy in terms of ASCVD prevention and risk reduction.

- In patients with clinically established ASCVD: high-intensity statin treatment (atorvastatin 40- 80 mg or rosuvastatin 20 - 40 mg daily) is recommended in patients ≤ 75 years; moderate-intensity statins (atorvastatin 10- 20 mg, or rosuvastatin 5 - 10 mg daily) in patients > 75 years;
- In patients with LDL-C levels ≥ 4.92 mmol/L: high-intensity statin treatment is recommended; moderate-intensity statins are considered if the patient is not a candidate for high-intensity statin treatment;
- In patients with diabetes, age 40-75 years (LDL-C levels of 1.8 - 4.9 mmol/L): moderate-intensity statin treatment is recom mended; high-intensity statin treatment is to be considered in patients with an estimated ASCVD risk ≥ 7.5%;
- In patients aged 40-75 years, with an estimated 10-year ASCVD risk ≥ 7.5%: moderate- to high-intensity statin treatment is recommended [4].

The statins demonstrate differences in terms of pharmacokinetic and pharmacodynamic properties that translates into clinical efficacy and side effects differences. Atorvastatin and rosuvastatin are the most commonly used statins in the clinical practice [5-7].

The motivation for our study was to address the question of performance capacity of the two first-line statins, atorva- and rosuvastatin, in high-intensity dose regiments, in terms of lipid-lowering efficacy and safety in the everyday settings in a mixed population, in primary and secondary prevention, different ages and both genders.

Materials and Methods

Study protocol

Designed as a prospective, open-label, interventional, single-center study, in which two comparators (atorvastatin and rosuvastatin) in four high-intensity treatment regiments were analyzed. The study was approved by the Institutional etical board, and statin naïve patients who gave their written informed consent, with an indication for statin treatment, were included.

Analyzed Variables

We analyzed: age, gender, risk factors for ASCVD, co-morbidities, EURO SCORE risk (for patients without confirmed CVD: http://www.heartscore.org), co-medications, lipoprotein panel: cholesterol (C), high-density (HDL-C), low-density (LDL-C), triglicerides (TG), Apolipoproteins (Apo) A1, and Apo B, fasting blood glucosae (FBG), markers of myocite injury: myoglobin and creatine phosphokinase (CPK), and markers of hepatic injury: aspartate and alanine aminotransferase (AST and ALT).

Two statins in four dose-regimens were comparatively analyzed:

- Group 1 - Atorvastatin 40 mg,
- Group 2 - Atorvastatin 80 mg;

- Group 3 - Rosuvastatin 20 mg, and
- Group 4 - Rosuvastatin 40 mg.

Methods

Data was collected from patients records, clinical examination and blood sampling, with samples collected at the study entry and after six months of treatment.

The major exclusion criteria were: hepatic enzymes (AST, ALT) ≥ 2 times above the upper limit of normal (ULN), active liver disease or jaundice; patients with a CPK value ≥ 3 times above the ULN, calculated creatinine clearance <30 mL/min, pregnancy and lactation, and simultaneous receivement of CYP3A4 inhibitors.

There were no drop-outs during the treatment period. Patients adherence to the therapy was monitored by close follow-up of the patients with schedualed once/twice monthly phone or office visits.

Statistic analysis

Data analysis was performed with the statistical program SPSS 19.0. Descriptive as numbers, percentages and means with standard deviations (SDs) were used. For comparative statistic, Chi2 test, t-test, one-way ANOVA, Bonferroni analysis of variance, paired samples t-test were used for pre-post treatment comparison, non-parametric tests (Mann-Whitney U, Kolmogorov-Smirnov, Kruskal-Wallis) for comparison of small or uneven groups, and variables that deviated from the normal distribution were used. Significance was determined at a level of < 0.05.

Results

We analyzed 154 patients with ASCVD or high and very high-risk profile, at mean age 60.5 ± 9.7 years, equally distributed across both genders, with males being younger in comparison to females 59.1 ± 9.9 vs 62.0 ± 9.3 (p = 0,064/ non-parametric 0.072). We observed a unimodal distribution, negatively skewed (-.641). The female group was skewed less negatively -.345 in comparison to the male -.962 (Figure 1), which correlates with the afore-mentioned age difference.

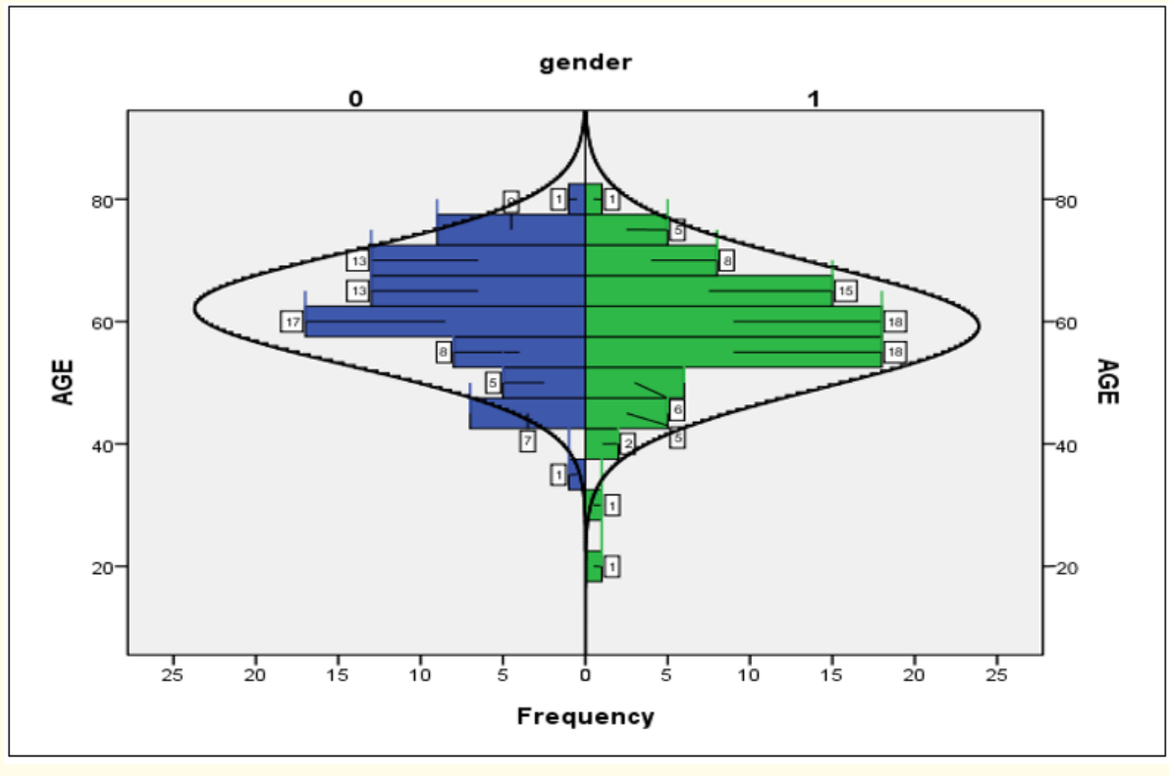

Figure 1: *Distribution of patients by gender and age.*

Abbreviations: 0 for female; 1 for male.

Patients were burdened with CVD risk factors: 72% hypertension, 85% overweight and/or obesity, 60% known untreated hyperlipidemia, 25% diabetes, 31% had ASCVD. Patients were severely co-medicated: 78% were receiving RAAS inhibitor, 85% aspirin, and nearly 11% were on dual antiplatelet therapy (DAPT). However, statistically significant inter-group difference was observed only for HLP and ASCVD presence, otherwise all treatment groups were with a similar risk profile (Table 1).

Statin treatment regiment	**Total 154 (100%)**	**Atorvastatin 85 (55.2%) 66 (42.8%) 21 (13.6%)**		**Rosuvastatin 69 (44.8%) 49 (31.8%) 18 (11.8%)**		**sig[a]**
Variable		**Group 1**	**Group 3**	**Group 3**	**Group 4**	**0.000**
Age	60.5 ± 9.7	62.1 ± 9.0	57.3 ± 7.4	60.1 ± 11.7	59.3 ± 8.0	ns
Age > 65y	49 (31.8%)	24 (15.6%)	3 (1.9%)	17 (11.1%)	5 (3.2%)	ns
Gender total	154 (100)	66 (42.9%)	21 (13.6%)	49 (31.8%)	18 (11.7%)	
male	80 (51,9%)	34 (22.1%)	15 (9.7%)	21 (13.6%)	10 (6.5%)	ns
female	74 (48,1%)	32 (20.8%)	6 (3.9%)	28 (18.2%)	8 (5.2%)	
BMI	28.4 ± 3.6	28.1 ± 3.5	29.4 ± 3.4	28.5 ± 4.2	27.8 ± 2.6	ns
Overweigh/Obesity (BMI ≥ 25)	117 (84.8%)	51 (37%)	17 (12.3%)	35 (25.4%)	14 (10.1%)	ns
Alcohol consumption (moderate)	11 (7.1%)	6 (3.9%)	1 (0.6%)	2 (1.3%)	2 (1.3%)	ns
Smoking	18 (11.7%)	11 (7.1%)	3 (1.9%)	4 (2.6%)	0	ns
Diabetes mellitus	39 (25.3%)	16 (10.4%)	4 (2.6%)	13 (8.4%)	6 (3.9%)	ns
Arterial hypertension	111 (72.1%)	49 (31.8%)	13 (8.4%)	35 (22.73%)	14 (9.1%)	ns
Hyperlipidemia	92 (59.7%)	45 (29.2%)	7 (4.5%)	30 (19.5%)	10 (6.5%)	0.042
Coronary Artery Disease	48 (31.2%)	21 (13.6%)	14 (9.1%)	9 (5.8%)	4 (2.6%)	0.001
Euro SCORE risk (mean)	7.0 ± 3.9	6.1 ± 2.3	7.5 ± 4.8	7.2 ± 4.4	7.9 ± 2.1	ns
EURO SCORE risk	111 (72.1%)	30 (19.5%)	32 (20.8%)	25 (16.2%)	24 (15.6%)	ns
• Intermediate (1 - 5)	21 (13.7%)	8 (5.2%)	7 (4.5%)	3 (1.9%)	3 (1.9%)	
• High (6 - 10)	47 (30.5%)	12 (7.8%)	11 (7.1%)	12 (7.8%)	12 (7.8%)	
• Very high (≥ 10)	43 (27.9%)	10 (6.5%)	14 (9.1%)	10 (6.5%)	9 (5.8%)	
Co-medications						
• RAAS inhibitors	121 (78.6%)	51 (33.1%)	12 (7.8%)	43 (27.9%)	15 (9.7%)	0.037
• Diuretics	57 (37%)	22 (14.3%)	8 (5.2%)	19 (12.3%)	8 (5.2%)	ns
• Beta blockers	82 (53.2%)	41 (26.6%)	10 (6.5%)	20 (13%)	11 (7.1%)	ns
• Ca-channel blockers	24 (15.9%)	8 (5.2%)	4 (2.6%)	7 (4.5%)	5 (3.2%)	ns
Antithrombotic						
• ASA	131 (85.1%)	58 (37.7%)	12 (7.8%)	44 (24.6%)	17 (11%)	0.014
• DAPT	17 (11%)	5 (3.2%)	8 (5.2%)	3 (1.7%)	1 (0.6%)	
• VKA	5 (3.2%)	2 (1.1%)	1 (0.6%)	2 (1.1%)	0	

Table 1: *Baseline characteristic of the study population.*

Abbreviations: ALT: Alanine Aminotransferase; Apo: Apolipoprotein; AST: Aspartate Aminotransferase; ASA: Aspirin; BMI: Body Mass Index; CPK: Creatine Phosphokinase; DAPT: Dual Antiplatelet Therapy; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; RAAS: Renin-Angiotensin-Aldosterone System; TG: Triglyceride.

a Only values with statistical significance ($p < 0.05$) are expressed as numbers.

Values are expressed as means with SDs: numbers and percentages.

Comparison was made between four dose-regiments, regarding their lipid-lowering efficacy (Table 2 and Figure 2) and safety (Table 4). Patients were nonequally distributed across treatment groups, groups 1 and 3 outweighed (74.7% of patients; $p < 0.000$). Furthermore, we compared their potency with respect to gender and age (Table 3). Patients from both genders were equally represented (59.9% males and 48.1% female, p = ns), while only one third of patients (31.8%) were at the age ≥ 65 years ($p < 0.000$).

Variable	Mean ± SD	Mean ± SD	Mean delta	sig[b]	Percentage change (%)
C mmol/L					
Group 1	6.17 ± 1.09	4.77 ± 1.03	-1.40	0.000	-22.70
Group 2	6.32 ± 1.45	4.41 ± 0.91	-1.90	0.000	-30.23
Group 3	6.26 ± 1.29	4.45 ± 0.79	-1.81	0.000	-28.91
Group 4	6.95 ± 1.39	4.12 ± 0.93	-2.83	0.000	-40.72
Total	6.31 ± 1.25	4.54 ± 0.95	-1.77	0.000	-28.05
[a]ANOVA sig /[g]Kruskal Wallis test [v]Bonferroni post hoc test	ns/ns	0.041/0.068 1 vs 4 0.047			
LDL-C mmol/L					
Group 1	4.13 ± 1.00	2.89 ± 0.11	-1.24	0.000	-30.03
Group 2	4.23 ± 1.40	2.77 ± 0.19	-1.46	0.000	-34.52
Group 3	4.74 ± 3.59	2.43 ± 0.11	-2.31	0.000	-49.41
Group 4	4.75 ± 1.29	2.31 ± 0.15	-2.44	0.000	-51.37
Total	4.41 ± 2.24	2.66 ± 0.84	-1.75	0.000	-39.68
[a]ANOVA sig /[g]Kruskal Wallis test [v]Bonferroni post hock test	ns/ns	0.007/0.024 1 vs 3 0.021 1 vs 4 0.044			
HDL-C mmol/L					
Group 1	1.16 ± 0.33	1.31 ± 0.04	+0.15	0.000	+12.93
Group 2	1.08 ± 0.24	1.32 ± 0.07	+0.24	0.000	+22.22
Group 3	1.11 ± 0.21	1.46 ± 0.07	+0.35	0.000	+31.53
Group 4	1.13 ± 0.14	1.59 ± 0.09	+0.46	0.000	+40.71
Total	1.13 ± 0.26	1.39 ± 0.33	+0.26	0.000	+23.00
[a]ANOVA sig/[g]Kruskal Wallis test [v]Bonferroni post hock test	ns/ns	0.004/0.021 1 vs3 0.075 1 vs 4 0.007 2 vs 4 0.056			
TG mmol/L					
Group 1	2.41 ± 1.19	1.62 ± 0.08	-0.79	0.000	-29.88
Group 2	2.75 ± 1.23	1.74 ± 0.14	-1.01	0.000	-34.73
Group 3	2.71 ± 1.77	1.59 ± 0.13	-1.13	0.000	-41.33
Group 4	2.25 ± 0.66	1.35 ± 0.11	-0.90	0.000	-40.00
Total	2.53 ± 1.37	1.59 ± 0.73	-0.94	0.000	-37.15
[a]ANOVA sig/[g]Kruskal Wallis test	ns	ns			
ApoA1 mg/L					
Group 1	1.46 ± 0.26	1.55 ± 0.24	+0.09	0.002	+6.16
Group 2	1.45 ± 0.30	1.56 ± 0.19	+0.11	ns	+7.59
Group 3	1.44 ± 0.23	1.68 ± 0.29	+0.14	0.000	+16.66
Group 4	1.38 ± 0.15	1.65 ± 0.19	+0.27	0.001	+19.56
Total	1.44 ± 0.24	1.61 ± 0.25	+0.17	0.000	+11.80
[a]ANOVA sig/[g]Kruskal Wallis test	ns	ns			
ApoB mg/L					
Group 1	1.00 ± 0.27	0.83 ± 0.28	-0.17	0.000	-17.00
Group 2	1.03 ± 0.39	0.94 ± 0.35	-0.90	ns	-8.74
Group 3	1.00 ± 0.24	0.79 ± 0.21	-0.21	0.000	-21.00
Group 4	1.09 ± 0.43	0.85 ± 0.41	-0.24	0.000	-21.02
Total	1.02 ± 0.30	0.83 ± 0.29	-0.19	0.000	-18.83
[a]ANOVA sig	ns	ns			

Table 2: *Comparative therapeutic efficacy of different dose-regiments of two comparators.*

Abbreviations: Apo: Apolipoprotein; C: Cholesterol; HDL-C: High Density Cholesterol; LDL-C: Low-Density Cholesterol; TG: Triglyceride.

Values are expressed as means with SDs, means with SDs of the change (delta) and percentage of change.

[a]ANOVA (one-way ANOVA) sig. [b]Paired samples t-test sig. [v]Bonferroni test of analyze of variance sig.[g]Kruskal Wallis test (non-parametric) sig.

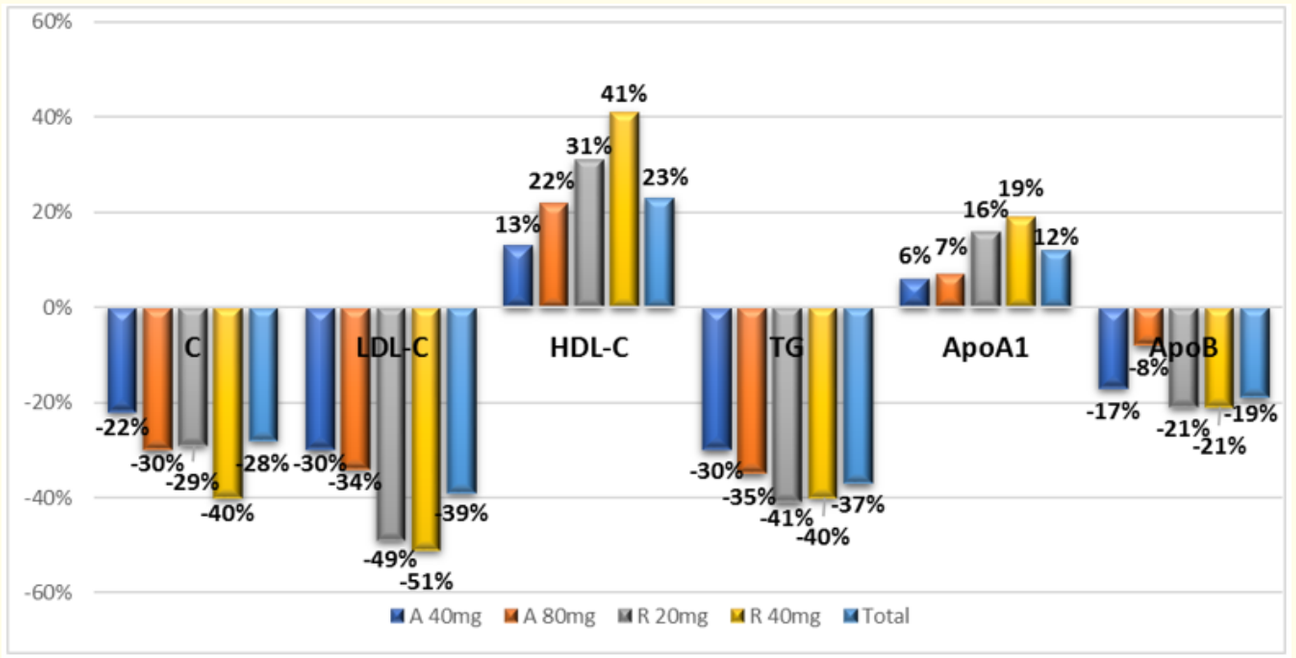

Figure 2: *Graphical presentation of therapeutic efficacy of different dose-regiments of two comparators.*

Abbreviations: *A: Atorvastatin; Apo: Apolipoprotein; C: Cholesterol; HDL: High-Density Lipoprotein; LHL: Low-Density Lipoprotein; R: Rosuvastatin.*

Therapeutic lipid-lowering efficacy

At the study entry there was no statistically significant difference between treatment groups in LP fractions. With respect to total C, 80 mg atorvastatin and 20 mg rosuvastatin demonstrated the same efficacy, with a mean reduction of 30 and 29% respectively (1:4 dose-ratio). Regarding the LDL-C lowering efficacy, a gradually increasing effect was observed with 30, 34, 49 and 51% reduction, respectively. HDL-C increasing was achieved as follows: 13, 22, 31 and 40% respectively, with rosuvastatin being more effective than atorvastatin in 1:3 and 1:2 ratio, in no-dose dependent manner. The beneficial effect on apoA1 and apoB was less prominent. The percent increase of ApoA1 was similar, 6-8% for atorvastatin, and 17-20% for rosuvastatin (1:3 dose-ratio). Same was for ApoB, where no significant inter-group differences in after-treatment mean values were observed, although rosuvastatin at any dose was more effective than atorvastatin. Considering TG, it seems that all doses of atorvastatin led to similar (around 30%), while all doses of rosuvastatin led to similar (around 40%) decrease (more than 1:2 dose-ratio) (Table 2).

No statistically significant gender differences existed in pretreatment LP values, while the only statistically significant difference between genders was observed as a function of the treatment in HDL-C levels, that were more increased in females (mean increase 0.27 vs 0.22; $p = 0.028$).

Patients at advanced age had lower levels of TG ($p = 0.006$), without significant differences, as compared to their younger peers in other LP fractions before treatment, and also as a result of the treatment the TG lowering effect was more pronounced in the same age group (-0.80 vs -1.03; $p = 0.025$). Moreover, when different treatment regiments were compared, in the group of patients on 20 mg rosuvastatin significantly higher pretreatment TG levels were observed in patients <65y, and the treatment effect was more pronounced (-1.29/ -0.8; p = 0,035/0.017) (Table 3).

Safety

The safety profile was evaluated through clinical signs and symptoms, by measuring biomarkers of hepatic and/or skeletal muscle injury, and fasting blood glycose (FBG) (Table 4). There were no treatment discontinuations or loss of follow-up, no major adverse effects, no muscle pain, nor significant increase of biomarkers of muscle or hepatic injury. Paired samples statistic demonstrated statistically significant difference in pre-post treatment levels of hepatic enzymes, but without clinical significance, and no single patient overcame the ULN. Also, no significant increase in FBG was observed after the six months-treatment (Table 4).

Dose regimen	Gender	Mean ± SD (before)	sig[a]	Mean ± SD (after)	sig[a]	Mean delta
Group 1						
C mmol/L	F/M	6.15 ± 1.25/6.19 ± 0.92	ns	4.69 ± 1.05/4.83 ± 1.02	ns	-1.46/-1.33
LDL-C mol/L	F/M	4.20 ± 0.16/4.06 ± 0.85	ns	2.88 ± 0.94/2.89 ± 0.85	ns	-1.32/-1.17
HDL-C mol/L	F/M	1.22 ± 0.29/1.12 ± 0.35	ns	1.37 ± 0.35/1.25 ± 0.29	ns	0.15/0.13
TG mmol/L	F/M	2.03 ± 0.71/2.77 ± 1.43	0.010/0.006	1.53 ± 0.55/1.71 ± 0.80	ns	-0.50/-1.06
ApoA1 mg/L	F/M	1.51 ± 0.26/1.42 ± 0.26	ns	1.61 ± 0.28/1.49 ± 0.19	ns	0.10/0.07
ApoB mg/L	F/M	0.98 ± 0.26/1.02 ± 0.28	ns	0.80 ± 0.26/0.85 ± 0.31	ns	-0.18/-0.17
Group 2						
C mmol/L	F/M	6.11 ± 1.10/6.40 ± 1.59	ns	4.47 ± 1.00/4.38 ± 0.91	ns	-1.64/-2.02
LDL-C mol/L	F/M	4.05 ± 1.02/4.30 ± 0.55	ns	2.81 ± 0.58/2.75 ± 0.98	ns	-1.24/-1.55
HDL-C mol/L	F/M	1.25 ± 0.32/1.02 ± 0.18	ns/0.044	1.42 ± 0.39/1.29 ± 0.29	ns	0.17/0.27
TG mmol/L	F/M	2.43 ± 0.87/2.87 ± 1.32	ns	1.69 ± 0.55/1.76 ± 0.67	ns	-0.74/-1.11
ApoA1 mg/L	F/M	1.71 ± 0.53/1.37 ± 0.17	ns	1.55 ± 0.37/1.56 ± 0.13	ns	-0.16/0.19
ApoB mg/L	F/M	1.16 ± 0.36/0.98 ± 0.40	ns	1.36 ± 0.36/0.81 ± 0.24	0.010/0.020	0.24/-0.17
Group 3						
C mmol/L	F/M	6.50 ± 0.98/5.93 ± 1.59	ns	4,54 ± 0.71/4,33 ± 0.89	ns	-1.96/-1.60
LDL-C mol/L	F/M	4.51 ± 0.98/5.05 ± 1.43	ns	2.51 ± 0.73/2.33 ± 0.75	ns	-2.00/-2.72
HDL-C mol/L	F/M	1.05 ± 0.17/1.18 ± 0.23	0.028/ns	1.47 ± 0.31/1.44 ± 0.29	ns	0.42/0.26
TG mmol/L	F/M	2.83 ± 1.98/2.56 ± 1.49	ns	1.68 ± 0.99/1.45 ± 0.68	ns	-1.15/-1.22
ApoA1 mg/L	F/M	1.42 ± 0.17/1.46 ± 0.29	ns	1.67 ± 0.21/1.69 ± 0.38	ns	0.90/0.23
ApoB mg/L	F/M	1.07 ± 0.21/0.91 ± 0.26	0.047/ns	0.82 ± 0.18/0.76 ± 0.25	ns	-0.25/-0.15
Group 4						
C mmol/L	F/M	6.78 ± 0.81/7.08 ± 1.76	ns	3.67 ± 0.69/4.47 ± 0.98	0.071	-3.11/-2.61
LDL-C mol/L	F/M	4.31 ± 0.76/5.10 ± 1.53	ns	2.07 ± 0.65/2.50 ± 0.63	ns	-2.24/-2.60
HDL-C mol/L	F/M	1.20 ± 0.15/1.07 ± 0.10	ns/0.049	1.80 ± 0.34/1.42 ± 0.29	0.025/0.034	0.60/0.35
TG mmol/L	F/M	1.89 ± 0.50/2.53 ± 0.66	0.040/0.034	1.07 ± 0.26/1.58 ± 0.45	0.014/0.021	-0.82/-0.95
ApoA1 mg/L	F/M	1.29 ± 0.18/1.43 ± 0.11	ns	1.73 ± 0.22/1.60 ± 0.16	ns	0.44/0.17
ApoB mg/L	F/M	0.63 ± 0.18/0.99 ± 0.56	ns	0.82 ± 0.18/0.76 ± 0.46	ns	-0.19/-0.23
Total						
C mmol/L	F/M	6.35 ± 1.08/6.27 ± 1.35	ns	4.51 ± 0.93/4.57 ± 0.97	ns	-1.65/-1.60
LDL-C mol/L	F/M	4.32 ± 1.04/4.49 ± 2.95	ns	2.64 ± 0.84/2.67 ± 0.85	ns	-1.60/-1.81
HDL-C mol/L	F/M	1.15 ± 0.25/1.11 ± 0.27	ns	1.46 ± 0.36/1.33 ± 0.30	0.017/0.028	+0.27/+0.22
TG mmol/L	F/M	2.35 ± 1.38/2.70 ± 1.34	ns	1.55 ± 0.75/1.64 ± 0.71	ns	-0.80/-1.03
ApoA1 mg/L	F/M	1.46 ± 0.25/1.42 ± 0.24	ns	1.64 ± 0.25/1.58 ± 0.26	ns	+0.18/+0.16
ApoB mg/L	F/M	1.02 ± 0.24/1.01 ± 0.35	ns	0.83 ± 0.27/ 0.84 ± 0.31	ns	-0.18/-0.16
Dose regimen	**Age**	**mean ± SD (before)**	**sig[a]**	**mean ± SD (after)**	**sig[a]**	**Mean delta**
Group 1						
C mmol/L	< 65/≥ 65	6.37 ± 1.00/5.83 ± 1.16	ns	4.92 ± 1.04/4.49 ± 0.97	ns	-1.45/-1.34
LDL-C mol/L	< 65/≥ 65	4.24 ± 1.02/3.92 ± 0.96	ns	2.99 ± 0.90/2.71 ± 0.86	ns	-1.25/-1.21
HDL-C mol/L	< 65/≥ 65	1.15 ± 0.31/1.19 ± 0.35		1.31 ± 0.32/1.29 ± 0.34	ns	+0.16/+0.10
TG mmol/L	< 65/≥ 65	2.62 ± 1.37/2.05 ± 0.65	ns	1.72 ± 0.78/1.43 ± 0.45	ns	-0.90/-0.62
ApoA1 mg/L	< 65/≥ 65	1.49 ± 0.26/1.41 ± 0.26	ns	1.57 ± 0.25/1.51 ± 0.24	ns	+0.08/+0.10
ApoB mg/L	< 65/≥ 65	1.04 ± 0.24/0.93 ± 0.31	ns	0.86 ± 0.29/0.77 ± 0.26	ns	-0.18/-0.16

Group 2						
C mmol/L	< 65/≥ 65	6.22 ± 1.52/6.88 ± 0.95	ns	4.29 ± 0.88/5.07 ± 1.00	ns	-1.95/-1.81
LDL-C mol/L	< 65/≥ 65	4.14 ± 1.48/4.77 ± 0.58	ns	2.74 ± 0.93/2.97 ± 0.51	ns	-1.40/-1.80
HDL-C mol/L	< 65/≥ 65	1.06 ± 0.22/1.23 ± 0.40	ns	1.32 ± 0.32/1.37 ± 0.38	ns	+0.26/+0.14
TG mmol/L	< 65/≥ 65	2.76 ± 1.32/2.67 ± 0.49	ns	1.70 ± 0.67/1.97 ± 0.16	ns	-1.06/-0.70
ApoA1 mg/L	< 65/≥ 65	1.39 ± 1.29/2.10 ± 0.11	0.017/ ns	1.57 ± 0.40/1.38 ± 0.36	ns	+0.18/-0.72
ApoB mg/L	< 65/≥ 65	1.01 ± 0.40/1.20 ± 0.38	ns	0.93 ± 0.37/0.99 ± 0.35	ns	-0.08/-0.21
Group 3						
C mmol/L	< 65/≥ 65	6.45 ± 1.43/5.91 ± 0.95	0.037/ 0.022	4.63 ± 0.87/4.13 ± 0.47	ns	-2.18/-1.78
LDL-C mol/L	< 65/≥ 65	4.39 ± 1.35/5.41 ± 1.87	ns	2.57 ± 0.78/2.18 ± 0.58	ns	-1.82/-3.23
HDL-C mol/L	< 65/≥ 65	1.12 ± 0.22/1.08 ± 0.18	ns	1.47 ± 0.27/1.43 ± 0.35	ns	+0.35/+0.35
TG mmol/L	< 65/≥ 65	3.07 ± 1.88/2.05 ± 1.36	0.054/0.004	1.78 ± 0.98/1.23 ± 0.49	0,035/0.017	-1.29/-0.82
ApoA1 mg/L	< 65/≥ 65	1.46 ± 0.25/1.29 ± 0.19	ns	1.73 ± 0.32/1.58 ± 0.23	ns	+0.27/-0.29
ApoB mg/L	< 65/≥ 65	1.02 ± 0.24/0.95 ± 0.25	ns	0.83 ± 0.21/0.72 ± 0.19	ns	-0.19/-0.23
Group 4						
C mmol/L	< 65/≥ 65	6.87 ± 1.64/7.14 ± 0.26	ns	3.91 ± 0.89/4.64 ± 0.93	ns	-2.96/-2.50
LDL-C mol/L	< 65/≥ 65	4.65 ± 1.51/5.02 ± 0.27	ns	2.21 ± 0.67/2.58 ± 0.63	ns	-2.44/-2.44
HDL-C mol/L	< 65/≥ 65	1.14 ± 0.15/1.10 ± 0.12	ns	1.60 ± 0.42/1.56 ± 0.22	ns	+0.46/+0.46
TG mmol/L	< 65/≥ 65	2.29 ± 0.73/2.13 ± 0.49	ns	1.30 ± 0.48/1.49 ± 0.37	ns	-0.99/-0.64
ApoA1 mg/L	< 65/≥ 65	1.37 ± 0.16/1.40 ± 0.17	ns	1.66 ± 0.17/1.63 ± 0.26	ns	+0.29/+0.23
ApoB mg/L	< 65/≥ 65	1.11 ± 0.46/1.02 ± 0.36	ns	0.84 ± 0.45/0.88 ± 0.33	ns	-0.37/-0.14
Total						
C mmol/L	< 65/≥ 65	6.43 ± 1.31/6.06 ± 1.09	ns	4.59 ± 0.99/4.42 ± 0.84	ns	-1.65/-1.60
LDL-C mol/L	< 65/≥ 65	4.32 ± 1.26/4.60 ± 3.52	ns	2.72 ± 0.87/2.53 ± 0.76	ns	-1.60/-1.81
HDL-C mol/L	< 65/≥ 65	1.12 ± 0.25/1.15 ± 0.29	ns	1.39 ± 0.33/1.38 ± 0.34	ns	+0.27/+0.22
TG mmol/L	< 65/≥ 65	2.74 ± 1.48/2.09 ± 0.94	0.006/0.005	1.68 ± 0.81/1.40 ± 0.47	0.025/0.050	-0.80/-1.03
ApoA1 mg/L	< 65/≥ 65	1.45 ± 0.24/1.43 ± 0.25	ns	1.64 ± 0.26/1.55 ± 0.23	ns	+0.18/+0.16
ApoB mg/L	< 65/≥ 65	1.04 ± 0.31/0.96 ± 0.28	ns	0.86 ± 0.30/0.77 ± 0.24	ns	-0.18/-0.16

Table 3. *Comparative therapeutic efficacy of a different dos-regiments of two comparators, as a function of gender and age group*

Abbreviations*: Apo: Apolipoprotein; C: Cholesterol; HDL-C: High-Density Cholesterol; LDL-C: Low-Density Cholesterol; TG: Triglyceride. Values are expressed as means with SDs, mean with SDs of the change (delta), and as percentages.*

[a]: Independent sample t-test sig, and Mann Whitney U test (non-parametric) are displayed (the second in the row being non-parametric test value, only one value is displayed if both test are ns).

Discussion

Clinical significance of lipid-modification

3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitors, known as statins, are effective drugs in the reduction of LDL-C and total cholesterol. LDL-C lowering, particularly with statins, results with ASCVD reduction in primary and secondary prevention, in a linear manner with the reduction amount. Studies have demonstrated that reduction of LDL-C for approximately 1 mmol/L is associated with 10% risk-reduction. Additionally, to their beneficial C and LDL-C lowering effects, statins improve endothelial function, enhance stability of atherosclerotic plaques, and inhibit inflammatory as well as thrombogenic responses [8]. Seven statins are approved for clinical use, with a three-part chemical structure: an analogue of the target enzyme substrate, HMG-CoA; a complex hydrophobic ring structure involved in binding of the statin to the reductase; side groups on the rings defining the drug solubility, and therefore many of their pharmacokinetic properties. Atorvastatin, fluvastatin, lovastatin, pitavastatin and simvastatin are relatively lipophilic compounds, while pravastatin and rosuvastatin are more hydrophilic, owing to their structure [9].

The most widely used are atorvastatin and rosuvastatin. Atorvastatin is a potent (lipophilic) statin that lowers LDL- C by nearly 30 - 50%, with a log-linear dose-response relationship [10]. Rosuvastatin is a methane-sulphonamide pyrimidine and N-methane sulfonyl

Parameter	Treatment group	Mean ± SD before treatment	Mean ± SD after treatment	sig[a]	sig[b]
Myoglobin	Group 1	35.44 ± 17.13	36.73 ± 14.93	ns	ns
(ng/ml)	Group 2	47.49 ± 13.95	45.13 ± 15.55		
	Group 3	46.79 ± 26.10	45.19 ± 22.11		
	Group 4	40.86 ± 19,17	39.12 ± 18,11		
	Total	53.23 ± 22.13	44.69 ± 40.91		
ANOVA sig		ns	ns		
CPK (IU)	Group 1	96.17 ± 47.19	102.06 ± 63.49	ns	ns
	Group 2	87.17 ± 34.24	97.17 ± 29.24		
	Group 3	108.54 ± 34.45	100.50 ± 44.50		
	Group 4	99.22 ± 19.11	97.17 ± 29.24		
	Total	93.66 ± 73.28	87.17 ± 35.22		
ANOVA sig		ns	ns		
AST (IU)	Group 1	23.24 ± 8.86	23.98 ± 6.97	ns	0.026
	Group 2	26.21 ± 15.68	27.42 ± 13.15		
	Group 3	21.89 ± 7.65	24.29 ± 9.13		
	Group 4	21.50 ± 5.18	23.00 ± 4.80		
	Total	23.00 ± 9.43	24.45 ± 8.62		
ANOVA sig		ns	ns		
ALT (IU)	Group 1	25.35 ± 10.80	28.10 ± 11.58	ns	0.005
	Group 2	33.53 ± 23.15	36.11 ± 25.12		
	Group 3	23.29 ± 10.95	24.53 ± 8.19		
	Group 4	22.31 ± 6.49	24.80 ± 8.05		
	Total	25.45 ± 13.23	27.67 ± 13.54		
ANOVA sig		0.025	0.012		
Post hoc sig[v]		3 vs 4 0.030	3 vs 4 0.011		
FBG mmol/L	Group 1	6.43 ± 1.59	6.44 ± 1.53	ns	ns
	Group 2	6.65 ± 2.23	6.58 ± 1.60		
	Group 3	6.83 ± 2.18	6.79 ± 1.59		
	Group 4	6.20 ± 0.65	6.26 ± 0.78		
	Total	6.57 ± 1.83	6.55 ± 1.83		
ANOVA sig		ns	ns		

Table 4: *Safety profile of a different dos-regiments of two comparators.*

Abbreviations*: AST: Lactate Dehydrogenase; ALT, Alanine Aminotransferase; CPK: Creatine Phosphokinase; FBG: Fasting Blood Glycose.*

Values are expressed as means with SDs.

[a]*ANOVA sig and Kruskal Wallis test (non-parametric), (columns).*

[b]*Paired samples t-test (rows).*

[v]*Bonferroni test of analyze of variance sig.*

pyrrole-substituted 3, 5-dihydroxy-heptenoate. Although the characteristic statin pharmacophore remains similar to other statins, the addition of a polar methane-sulphonamide group provides low lipophilicity (high hydrophilicity) and enhanced interaction with HMG-CoA reductase, improving its' binding affinity to the enzyme, highest among statins. Due to its' low lipophilicity and, therefore, low penetration into extrahepatic tissues, the incidence of muscle side effects is lower [11]. Rosuvastatin reduces LDL-C more aggressively, with a better attenuation of inflammation and oxidative stress parameters, compared with atorvastatin. There are data confirming its' ability to increase ApoA1 (known to act as a lipoprotein structure stabilizer, having anti-inflammatory and antioxidant properties) [12].

Lipid-lowering efficacy

Primary treatment targets for statins are total and LDL-C. Many differently designed randomized clinical trials (RCTs), meta-analysis, systematic reviews, and a small-scale study demonstrate lipid-lowering advantages of rosuva- versus atorvastatin. A meta-analysis of randomized controlled trials on over 20,000 patients published by Wlodarczyk in 2008, summarized 28 comparisons of 1:1, 20 comparisons of 1:2, and 6 comparisons of 1:4 dose ratios of rosuvastatin and atorvastatin. Rosuvastatin was found to be more efficacious than atorvastatin in 1:1 and 1:2 dose-ratio, and similarly efficacious in 1:4 dose-ratio, in the same time with no significant differences in side effects at any dose-ratio [13]. The Beners' study, on high-risk diabetic patients, reported dose equivalence of 20 mg rosuvastatin to higher than 40 mg atorvastatin [7].

In the systematic review published in the Cochran database in 2014, comparison of different dose-regiments of rosuvastatin demonstrated dose-dependent linear reduction of LDL-C and non-HDL-C between 46 - 55%, and an increase of HDL-C of 7%, without the same dose-dependent effect. In comparison with the most widely used atorvastatin, rosuvastatin demonstrates three-fold greater potency [14]. Several RCTs: Measuring effective reductions in cholesterol using rosuvastatin therapy (MERCURY) trial, Statin Therapies for Elevated Lipid Levels compared Across doses to Rosuvastatin (STELLAR) trial, and Prospective study to evaluate the Use of Low doses of the Statins Atorvastatin and Rosuvastatin (PULSAR), were designed to compare rosuvastatin (10, 20, 40, or 80 mg), atorvastatin (10, 20, 40, or 80 mg), pravastatin (10, 20, or 40 mg), and simvastatin (10, 20, 40, or 80 mg), across dose ranges, in their LDL-C lowering potency [15-17]. In the STELLAR trial, rosuvastatin, across all doses, was the most effective at reducing LDL-C in comparison to all other statins. Both, The MERCURY and STELLAR studies reported that 10 mg rosuvastatin is effective in LDL-C goal achievement in hypercholesterolemic and high-risk diabetic patients [15,16]. Bener reported that rosuvastatin at the dose of 10 mg was more effective in reducing LDL-C (28.6%) than atorvastatin and pravastatin at doses of 40 mg, (15.9% and 11.59% respectively; $p < 0.001$) [7]. Arshad demonstrated 10% greater reduction of LDL-C with rosuvastatin over atorvastatin in the Pakistani population (Asians are known to share genetic differences resulting in pharmacokinetic and pharmacodynamic influences on the statins, with possible differences in clinical efficacy and safety) [5]. In 2013 Naci published a systematic review of 181 placebo-controlled and active-comparator trials including 256 827 individuals, studding the dose-comparative effects of different statins on the lipid-lowering effects. Dose-dependent total and LDL-C reduction properties of statins were reported, the most consistent one achieved with atorvastatin at >40 mg, rosuvastatin at >10 mg, and simvastatin at > 40 mg as dose equivalents [18]. Kuznecova demonstrated dose equivalence of 10 mg rosuvastatin with 40 mg atorvastatin in terms of LDL-C reduction (-44.0% versus -50%) in a small-scale study in patients with acute coronary syndrome [19]. Baseline LDL-C and the choice and dose of a statin drug are important for LDL-C goal achievement. The present analysis may allow prediction of individual patient response to different statins at different doses. In the VOYAGER meta-analysis, Karlson and co-authors determined doses of rosuvastatin, atorvastatin and simvastatin that induce equal reductions in LDL-C and non-HDL-C and concluded that each rosuvastatin dose is equivalent to doses 3- 3.5 times higher for atorvastatin and 7 - 8 times higher for simvastatin [20].

Our data was consistent with the aforementioned studies in favor of higher lipid-lowering potency of rosuvastatin. With respect to total cholesterol, 20 mg rosuvastatin was equipotent to 80 mg atorvastatin (30 and 29% reduction respectively), 1:4 ratio was observed. However, with respect to LDL-C lowering, rosuvastatin (20/40 mg) was more effective, leading to 49 and 51% mean reduction respectively, as compared with 30 and 34% mean reduction achieved with 40/80 mg atorvastatin ($p < 0.000$).

Considering effects on HDL-C, there are conflicting data from the literature. Some studies reported mild reduction of HDL-C with statins, like the studies by Benet, Arshad, and Barakat (performed on diabetic cohort of Qatari patients) [7,5,21]. Different statins vary in their HDL-C raising ability, which is also highly dependable of baseline HDL-C and TG levels, and closely correlated with the study population structure, mostly the presence of diabetes. In the presence of diabetes, HDL-C response to statins is blunted [5]. However, even in diabetic patients, rosuvastatin demonstrated advantages over atorvastatin. In the PULSAR Study (50% patients with DM and 50% with metabolic syndrome), 10 mg rosuvastatin resulted with a 6,5% mean HDL-C increase, while in the STELLAR Study 40 mg rosuvastatin resulted with 10,5% mean HDL-C increase [16,17]. Weng., *et al*., described around a 10% mean increase of HDL-C with rosuvastatin, and 5-6% with atorvastatin, in no dose-dependent manner [22].

We are reporting 31 and 40% increase of HDL-C for 20 and 40 mg rosuvastatin respectively, with a less prominent effect with 40 and 80 mg atorvastatin (12 and 22% increase), with 1:3 and 1:2 dose-ratios observed. Our data differs significantly from the literature data, and we can only speculate in an attempt to explain these results with the risk profile of the study population: only 30% older population, 25% diabetic patients, only Caucasians, good patients' adherence to the treatment regimen, etc.

With respect to TG modification, Wang, in his meta-analysis, reports similar TG reduction effect at equivalent doses (1:2 ratio), to the maximum of 30% [22]. In the PULSAR study 10mg rosuvastatin produced a similar reduction as 20 mg atorvastatin, 18 vs 19%, (dose ratio 1:2) [17], and in The STELLAR study the mean percentage reduction was 24 and 26% respectively for rosuvastatin, 26 and 28% for atorvastatin in high-dose regiments (1:2 ratio) [16]. However, in specific subset of diabetic patients targeting TG and HDL-C is a significant challenge. The results of the use of rosuvastatin versus atorvastatin in type 2 diabetes mellitus (URANUS) study, the superior benefit of aggressive lipid-lowering therapy for high-risk patients using statins (SUBARU) study and a study to verify the efficacy of rosuvastatin for hypercholesterolemia (ASTRO-2), failed to demonstrate a difference in the TG lowering ability. In the studies of Bener and Baracat, the most pronounced reduction of TG levels (25.17%; $p < 0.001$) was achieved with 10 mg rosuvastatin, whereas 20 mg produced only 16% reduction, while percent of reduction with 10, 20 and 40 mg atorvastatin was 17, 16 and 18% respectively. High dose-regiments were not used in this study [7,21].

TG lowering potency for atorvastatin in our subjects was 30 and 35% across dose ranges, and 41 and 40% respectively for rosuvastatin. So, the demonstrated potency was higher for rosuvastatin in 1:2 dose-ratios.

Takagi's meta-analysis of RCTs comparing these two statins in terms of improving Apo profiles (ApoA-I levels, ApoB levels, and ApoB/A-I ratios), demonstrated that rosuvastatin might increase ApoA-I at all dose-ratios, and decrease ApoB levels and ApoB/A-I ratios in the 1/1 and 1/2 dose-ratio versus atorvastatin. Only higher dose atorvastatin appeared to be more effective in ApoB (1/4 and 1/8 dose ratio) and Apo B/A-I ratios (1/8 dose ratio) decrease [23]. Non-inferiority of 20 mg rosuvastatin versus 80 mg atorvastatin in reducing Apo/ApoA-1 ratio was demonstrated in the CENTAURUS study [24].

We demonstrated better performance of rosuvastatin (16 and 19% increase) in comparison with atorvastatin (6 and 7% increase) for ApoA1, and (21 and 21% decrease) as compared to atorvastatin (17 and 8% decrease) for ApoB. Lack of consistency of the treatment effect across dose-regiments of atorvastatin was evident.

Dose considerations are recommended in the elderly patients with respect to their co-morbidities, co-medications profile, while in the same time targeting lipid-lowering and ASCVD risk reduction. In the study of Chen., *et al*, low- to moderate-dose regiments of atorvastatin and rosuvastatin were found to be effective in lipid-lowering of LDL-C and non-HDL-C in older patients. Moderate-intensity atorvastatin led to a more pronounced increase of HDL-C ($p < 0.049$), ApoA1 ($p < 0.050$), and decrease of ApoB ($p < 0.022$) levels in our elderly cohort of patients [25].

In our study 30% of patients were at the age ≥ 65 years, treated with high-dose regiments. With respect to the lipoprotein profile, the only statistically significant difference was observed for TG ($p = 0.006$), being lower in older patients, but with a more pronounced response to the treatment (0.025). No differences in other LP lowering treatment effects were observed in comparison to their younger pares.

With respect to gender differences, LDL-C levels are typically lower in women until menopause, when levels increase (3 mmol/L to 3.7 mmol/L). HDL-C levels are approximately 0.3 mmol/L higher in women than in men, while elevated TGs may be a more significant risk factor in women, compared to men. In the STELAR study, in the sub-group analysis of female subjects' dose-related decrease of LDL-C levels ranged from 21% to 57% ($p < 0.002$ rosuvastatin vs. all comparators), with similar pattern for high-intensity regiments: 53% and 57% reduction with 20/40 mg rosuvastatin, and 47% and 51% with 40/80 mg atorvastatin [6]. Rosuvastatin 20 mg produced statistically greater LDL-C reductions, compared with atorvastatin 20 mg and 40 mg ($p < 0.002$ for both comparisons) [26].

No gender difference in LP profile was observed in our subjects. However, treatment effect on HDL-C was more pronounced in females ($p = 0.017$), more specific in the 40 mg rosuvastatin treatment group ($p = 0.025$), as opposite to TG where males responded better ($p = 0.014$), more importantly because in this treatment arm TGs before the treatment were higher as compared to females ($p = 0.040$).

Safety

The adverse effects of statins are dose, type and therapy duration dependent. Arshad reported a very low rate of side effects, with tolerability resulting with no treatment withdrawals. Body aches and pains were reported, but no laboratory evidence of myositis or liver function deterioration [5]. When analyzed by gender, statins were proven to be well tolerated in women and older population also [6].

Even high-intensity statin regiments were demonstrated to be safe and free of major side-effects, as demonstrated in the LUNAR study [27-29].

The unfavorable effect of statins on glucose metabolism and the risk of diabetes is widely elaborated. A potentially preferable effect of the hydrophilic statins: pravastatin, rosuvastatin and pitavastatin is described, as compared to lipophilic statins, including atorvastatin and simvastatin [30].

In our study both comparators in all dose-regiments were safe enough with no significant side effects reported.

Limitations of the Study

This study has several limitations that may influence the results. For a more powered analysis we need a larger sample size and balanced groups in the number of subjects enrolled in each treatment group. In terms of therapeutic efficacy, we did not analyze biomarkers of inflammation, and for the safety analysis we did not perform a measurement of HbA1c. In terms of gender presentation, females were well represented in our study, but patients at advanced age were underrepresented, so it may influence the results. We would like to underline that this was not designed as a clinical outcome trial.

Conclusion and Relevance

According to the results it seems that rosuvastatin is more effective than atorvastatin in total cholesterol lowering in a 1:4 ratio. The effectiveness, with respect to LDL-C, demonstrates linear progression, with rosuvastatin being more effective, as compared to atorvastatin at any dose, while with respect to HDL-C, rosuvastatin demonstrated to be more effective, but in nonlinear manner. The effects on ApoA1 and Apo and TG were persistent across both dose-regiments, as opposite to atorvastatin. No major side effects were observed.

The major clinical relevance of our findings lies in the fact that it seems that 20 mg rosuvastatin can be prescribed with the same, if no better, therapeutic efficacy that can be provided with 80 mg atorvastatin in total and LDL-C lowering treatment.

Conflict of Interest Statement

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Volume 7 Issue 1 January 2019