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Research Article

Efficacy and cost-effectiveness of generic rosuvastatin compared with the brand in patients with stable coronary artery disease

Rehab ElHiny[1], Amr S. Amin[2], Hend M. Moness[3], Sahar B. Hassan[4], Mohamed M. Abdel-Latif[4], Hatem A. Sarhan[5]

[1]Clinical Pharmacy Department, Faculty of Pharmacy, Minia University, Minia, Egypt; [2]Cardiology Department, Faculty of Medicine, Minia University, Minia, Egypt; [3]Clinical Pathology Department, Faculty of Medicine, Minia University, Minia, Egypt; [4]Clinical Pharmacy Department, Faculty of Pharmacy, Assiut University, Assiut, Egypt; [5]Department of Pharmaceutics, Faculty of Pharmacy, Minia University, Minia, Egypt

ABSTRACT

Background: Statins are the mainstay drugs that are widely used to lower lipid levels among patients with cardiovascular diseases. Cost-effectiveness is questionable among branded and generic market products.

Aim: The study aims to evaluate the efficacy and cost-effectiveness of the branded and generic rosuvastatin products available in the Egyptian market.

Patients and methods: Ninety patients with stable coronary artery disease (low to intermediate risk zero according to treadmill duke score risk stratification) were divided (1:1:1) to either receiving the brand-name rosuvastatin or one of the two generic rosuvastatin medicines. LDL-C, total cholesterol, triglycerides, HDL-C levels and liver enzymes were tested at the enrolment and after 6 months. Major Adverse Cardiovascular Events (MACE) were monitored during the follow-up period. Average cost-effectiveness ratio and Incremental Cost-Effectiveness Ratio (ICER) were estimated for branded versus each generic. The output of ICERs was the percentage reduction in LDL-C.

Results: After 6 months of statin treatment initiation, all lipid parameters were reduced significantly compared with baseline levels. There was a significant difference in LDL-C reduction between the branded and generic groups ($P<0.01$) but insignificant differences were reported in triglycerides levels ($P=0.731$) and HDL ($P=0.167$) among the three groups. All three statins were safe concerning liver enzymes and no observed major adverse cardiovascular events. Incremental cost-effectiveness ratios of the branded versus each generic were 157.7 and 62 Egyptian pounds per additional 1% decrease in LDL-C.

Conclusion: Despite the higher lipid-lowering efficacy of the branded rosuvastatin, the lower cost of generic medicines can be beneficial in certain patients.

Keywords: Rosuvastatin; Generics; Safety; Efficacy; Cost-effectiveness; Egypt.

INTRODUCTION

Coronary Artery Disease (CAD) is deemed the major leading reason for death globally [1]. More than 500,000 deaths from CAD is accounted for the united states [2]. The WHO report published in 2017 has shown that deaths resulted from coronary heart disease in Egypt reached 126,312 or 24.58% of total deaths. Also, it has been demonstrated that cardiovascular diseases are the main cause of death in Egypt as it accounts for 46% of total deaths [3].

Patients with Stable Coronary Artery Disease (SCAD) are at high risk of recurrent cardiovascular events [4]. Atorvastatin, pravastatin, simvastatin, and rosuvastatin are the available statins, of which the superiority of rosuvastatin in LDL-C, total cholesterol reduction and reaching LDL-C goals has been proven [5,6]. Rosuvastatin is also the cost-effective choice compared to simvastatin, atorvastatin, pitavastatin and pravastatin in patients with high, moderate and low-risk patients [7-9]. Generic statins had been approved depending on their bioequivalence with branded drugs [10].

Correspondence to: Hatem Sarhan, Department of Pharmaceutics, Faculty of Pharmacy, Minia University, Minia, Egypt, Tel: +0020862369075; E-mail: Ha_sarhan@yahoo.com

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The current study aims to evaluate the efficacy and the cost-effectiveness of the brand-name and generic rosuvastatin in patients with stable coronary artery disease (low-intermediate risk ≥ zero according to treadmill duke score risk stratification of cardiovascular events.

MATERIALS AND METHODS

Study patients

This pilot study was approved by the Commission on the Ethics of Scientific Research, Faculty of Pharmacy, Minia University. Out of 600 patients who underwent treadmill stress test to rule out CAD at the cardiology department, Minia University Hospital from September 2018 to December 2019, 90 Egyptian male and female subjects aged 40-71 years were eligible for the study. The inclusion criteria involved patients with SCAD [low to intermediate risk ≥ zero according to treadmill duke score risk stratification [11] who had at least moderate physical fitness, no disabling comorbidities, no resting ECG changes and did not receive any lipid-lowering agents before enrolment. Informed consent was received from all the patients before the enrolments, then they were subjected to follow-up period for 6 months. Indication for coronary angiography, history of coronary intervention or coronary bypass graft surgery, hepatic dysfunction, moderate to severe renal impairment with creatinine clearance 60 ml/min using Cockcroft-Gault formula were the exclusion criteria.

Study design

Ninety patients were split into 30 patients in each group of the generic rosuvastatin; Novistoric 20 mg (group II), Epirovastin 20 mg (group III) and the brand-name rosuvastatin Crestor 20 mg (group I). All patients received 20 mg of each rosuvastatin once daily in the evening for 6 months.

Patients were subjected to

General and local cardiac examination: Full detailed clinical evaluation including full analysis of the chest pain, risk factors of CAD, history intervention or CABG and history of other system affection, general and local examination were done.

Transthoracic Echocardiogram: Transthoracic Echocardiogram examinations were performed by using general electric vivid 3 ultrasound. The measurements represented a mean of at least three consecutive cardiac cycles. Assessment of Left Ventricular Ejection Fraction (LVEF) was performed by M-mode method. Doppler and colour flow across the different valves were assessed.

Stress ECG (Treadmill Stress Test): Patients were subjected to exercise testing according to standard Bruce protocol; resting heart rate, blood pressure measurements and 12-lead ECG were examined before exercise. All subjects performed exercise testing till the endpoints of severe fatigue, limiting angina, serious arrhythmia or ST-segment deviation (depression or elevation). Exercise time in (min) was defined as the duration of exercise for patients performing this protocol [11].

Duke treadmill score equation: The equation used for the Duke Treadmill Score (DTS) calculation is DTS = exercise time – (5X ST. deviation) – (4X exercise angina) where zero indicates no angina during exercise, 1 is non-limiting angina, 2 indicates exercise limited angina. Score typically ranges from -25 to +15 these values were corresponding to low risk (with a score of ≥ 5), intermediate-risk (with a score ranging from +4 to -10) and high risk (with a score of ≤ -11) [12].

Lab Investigations: Fasting and 2-hour postprandial blood glucose, renal function, serum creatinine level, creatinine clearance (CrCl) (Cockcroft-Gault Formula), liver enzymes (Serum alanine aminotransferase (ALT) & Serum aspartate aminotransferase (AST), abdominal ultrasound were done.

Lipid Profile: Lipid profile; Total Cholesterol TC (mg/dl), Triglycerides TG (mg/dl), Low-Density Lipoprotein LDL-C (mg/dl) and High-Density Lipoprotein HDL-C (mg/dl). All parameters of liver function tests and lipid profile were done using a fully automated clinical chemistry auto-analyser system Kone Lab 60i (Thermo electron incorporation, Finland). LDL is evaluated by friedewald formula unless the triglycerides level was above 400 mg/dl [12].

Patients' Monitoring and Follow-Up

The study group participants were followed-up every month for six months in the out-patient cardiology department and were also interviewed weekly through telephone calls during the follow-up period. The follow-up evaluation included a medical history review concerning any major cardiovascular events (hospitalization by acute coronary syndrome either MI or unstable angina, Percutaneous Intervention (PCI), Coronary Artery Bypass Grafting (CABG), stroke or any other cause of mortality) and any other side effects (abdominal pain, headache, stomach ache, muscle pain and nausea). Physical examination included blood pressure and ECG was done besides assessment of any medical therapy updated.

Costs Analysis: Consistent with the analysis perspective, the direct medical costs of lipid-lowering therapy were included in the analysis. Six months total cost of each treatment was estimated based on the direct medical and non-medical cost incurred throughout the study. They have included the cost of each rosuvastatin product used by one patient and the estimated costs of outpatient clinic visits and laboratory monitoring per patient. The Average Cost-Effectiveness Ratio (ACER) was calculated by dividing the six months total cost of each treatment by the percentage reduction in total cholesterol and LDL-C for each patient. The ratio demonstrated the cost per 1% reduction in total cholesterol and LDL-C level. The output of the Incremental Cost-Effectiveness Ratio (ICER) was total cost and the average percentage change in LDL-C. The incremental cost-effectiveness ratios were calculated for brand-name versus each generic rosuvastatin.

The estimated costs in dollars are calculated depending on the average exchange rate in 2018-2019=17.3 Egyptian pounds.

Statistical Analysis: The collected data was revised, coded, tabulated and introduced. Data analysis was done using SPSS program (Statistical Package for Social Sciences) software version 25. Continuous variables are expressed as mean and standard deviation for normal distribution or as a median and interquartile range for skewed distribution. Categorical data are expressed as number and percentage. For continuous data One Way ANOVA test followed by Post Hoc test or Kruskal Wallis test followed by Mann Whitney test were used for comparison between groups. Paired Sample T-test or Wilcoxon Signed-Rank test was used for comparison between the two times within the same group.

RESULTS

Demographics and Baseline Characteristics

The present study included 90 patients. The demographic characteristics, risk factors and the anti-ischemic medications of the study groups were summarized in Table 1. There was no significant difference between the three study arms in baseline levels in both lipid parameters (total cholesterol, triglycerides, HDL and LDL) and liver enzymes (alanine aminotransferase and aspartate aminotransferase), as shown in Table 2.

Efficacy Analysis

Table 3 shows the percentage changes in lipid profile parameters including total cholesterol, triglycerides, HDL and LDL in each arm of the three study arms after 6 months of treatment. The lipid-lowering percentage was higher in the brand name Crestor 20 mg group when compared with two generic groups. The analysis revealed that there was a significant difference in the reducing percentage of LDL-C between the two generics rosuvastatin groups; group II and group III [P*=0.022] and between the two generics rosuvastatin (group II and group III) when compared with the brand name group I as well [P**=0.041] and [P***<0.001] respectively. The decrease in the percentage of triglycerides and the increase in the percentage of HDL-C were insignificantly different between the three groups (P=0.731) and (P=0.167) respectively.

Safety Analysis

Table 4 shows the percentage of increase in liver enzymes in the three study groups. The changes in the three study arms in both AST and ALT post-treatment were not clinically significant as they were within the normal ranges and did not indicate for either dose adjustment or treatment discontinuation.

Patients Monitoring and Follow-Up during the Study Period

No Major Adverse Cardiovascular Events (MACE) which were noted throughout the 6 months follow-up period.

Cost analysis

The total costs were 2254 Egyptian pounds for Crestor 20 mg/day, 849.6 Egyptian pounds for Novistoric 20 mg/day and 833.57 Egyptian pounds for Epirovastin 20 mg/day (Table 5).

The cost-effectiveness analysis revealed that Novistoric 20 mg/day has the least cost 28 Egyptian pounds per percentage point decrease in LDL-C followed by Epirovastin 20 mg/day as it costs 51 Egyptian pounds while the brand-name costs 57.5 Egyptian pounds (Table 6).

Crestor has incremental cost 1404 Egyptian pounds per patient with incremental effectiveness of 1% reduction in LDL-C, providing ICER of 157.79 Egyptian pounds per additional 1% reduction in LDL-C compared to Novistoric 20 mg. however, it has an incremental cost 1420.4 Egyptian pounds per patient with incremental effectiveness of 1% reduction in LDL-C, providing ICER of 62 Egyptian pounds per additional 1% reduction in LDL-C compared to Epirovastin 20 mg (Table 7).

Table 1: The demographic characteristics, CAD Risk factors and the anti-ischemic medications used among the studied groups.

Parameters		Group I Crestor 20 mg	Group II Novistoric 20 mg	Group III Epirovastin 20 mg	P-value
		N=30	N=30	N=30	
Age	Mean SD	(43-70) 56.7 ± 8.1	(41-71) 55.1 ± 8.5	(40-70) 54.3 ± 9.2	0.551
Sex	Male Female	17(56.7%) 13(43.3%)	20(66.7%) 10(33.3%)	16(53.3%) 14(46.7%)	0.551
HTN	No Yes	1(3.3%) 29(96.7%)	3(10%) 27(90%)	4(13.3%) 26(86.7%)	0.522
DM	No Yes	22(73.3%) 8(26.7%)	24(80%) 6(20%)	25(83.3%) 5(16.7%)	0.627
Smoking	No Yes	25(83.3%) 5(16.7%)	26(86.7%) 4(13.3%)	27(90%) 3(10%)	0.925
BMI	Range Mean ± SD	(24-43) 31.3 ± 5	(22.4-43) 32.2 ± 5.8	(24-44.5) 30.9 ± 5.4	0.638
Waist circumference	Range Mean ± SD	(86-120) 94.6 ± 7.9	(80-132) 99.1 ± 13	(70-124) 93 ± 10.4	0.076
Aspirinc	No Yes	0(0%) 30(100%)	0(0%) 30(100%)	0(0%) 30(100%)	-
Beta-blockers	No Yes	1(3.3%) 29(96.7%)	1(3.3%) 29(96.7%)	2(6.7%) 28(93.3%)	1
ACEI	No Yes	20(66.7%) 10(33.3%)	19(63.3%) 11(36.7%)	17(56.7%) 13(43.3%)	0.718
Trimetazidine	No Yes	27(90%) 3(10%)	27(90%) 3(10%)	25(83.3%) 5(16.7%)	0.780
Nicorandil	No Yes	30(100%) 0(0%)	29(96.7%) 1(3.3%)	29(96.7%) 1(3.3%)	1

HTN: Hypertension; DM: Diabetes Mellitus; BMI: Body Mass Index; ACEI: Angiotensin-Converting Enzyme Inhibitors.

Table 2: Baseline levels of lipid parameters and liver enzymes among the study groups.

Pretreatment		Group (I) Crestor 20 mg	Group(II) Novistoric 20 mg	Group(III) Epirovastin 20 mg	P-value
		N=30	N=30	N=30	
Total cholesterol	Range Mean ± SD	(168-281) 227.6 ± 31.7	(158-305) 217 ± 34.7	(163-275) 214.5 ± 33.6	0.273
Triglycerides	Range Mean ± SD	(75-308) 152.5 ± 52.5	(69-236) 135 ± 41.6	(60-228) 142.4 ± 51.3	0.384
HDL	Range Mean ± SD	(30-60) 42.33 ± 8.34	(30-58) 45.8 ± 7.88	(33-60) 45.83 ± 7.86	0.159
LDL	Range Mean ± SD	104-204) 154.8 ± 27.8	(111-229.2) 144.2 ± 30.5	(112-201) 140.4 ± 27.8	0.138
Aspartate aminotransferase	Median (IQR)	20 (16.5-24.8)	20.5 (17.8-30.3)	21.5 (17.5-27)	0.598
Alanine aminotransferase	Median (IQR)	19.5 (14.5-22)	19 (13.8-29.3)	17 (11.8-24)	0.412

HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; SD: Standard Deviation; (IQR): Interquartile Range.

Table 3: The percentage changes in lipid parameters after 6 months.

Parameters		Group I Crestor 20 mg	Group II Novistoric 20 mg	Group III Epirovastin 20 mg	P*	P**	P***
		N=30	N=30	N=30			
Total cholesterol, %	Median (IQR)	28.8 (25-31)	20 (8.3-30.8)	10.8 (9.4-17.6)	0.112	0.023	<0.001
Triglycerides,%	Median (IQR)	18.7 (15.4-20)	15 (4.3-30.3)	15 (5.1-32.8)	0.728	0.468	0.584
High-density lipoprotein (HDL), %	Median (IQR)	4.7 (0-10)	8.4 (0-14.3)	7.1 (3.2-12.9)	0.766	0.109	0.098
Low-density lipoprotein (LDL),%	Median (IQR)	39.2 (34.3-45)	30.3 (13.9-44.4)	16.3 (11.8-26.3)	0.022	0.041	<0.001

P*: P-value between groups (II & III); P**: P-value between groups (II & I); P***: P-value between groups (III & I).

Table 4: Percentage changes in aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Parameters		Group I Crestor 20mg	Group II Novistoric 20mg	Group III Epirovastin 20mg	P□	P□□	P□□□
		N=30	N =30	N=30			
AST,%	Median (IQR)	0 (0-0.8)	8.6 (0-18.5)	7.5 (0-15.4)	0.757	0.001	0.001
ALT,%	Median (IQR)	8.2 (0-13.6)	7.3 (0-29.8)	14 (7.9-30.4)	0.142	0.810	0.024

P*: P-value between groups (II and III); P**: P-value between groups (II & I); P***: P-value between groups (III & I), AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; (IQR): Interquartile Range

Table 4: Percentage changes in aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Type of cost	Crestor 20 mg, Cost	Novistoric 20 mg, cost	Epirovastin 20 mg, cost
Outpatient visit	10	10	10
Total visits/6 month	60	60	60
Laboratory investigations			
Total Cholesterol	20	20	20
Total cost (pre &post treatment)	40	40	40
LDL	20	20	20
Total cost (pre &post treatment)	40	40	40
Liver enzymes	80	80	80
Liver enzymes pre & post treatment	160	160	160
Drug cost/ 6months	1954	549.6	533.57
Total cost (Egyptian pounds)	2254	849.6	833.57
Total cost ($)	130	49	48

LDL: Low-Density Lipoprotein; $: Dollars

Table 6: Costs and average cost-effectiveness ratio (ACER) in terms of 1 % reduction in LDL-C and total cholesterol.

Intervention	Costs			Average effectiveness (% of LDL-C reduction after 6 months)	ACER (Egyptian pounds)	ACER ($)	Average effectiveness (%reduction of cholesterol after 6 months)	ACER (Egyptian pounds)	ACER ($)
	Costs for 6 months	Other costs	Total cost						
Crestor 20 mg	1954	300	2254	39.2 (34.3-45)	57.5 (50.1-65.8)	3.3 (2.9-3.8)	28.8 (25-31)	78.3 (73-90.2)	4.5 (4.2-5.2)
Novistoric 20 mg	549.6	300	849.6	30.3 (13.9-44.4)	28.1 (19.1-61)	1.6 (1.1-3.5)	20 (8.3-30.8)	43 (27.6-103)	2.5 (1.6-6)
Epirovastin 20 mg	533.57	300	833.57	16.3 (11.8-26.3)	51.1 (31.7-71)	2.9 (1.8-4.1)	10.8 (9.4-17.6)	77.2 (47.5-88.6)	4.5 (2.7-5.1)

ACER: Average Cost-Effectiveness Ratio; $: Dollar

Table 7: The incremental cost effectiveness (ICER) analysis.

Treatment	Total cost	Incremental effectiveness*	Incremental cost**	Incremental cost-effectiveness ratio***	Incremental Cost-effectiveness ratio***
Novistoric	849.6 Egyptian pounds	8.9	1404.4 Egyptian pounds	157.7 Egyptian pounds	9.1 $
Epirovastin	833.57 Egyptian pounds	22.9	1420.4 Egyptian pounds	62.02 Egyptian pounds	3.58 $

 Effectiveness of branded-Effectiveness of generic (branded is more effective than generic); **Cost of branded – Cost of generic; *** Cost per percentage reduction in LDL-C (Incremental cost effectiveness ratio = Incremental cost / incremental effectiveness).

DISCUSSION

Rosuvastatin has been proven to be the most effective statin in decreasing LDL-C level and frequently prescribed drug in clinical practice. It reduced LDL-C significantly higher than the other counterpart drugs according to STELLAR trial in addition to its beneficial effect in primary and secondary prevention [13-15]. In our experience the main reasons for interruption of statins are the lack of perception of the benefits of using statins within patients, the idea of life long treatment with statins is not welcomed by patients and the high price of statins especially the brand-name drug. Therefore, the financial affordability of generic statin becomes the only solution to these problems.

In the current study, LDL-C level was reduced by 16.3% (11.8-26.3) and 30.3% (13.9-44.4) in Epirovastin 20 mg and Novistoric 20 mg respectively, however, the reduction was by 39.2% (34.3-45) in Crestor 20 mg.

Rafeeq et al. have reported a reduction of 57.53% in the percentage of LDL-C from baseline [16]. Similarly, It has been reported that rosuvastatin 20 mg decrease LDL-C by 53% and 52% respectively [14,17]. The percentage of changes in lipid profile showed slight variation comparable to our findings. The variability explained by differences in the sampled population as Inter-individual variations resulting from genetic variability demonstrated by the effect of gene polymorphism in the pharmacokinetics of rosuvastatin and thus the lipid-lowering efficacy [18,19].

According to Bacquer et al. the difference in the baseline of LDL-C value contributed to the inter-individual variability in the LDL-C reduction response toward a fixed dose of statins treatment. As reported the LDL-C reduced by 31% in response to atorvastatin 40 mg and rosuvastatin 20 mg although the predicted reducing percentages were 48%-49% [20].

In this study, the change of triglycerides level among the three study arms was relatively comparable to the reported decreasing percentages in many studies. Schneck et al. demonstrated that rosuvastatin 20 mg reduced triglycerides by 18.4% [21]. Although, Ballantyne et al. have reported that the reduction was by 21.6% with the same dose after 16 weeks of treatment [22].

Regarding the difference in the efficacy of Crestor group when compared with other generic groups, there was a lack in the published data of comparative studies concerning the efficacy of generic rosuvastatin, especially in the Egyptian market. It has been reported that both generic rosuvastatin products showed high lipid-lowering efficacy and tolerability in high and very high-risk patients as for LDL reduction was 34.2% after 3 months with Roswera and 35% after 2 months with Superstate [23,24].

A statistically significant increase in both ALT and AST levels in the three study arms was reported, but these changes were not clinically significant as it did not reach 2 times the upper limit of the normal values in the three groups with no need for treatment discontinuation. Betto et al. have reported that generic rosuvastatin was a well-tolerated, although rosuvastatin therapy produced a statistically significant elevation in the levels of serum aminotransferases, the observed changes were not clinically significant since mean levels remained within the normal range [24]. These findings were supported by several trials in which no clinically significant elevation of levels occurred [25,26]. In this study, No major adverse cardiovascular events were observed during the 6 months treatment in the three study arms. In a study by Shaheen et al. assessing the difference in the economic impact of using generic rosuvastatin and brand-name rosuvastatin, they have reported that the cost of generic rosuvastatin was higher than the brand-name on concerning the cardiovascular events [27]. These findings reflected the superiority of the brand-name in reducing the cardiovascular event than the generic prescribing. In our study, a specific sector of low to intermediate-risk SCAD patients was included in evaluating the generic name medication but if we included intermediate to high and high-risk groups in our study they might lead to therapeutic failure of the generic groups in

preventing cardiovascular events compared with brand-name one in addition to short follow up period.

Olsson et al. reported that the reduction of 1% in LDL-C resulted in a decrease in the risk of major coronary events by 1.7% while the reduction of 1% in cholesterol resulted in a decrease in the incidence of major coronary events by 1.9% [28].

For time being, there is no study touched the point of the cost-effectiveness of generic rosuvastatin in the Egyptian market in patients with low to intermediate risk cardiovascular events according to Duke Score risk stratification ≥ zero.

For minimizing the cost-effectiveness ratio of statin therapy Morrison and Glassberg recommended using the least cost statin for patients with low risk of cardiovascular disease and patients with lower baseline LDL-C levels while the most effective statins for patients with high-risk CVD and patients with high baseline LDL-C level [29].

Although our study was small-sized with short follow-up period in evaluating lipid-lowering efficacy of generic rosuvastatin in preventing adverse cardiovascular effect in a specific sector of stable coronary artery disease, the results were promising for a better prospect for low to intermediate risk SCAD patients because of the price affordability of the generic rosuvastatin compared to the brand-name Crestor.

Further studies with a larger number of patients and long follow up period are needed for proper evaluation of the real benefits of generic rosuvastatin in adverse cardiovascular events prevention compared with brand type in low to intermediate risk and intermediate to high-risk CAD Patients in real-world practice. The Egyptian market contains several generic rosuvastatin products at different prices. We discussed two of them only which have the least cost. Further studies should be established to evaluate the economic impact of using generic medicines besides the clinical aspects.

CONCLUSION

Both the original and generic rosuvastatin were effective in lowering all lipid parameters in Egyptian patients with stable coronary artery disease. All three statins were safe concerning cardiac and liver functions. Despite the superiority of brand-name over Novistoric 20 mg and Epirovastin 20 mg in lipid-lowering efficacy, this was not reflected in the ability of generic rosuvastatin in preventing adverse cardiovascular events adding to their lower costs that helps in medication adherence for patients with low-intermediate risk SCAD.

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DISCLOSURE

The brand-name Crestor and the two generic Novistoric and Epirovastin drugs were not supplied from the manufacturers. None of the authors had any contractual agreement with the pharmaceutical companies. Funding is none declared.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Commission on the Ethics of Scientific Research, Faculty of Pharmacy, Minia University, approval reference number 35/2018.

REFERENCES

1. Cordero A, Galve E, Bertomeu-Martínez V, Bueno H, Fácila L, Alegría E, et al. Trends in risk factors and treatments in patients with stable ischemic heart disease seen at cardiology clinics between 2006 and 2014. Rev Esp Cardiol. 2016; 69 (4): 401-407.
2. Benner JS, Smith TW, Klingman D, Tierce JC, Mullins CD, Pethick N, et al. Cost-effectiveness of rosuvastatin compared with other statins from a managed care perspective. Value in Health. 2005; 8 (6): 618-628.
3. Turk-Adawi K, Sarrafzadegan N, Fadhil I, Taubert K, Sadeghi M, Wenger NK, et al. Cardiovascular disease in the Eastern Mediterranean region: Epidemiology and risk factor burden. Nature Reviews Cardiology. 2018; 15 (2): 106-119.
4. Leibowitz M, Karpati T, Cohen-Stavi CJ, Feldman BS, Hoshen M. Association between achieved low-density lipoprotein levels and major adverse cardiac events in patients with stable ischemic heart disease taking statin treatment. JAMA Internal Medicine.2016. 176 (8): 1105-1113.
5. McKenney JM, Jones PH, Adamczyk MA, Cain VA, Bryzinski BS. Comparison of the efficacy of rosuvastatin versus atorvastatin, simvastatin, and pravastatin in achieving lipid goals: Results from the STELLAR trial. Current medical research and opinion. 2003;19 (8): 689-698.
6. Paoletti R, Fahmy M, Mahla G, Mizan J, Southworth H. Rosuvastatin demonstrates greater reduction of low-density lipoprotein cholesterol compared with pravastatin and simvastatin in hypercholesterolaemic patients: A randomized, double-blind study. Journal of Cardiovascular Risk, 2001; 8 (6): 383-390.
7. Jeong Y, Kim H, Baik S, Kim T, Yang S. Analysis and comparison of the cost‐effectiveness of statins according to the baseline low‐density lipoprotein cholesterol level in Korea. Journal of Clinical Pharmacy and Therapeutics. 2017; 42 (3): 292-300.
8. Hirsch M, O'donnell J, Olsson A. Rosuvastatin is cost-effective compared with atorvastatin in reaching cholesterol goals. International journal of cardiology. 2005; 104 (3): 251-256.
9. Scharplatz M C, Ramanathan K, Frial T, Beamer B, Gandhi S. Cost-effectiveness analysis of rosuvastatin versus atorvastatin, simvastatin, and pravastatin from a Canadian health system perspective. Clinical Therapeutics. 2008; 30 (7): 1345-1357.
10. Iosifescu A, Halm EA, McGinn T, Siu AL, Federman AD. Beliefs about generic drugs among elderly adults in hospital-based primary care practices. Patient Education and Counselling. 2008; 73 (2): 377-383.
11. Kwok JMF, Miller TD, Hodge DO, Gibbons RJ. Prognostic value of the Duke treadmill score in the elderly. Journal of the American College of Cardiology. 2002. 39 (9): 1475-1481.
12. Mark DB, Shaw L, Harrell Jr FE, Hlatky MA, Lee KL. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. New England Journal of Medicine. 1991; 325 (12): 849-853.
13. Albert MA, Glynn RJ, Fonseca FA, Lorenzatti AJ, Ferdinand KC. Race, ethnicity, and the efficacy of rosuvastatin in primary prevention: The Justification for the Use of Statins in Prevention:

An Intervention Trial Evaluating Rosuvastatin (JUPITER) trial. American Heart Journal. 2011; 162 (1): 106-114.

14. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial). The American Journal of Cardiology. 2003; 92 (2): 152-160.

15. Crouse Iii JR, Grobbee DE, O'Leary DH, Bots ML, Evans GW et al. Measuring effects on intima media thickness: An evaluation of rosuvastatin in subclinical atherosclerosis: The rationale and methodology of the METEOR study. Cardiovascular Drugs and Therapy. 2004; 18 (3): 231-238.

16. Rafeeq M, Habib H, Murad H, Gari M, and Gazzaz Z. Effect of rosuvastatin on dyslipidemia and other parameters associated with metabolic syndrome in Saudi patients. Nigerian journal of clinical practice. 2017; 20 (4): 445-453.

17. Olsson AG, Istad H, Luurila O, Ose L, Stender S. Effects of rosuvastatin and atorvastatin compared over 52 weeks of treatment in patients with hypercholesterolemia. American Heart Journal. 2002; 144 (6): 1044-1051.

18. Lee HK, Hu M, Lui SS, Ho CS, Wong CK. Effects of polymorphisms in ABCG2, SLCO1B1, SLC10A1 and CYP2C9/19 on plasma concentrations of rosuvastatin and lipid response in Chinese patients. Pharmacogenomics. 2013; 14 (11):1283-1294.

19. Rose R, Neuhoff S, Abduljalil K, Chetty M, Rostami H A. Application of a physiologically based pharmacokinetic model to predict OATP1B1 related variability in pharmacodynamics of rosuvastatin. CPT: pharmacometrics & systems pharmacology. 2014; 3 (7): 1-9.

20. Bacquer DD, Smedt DD, Reiner Z, Tokgozoglu L, Clays E. Percentage low-density lipoprotein-cholesterol response to a given statin dose is not fixed across the pre-treatment range: Real world evidence from clinical practice: Data from the ESC-EORP EUROASPIRE V Study. Eur J Prev Cardiol. 2020; 27 (15):1630-1636.

21. Schneck DW, Knopp RH, Ballantyne CM, McPherson R, Chitra RR. Comparative effects of rosuvastatin and atorvastatin across their dose ranges in patients with hypercholesterolemia and without active arterial disease. Am J Cardiol. 2003; 91 (1): 33-41.

22. Ballantyne CM, Bertolami M, Garcia HRH, Nul D, Stein EA. Achieving LDL cholesterol, non-HDL cholesterol, and apolipoprotein B target levels in high-risk patients: Measuring Effective Reductions in Cholesterol Using Rosuvastatin therapy (MERCURY) II. American Heart Journal. 2006; 151 (5): 975-975.

23. Naydenov S, Runev N, Manov E, Shabani R, Donova T. Lipid-lowering potency and tolerability of generic rosuvastatin in Bulgarian patients with high and very high risk. J Cardiovasc Dis Diagn. 2014; 216 (2): 2.

24. Betto M, Fares J, Saliba N, and Ballout H, Efficacy and safety of a generic rosuvastatin in a real-world setting: Prospective, observational clinical study in Lebanese patients. Annals of Saudi Medicine, 2017. 37(5): 366-374.

25. Kapur NK, Musunuru K. Clinical efficacy and safety of statins in managing cardiovascular risk. Vascular health and risk management. 2008; 4 (2): 341.

26. Adhyaru BB, Jacobson TA. Safety and efficacy of statin therapy. Nature Reviews Cardiology, 2018; 15 (12): 757-769.

27. Shaheen S, Elserafy AS, Amin M, Hassan R, Issak ER. Brand versus Generic Rosuvastatin in Egyptian Patients with Hyperlipidemia; Cost-Minimization Analysis. International Journal of Clinical Medicine. 2019; 10 (12): 631-638.

28. Olsson AG. Statin therapy and reductions in low-density lipoprotein cholesterol: Initial clinical data on the potent new statin rosuvastatin. The American Journal of Cardiology. 2001; 87 (5): 33-36.

29. Morrison A, Glassberg H. Determinants of the cost-effectiveness of statins. Journal of Managed Care Pharmacy. 2003; 9 (6): 544-551.