Switching from High-Efficacy Lipid-Lowering Therapies [Atorvastatin or Rosuvastatin] to Simvastatin and the Results on Low-Density Lipoprotein Cholesterol Level

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Background: *In Thai National List of Essential Drugs in 2010, simvastatin is the only medication on the list for the statin group. Patients who previously prescribed other groups of statin were recommended to switch to simvastatin.*
Objective: *Comparison of lipid low-density lipoprotein cholesterol (LDL) levels before and after switching from rosuvastatin or atorvastatin to simvastatin.*
Material and Method: *The study was a retrospective observational study performed in patients older than 18 year-old who were enrolled as an outpatient at Siriraj Hospital during October 2009 and October 2010. From these patients who were switched from atorvastatin or rosuvastatin to simvastatin, LDL level was compared between before and after switching to simvastatin.*
Results: *Of 276 patients who were switched from atorvastatin to equivalent dose simvastatin, LDL levels increased from 106.20±33.47 mg/dl to 109.61±39.62 mg/dl (p = 0.089). Of 228 patients who were switched from rosuvastatin to a less than equivalent dose simvastatin, LDL levels increased from 112.73±45.94 mg/dl to 114.49±42.70 mg/dl (p = 0.437).*
Conclusion: *In the patients who were switched from atorvastatin and rosuvastatin to simvastatin, LDL levels before and after being switched was not significantly different. Moreover, patients who had switched from rosuvastatin to a less than equivalent dose of simvastatin still had no significant increases in LDL levels after switching.*

Keywords: *Statin, Simvastatin, Atorvastatin, Rosuvastatin, LDL*

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Cardiovascular disease is the leading cause of death around the world. The high levels of blood LDL increase the risk of cardiovascular disease. The importance of reducing LDL levels is for the prevention of coronary artery disease. The Adult Treatment Panel III of the National Cholesterol Education Program has recommended an LDL goal less than 100 mg/dl in high risk persons and less than 70 mg/dl in very high risk persons[1,2].

In 2006 American College of Cardiology/ American Heart Association secondary prevention statement for patients with coronary and other artherosclerotic vascular disease further endorses these goals by stating that an LDL goal of less than 70 mg/dl was reasonable[1,2]. These guidelines recommend treatment targets and advocated the use of statins as the lipid modifying agents of choice. The statin groups prescribed in Siriraj Hospital were simvastatin, atorvastatin, rosuvastatin, pravastatin and fluvastatin. Siriraj Hospital has an increasing number of patients with hyperlipidemia who switched to a different statin. Multinational clinical trials have demonstrated that switching to more efficacious statins improves goal achievement[3,4]. However, little is known about the LDL level effects when patients are switched form one statin to another.

In Thai National List of Essential Drugs in 2010, simvastatin is the only medication in the list for the statin group. Patients who were previously prescribed other groups of statin were recommended to switch to simvastatin.

This raises the question about the difference in LDL levels in patients who switch from atorvastatin or rosuvastatin to simvastatin in equivalent doses and complications caused by switching medication.

Objective

1) The primary objective: Comparison of LDL levels before and after switching from rosuvastatin or atorvastatin to simvastatin in an equivalent dose.

2) The secondary objective: To discover complications caused by the drug.

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Material and Method

Study population

The authors enrolled patients aged at least 18 years old who were treated in Siriraj Hospital and were switched from rosuvastatin or atorvastatin to simvastatin in equivalent dose (Table 1) during October 2009 and October 2010. Patients include in this study had prescriptions with at least 90 days supply for atorvastatin or rosuvastatin. Switcher also needed prescription of at least 90 day supply for simvastatin starting at the switch date. Patients were required to have calculated LDL results before switching and at least 90 days after switching. The patients who had concomitant use of other lipid lowering therapy were excluded.

Sample size calculation

The present study compared LDL levels before and after switching from atorvastatin or rosuvastatin to simvastatin; therefore, the formula that is reasonable for sample size calculation is calculated by comparing mean of dependence two groups. Previous study showed that in patients with heart disease receiving Rosuvastatin, the average LDL level before switching to simvastatin was 90.3 mg/dl and the average LDL levels after switching to simvastatin was 96.7 mg/dl, with a mean difference of level 6.5 mg/dl of LDL and standard deviation of 7.2 mg/dl[3]. The authors determined type I error (α) = 0.05 and type II error (β) = 0.20. Using compare mean of dependence two groups method for calculation we have a sample size of at least 228 patients per group. By increasing the sample size 20% to prevent data loss, the sample size became 274 people per group.

Study design and protocol

The authors retrospectively enrolled patients aged at least 18 years old who were treated in Siriraj Hospital and were switched from rosuvastatin or atorvastatin to simvastatin in equivalent dose during October 2009 and October 2010. The medical records were searched via the Siriraj Computer Center for patients who were switched from rosuvastatin or atorvastatin to simvastatin from October, 2009 to October, 2010. Patients who received rosuvastatin or atrovastatin for less than three months, patients who did not have LDL testing at least 90 days after receiving medication and patients who receiving concomitant use of other lipid lower therapy were excluded. Basic information (age, sex, race, underlying disease), dose of rosuvastatin/atorvastatin/simvastatin, LDL level before and after being switched and reported side effects of the medication were collected. The LDL levels before and after switching from rosuvastatin or atorvastatin to simvastatin were compared.

Statistical analysis

Data were analyzed by using SPSS version 17.0 statistical comparison of low density lipoprotein cholesterol paired t-test or Wilcoxon signed rank test and *p*-value less than 0.05 was considered statistically significant.

Results

A total of 6,298 patients who received atorvastatin therapies switched to simvastatin in equivalent doses during the observation period. There were 1,588 patients who were prescribed with medication at least 90 days before and after switching therapies and 288 patients who had both baseline and follow-up LDL values without any other concomitant lipid lowering therapies. One hundred and forty patients who received rosuvastatin switched to simvastatin in equivalent dose during the observation period and only 20 patients had both baseline and follow-up LDL level. Most of the patients had been switched from

Table 1. Relative LDL-lowering efficacy of Statin and Statin-based therapies*

Atorva	Fluva	Pitava	Lova	Prava	Rosuva	Vytorin®a	Simva	% decrease LDL-C
-	40 mg	1 mg	20 mg	20 mg	-	-	10 mg	30%
10 mg	80 mg	2 mg	40/80 mg	40 mg	-	-	20 mg	38%
20 mg	-	4 mg	80 mg	80 mg	5 mg	10/10 mg	40 mg	41%
40 mg	-		-	-	10 mg	10/20 mg	80 mg	47%
80 mg	-		-	-	20 mg	10/40 mg	-	55%
	-		-	-	40 mg	10/80 mg	-	63%

LDL-C = low-density lipoprotein cholesterol

* Data from http://www.fda.gov

rosuvastatin 5 mg to simvastatin 20 mg or rosuvastain 10 mg to simvastatin 40 mg, which is less than the equivalent dose. If we used switching from rosuvastatin 5 mg to simvastatin 20 mg or rosuvastain 10 mg to simvastatin 40 mg (less than equivalent dose), we had 5,267 patients switched from rosuvastatin to simvastatin in the observational period. There were 412 patients for whom who were prescribed with medication at least 90 days before and after switching therapy and 228 patients who had both baseline and follow-up LDL values without any other concomitant lipid lowering therapies (Fig. 1).

Baseline characteristic were shown in Table 2. There were more females than males and most of the patients had hypertension. More patients had stroke, ischemic heart disease and diabetes mellitus in the atorvastatin group.

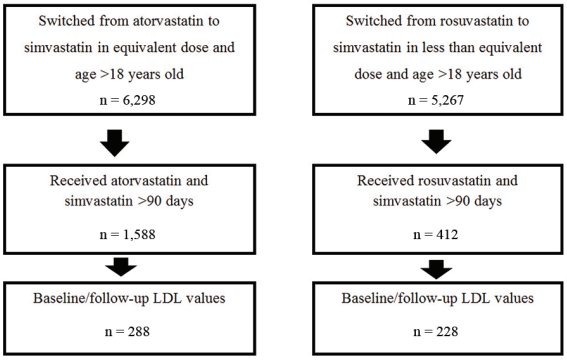

Fig. 1 Baseline characteristic were shown in Table 2. There were more female than male and most of the patients had hypertension. There were more patients who had stroke, ischemic heart disease and diabetes mellitus in the atorvastatin group.

Table 2. Baseline characteristics

	Atorvastatin (n = 288)	Rosuvastatin (n = 228)
Sex		
Male	109 (38%)	82 (36%)
Female	179 (62%)	146 (64%)
Age (years)	61±22	64±26
Nationality		
Thai	279 (97%)	207 (91%)
Chinese	9 (3%)	21 (9%)
Underlying disease		
Hypertension	222 (77%)	164 (72%)
Dyslipidemia	236 (82%)	187 (82%)
Stroke	37 (13%)	7 (3%)
Ischemic heart disease	89 (31%)	57 (25%)
Diabetes mellitus	150 (52%)	87 (38%)

Patients who were switched to simvastatin from atorvastatin showed increases in total cholesterol and LDL level but these did not reach statistically significant levels (Table 4).

Patients who were switched to simvastatin from rosuvastatin had a total cholesterol level that increased significantly. LDL level had increased but did not reach statistical significance. The LDL level is not normally distributed, so the Wilcoxon signed ranks test was applied and showed no significant difference at *p*-value of 0.47.

Table 3. Lipid profile in patients who were switched from atorvastatin to equivalent dose of simvastatin

Lipid profile	Lipid level before switching (mean ± SD)	Lipid level after switching (mean ± SD)	Lipid level change (mean ± SD)	95% confidence interval	*p*-value
Total cholesterol	181.5±38.6	188.8±47.3	7.2±40.2	1.6 to 12.9	0.012
Triglyceride	130.5±60.5	128.3±67.7	-2.1±51.5	-9.3 to 5.0	0.552
HDL	53.9±15.4	54.4±15.2	0.4±8.1	-0.7 to 1.5	0.459
LDL	106.2±33.4	109.6±39.6	3.4±33.1	-0.5 to 7.3	0.089

HDL = high-density lipoprotein; LDL = low-density lipoprotein

Table 4. Lipid profile in patients who were switched from rosuvastatin to less than equivalent dose of simvastatin

Lipid profile	Lipid level before switching (mean ± SD)	Lipid level after switching (mean ± SD)	Lipid level change (mean ± SD)	95% confidence interval	*p*-value
Total cholesterol	189.8±52.6	192.7±49.7	2.8±44.4	-3.8 to 9.6	0.398
Triglyceride	141.2±69.4	137.1±68.5	-4.0±63.1	-13.5 to 5.4	0.397
HDL	56.0±26.3	54.6±19.7	-1.4±17.1	-4.1 to 1.1	0.271
LDL	112.7±45.9	114.4±42.7	1.7±38.4	-3.2 to 6.7	0.490

Discussion

In the present study, the authors found that after switching from atorvastatin to simvastatin in an equivalent dose and roruvastatin to simvastatin in a less than equivalent dose, the LDL level did not change significantly in this group of patients. In our population, 38-52% had diabetes, 25-31% had ischemic heart disease and 3-13% had prior stroke, which are classified as high-risk patients. Prior study shows switching from simvastatin 20-40 mg to rosuvastatin 10-20 mg produced greater reductions in LDL-C and total cholesterol in very high-risk patients[5].

The differences in individual response to statins may also be reflected in risk factors and current therapy which can lead to a switch to less efficacious doses leading to higher LDL level and lower goal attainment rates[6-10]. Another study found rosuvastatin achieves greater percent LDL reduction than simvastatin as a switch therapy in a real world clinical practice setting. The need to select the statin to switch to base on additional need percent LDL reduction to meet individual target[11].

In the present study, it was found that in switching from atorvastatin to simvastatin in equivalent doses, the LDL levels were not significantly different. The study enrolled patients who were not at very high risk of cardiovascular disease and the initial mean LDL levels before being switched from atorvastatin were 106.20 mg/dL and in the rosuvastatin group 112 mg/dL. Therefore, switching to simvastatin may be appropriate for patients who need to maintain their LDL levels on another statin and for patients who need a smaller additional LDL reduction to achieve an individual LDL target goal.

Conclusion

In the patients who were switched from atorvastatin and rosuvastatin to simvastatin, LDL level before and after switching, was not significantly different. Moreover, patients who had switched from rosuvastatin to a less than equivalent dose of simvastatin still did not experience any significant increase in LDL levels after switching.

Study limitations

1. This trial is a retrospective observational study so several confounding factors could occur during the study, such as actual compliance with prescribed medication.

2. The authors did not have baseline LDL levels before starting lipid-lowering therapy and did not have data on other risks of heart disease, such as smoking and Framingham risk scores.

What is already known on this topic?

The high levels of blood LDL increase the risk of cardiovascular disease. LDL-lowering potency of statin varies between agents.

What this study adds?

Switching from atorvastatin to simvastatin in an equivalent doses and rosuvastatin to simvastatin in a less than equivalent dose, the LDL level did not significantly change in this specific group of patient.

Potential conflicts of interest

None.

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การเปลี่ยนแปลงของระดับไขมันในเลือดหลังการเปลี่ยนยาจาก atorvastatin หรือ rosuvastatin เป็น simvastatin

ศุภนัชญา กางการ, วรางคณา บุญญพิสิฎฐ์

ภูมิหลัง: *ระดับไขมัน low density lipoprotein มีผลต่อการลดระดับความเสี่ยงของโรคหัวใจและหลอดเลือด ทำให้ยาในกลุ่มสเตติน [statin] เข้ามามีบทบาทเนื่องจากมีหลักฐานชัดเจนถึงประสิทธิภาพในการลดระดับไขมัน แต่บัญชียาหลักแห่งชาติ พ.ศ. 2554 ได้กำหนดให้มีเพียง simvastatin เพียงตัวเดียวที่อยู่ในบัญชียาหลักแห่งชาติ ทำให้ผู้ป่วยที่ได้รับยากลุ่มอื่นต้องเปลี่ยนกลับมาใช้เป็น simvastatin โดยเปลี่ยนยาจาก atorvastatin, rosuvastatin เป็น simvastatin*

วัตถุประสงค์: *วัตถุประสงค์ของการศึกษาคือ เปรียบเทียบระดับไขมัน low density lipoprotein cholesterol (LDL) ก่อนและหลังการเปลี่ยนยาจาก rosuvastatin หรือ atorvastatin เป็น simvastatin*

วัสดุและวิธีการ: *เป็นการศึกษาแบบ retrospective observational study โดยทำในผู้ป่วยอายุมากกว่า 18 ปี ที่เข้ารับการรักษาพยาบาลเป็นผู้ป่วยนอกของโรงพยาบาลศิริราช ที่ได้รับยา atorvastatin หรือ rosuvastatin แล้วเปลี่ยนเป็นยา simvastatin ในขนาดยาที่มีผลลด LDL ได้เท่ากัน ช่วงระยะเวลาตั้งแต่เดือนตุลาคม พ.ศ. 2553 ถึง ตุลาคม พ.ศ. 2554*

ผลการศึกษา: *ผู้ป่วยที่ได้รับยา atorvastatin แล้วเปลี่ยนเป็น simvastatin ในขนาดเท่ากันจำนวน 276 ราย พบระดับไขมัน low density lipoprotein เพิ่มขึ้นจาก 106.20±33.47 mg/dl เป็น 109.61±39.62 mg/dl (p = 0.089) ส่วนในกลุ่มผู้ที่ได้รับการเปลี่ยนยาจาก rosuvastatin เป็น simvastatin จำนวน 228 ราย พบว่าระดับไขมัน LDL เพิ่มขึ้นจาก 112.73±45.94 mg/dl เป็น 114.49±42.70 mg/dl (p = 0.437)*

สรุป: *การเปลี่ยนยาจาก atorvastatin หรือ rosuvaststin เป็น simvastatin ในขนาดเทียบเท่านั้น ไม่มีความแตกต่างกันของระดับไขมัน อีกทั้งการเปลี่ยนขนาดยาของ rosuvastatin เป็น simvastatin ที่ขนาดน้อยกว่าขนาดเทียบเท่า กลับมีผลต่อระดับไขมันไม่แตกต่างกัน*