Efficacy of Statins in Dyslipidemia: A Non interventional comparative study in a tertiary care hospital, Ajman, UAE

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Original Article

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Abstract

Background

The reduction of serum total cholesterol and LDL-cholesterol levels varies with different statins. The objective of the present study was to compare the efficacy of Simvastatin, Atorvastatin and Rosuvastatin in the treatment of newly diagnosed dyslipidemia.

Material and Methods:

A prospective, non-interventional 12-week study was conducted after approval from the Ethics Committee. A total of 70 patients with newly diagnosed dyslipidemia receiving 20mg of Simvastatin, Atorvastatin or Rosuvastatin were included. The primary efficacy measure was reduction of lipid levels from the initial baseline values at the end of 12 weeks with the respective Statins. Data was analyzed using descriptive statistics, Paired -t test, and analysis of variance (ANOVA).

Results:

Of total 70 patients, 14 patients received Simvastatin; 40 patients received Atorvastatin and 16 patients received Rosuvastatin. Demographic and baseline clinical characteristics were similar between the three groups.

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Significant reduction in lipid levels (total cholesterol, and LDL) was seen within the three treatment groups ($p<0.01$). However, statistically significant difference in the reduction lipid levels was not observed between the three groups.

Conclusion:

We found no significant difference in the reduction of lipid levels between Simvastatin, Atorvastatin or Rosuvastatin patients with newly diagnosed dyslipidemia.

Keywords:

Atorvastatin, Simvastatin, Rosuvastatin, Dyslipidemia

Background:

Cardiovascular diseases (CVD) are the leading cause of mortality in the developed and in most of the developing world. The World Health Organization (WHO) estimates that dyslipidemia is associated with more than half of global cases of ischemic heart disease and more than 4 million deaths per year[1]. Prevalence of hypercholesterolemia in Arab world ranges from 2.7-51.6%[2]. In the United Arab Emirates, the prevalence of hypercholesterolemia is estimated to be around 39.6%[3].

Statins are now the established first-line cholesterol-lowering drugs due to their effectiveness and safety[4]. Treatment with statins has shown reduction in the recurrence of cardiovascular events, cardiovascular death and all-cause mortality in patients with hypercholesterolemia[5]. The effects on the cholesterol levels vary with different statins. The dose-response relationship of all statins seems to be relatively flat, however, with a 15% to 30% further decrease in cholesterol with every doubling of the dose[6].

Studies have reported ethnic differences in the response to statins, Among the Japanese patients very low doses of Simvastatin brought about 20% reduction in total cholesterol and 25% of LDL-C[7]. Similarly with rosuvastatin among the Asian population, low doses are preferred. Some of the comparative trials have demonstrated superiority of Rosuvastatin over Atorvastatin and Simvastatin in lowering the serum total cholesterol and LDL-cholesterol concentrations[6,8,9]. However, limited studies on Statin therapies in hypercholesterolemia have been published from the Middle East. This study compared the efficacy of atorvastatin, simvastatin and Rosuvastatin in the treatment of newly diagnosed dyslipidemia among patients reporting to Cardiology Department of a tertiary care center.

Material and Methods:

Study design and the participants:

A non-interventional study was carried out among adult patients with newly diagnosed dyslipidemia reporting to the Department of Cardiology from January 2012. All patients were screened based on the inclusion criteria and recruited into the study after obtaining the informed consent. Their baseline serum lipid levels (total cholesterol, triglycerides, LDL and HDL levels), fasting blood sugar levels (FBS), HbA1c levels, serum creatinine levels, Liver function test (aspartate transaminase (AST) and alanine transaminase (ALT)) were recorded. The patients were followed up after three months (12 weeks) of treatment, during this visit serum lipid levels were recorded assess the reduction of lipid level with the respective Statins. The liver function test and serum creatinine levels were also assessed.

Data collection:

A Case Record Form (CRF) was used for the data collection. The socio-demographic characteristics, laboratory reports of biochemical parameters, treatment details, baseline and end of treatment lipid parameters were collected. Patients receiving 20 mg of Simvastatin, Atorvastatin or Rosuvastatin were followed up after 12 weeks of initiating treatment to assess the efficacy.

Inclusion criteria:

The patients of both gender, age above 20 years, newly diagnosed dyslipidemia and willing to participate in the study were included.

Exclusion criteria:

The patients with secondary hyperlipoproteinemias, active liver disease and renal insufficiency were not included

Sample size calculation:

To detect a minimum difference of 25mg in LDL levels with a standard deviation of 20mg and the power of the study at 80% and a statistical significance of p value <0.05, a sample of 14 patients in each treatment arm was estimated.

Outcome Variable:

The outcome variables included in this study were total cholesterol, triglycerides, LDL and HDL levels after 12 weeks of treatment.

Explanatory variable:

The explanatory variable was 20mg statin (Atorvastatin, Simvastatin or Rosuvastatin)

Ethical committee approval: Ethical review board approval was obtained for the study and all patients provided written informed consent.

Data management and statistical analysis: SPSS version 21 software (Chicago, Illinois, USA) was used for data analysis. Data was analyzed using descriptive statistics, Paired -t test, and analysis of variance (ANOVA).

Result:

Of total 70 patients included in the study, 14 patients received Simvastatin; 40 patients received Atorvastatin and 16 patients received Rosuvastatin. Table-1 details the demographic and baseline clinical characteristics of study patients in each group and these were comparable between the three groups. The mean age of the patients was approximately 43 years and males were the majority in all the three groups. More than half of the patients were of Arab ethnicity 38(54.3%) followed by Asians 18 (25.7%).

Males formed the majority in all the three groups, 12 (85.7%) in Simvastatin, 40 (72.5%) in Atorvastatin, 14 (87.5%) in Rosuvastatin groups

Table 1: Demographics and baseline characteristics for the three treatment groups

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Baseline characteristics	Simvastatin (n=14)		Atorvastatin (n=40)		Rosuvastatin (n=16)		p value
	Mean	SD	Mean	SD	Mean	SD	
Mean Age (in years)	40.0	9.3	46.4	10.0	43.8	7.3	NS
Serum Creatinine (mg/dl)	0.9	0.14	0.8	0.16	0.9	0.14	NS
Total cholesterol (mg/dl)	204.5	38.6	236.8	28.0	241.0	44.0	NS
Triglycerides(mg/dl)	139.5	42.0	154.7	58.0	140.0	47.0	NS
LDL(mg/dl)	140.0	33.8	161.8	28.0	167.0	44.0	NS
HDL(mg/dl)	43.79	7.2	44.2	8.7	46.0	9.6	NS
ALT (IU/l)	27.3	10.1	23.0	14.1	23.9	10.1	NS
AST(IU/l)	20.8	4.6	21.0	5.6	23.2	6.7	NS
FBS(mg/dl)	110	28	111.0	29.0	108.0	21.0	NS
HbA1c%	6.9	1.8	7.6	2.0	7.6	2.2	NS

×NS p>0.05, statistically not significant

Table 2: Baseline lipid parameters and percent change at the end of 12 weeks

Drug group	Lipid parameters	Baseline (mg/dl)	% change	p value
Simvastatin (n=14)	Total cholesterol	204.5	17.3	<0.01
	Triglycerides	139.5	8.4	NS
	LDL	140	24.5	<0.01
	HDL	43.79	-0.6	NS
Atorvastatin (n=40)	Total cholesterol	236.8	21.0	<0.001
	Triglycerides	154.75	12.1	NS
	LDL	161.8	29.8	<0.001
	HDL	44.2	-2.3	<0.05
Rosuvastatin (n=16)	Total cholesterol	241.1	16.0	<0.001
	Triglycerides	139.4	9.78	NS
	LDL	167.4	21	<0.001
	HDL	46	-0.8	NS

×NS p>0.05, statistically not significant
*p<0.05, statistically significant
†p<0.01, statistically significant

Simvastatin, Atorvastatin and Rosuvastatin reduced total cholesterol by 17.3%, 21% and 16% and LDL-cholesterol levels by 24.5%, 29.8% and 21% respectively and this reduction within each group was statistically significant (p<0.01). All the three statins increased the HDL levels; however, the rise was not statistically significant (Table-2). Statistically significant difference in the reduction of lipid levels was not observed between the three groups of statins of milligram- equivalent doses.

Discussion

Comparison between Simvastatin, Atorvastatin and Rosuvastatin and LDL levels

At the end of 12 weeks treatment with 20 mg Simvastatin, Atorvastatin and Rosuvastatin, total cholesterol and LDL-cholesterol levels reduced significantly within each group (p<0.01). There was no significant difference in the levels between the three groups of patients with hypercholesterolemia receiving of Simvastatin, Atorvastatin or Rosuvastatin in milligram- equivalent doses. In contrast to this finding, previous studies reported superiority of Rosuvastatin in improving the lipid profile of patients with hypercholesterolemia over Simvastatin and Atorvastatin in milligram-equivalent doses[8,10]. Binbrek AS et al documented greater reductions in LDL-C levels with a starting dose (10 mg) of Rosuvastatin compared with atorvastatin 10 mg[11]. Studies from Qatar, Pakistan and Greece also reported similar findings of significant reduction in low-density lipoprotein cholesterol and total cholesterol levels with Rosuvastatin[12-14].

Comparison between Simvastatin, Atorvastatin and Rosuvastatin and HDL levels

We observed that all the three groups increased the HDL levels however the rise was not statistically significant. Previous reports also noted increase in the high-density lipoprotein cholesterol in the Rosuvastatin groups were greater compared with all other groups[8,10-14].

Rosuvastatin and effect on lipid levels

In comparison to prior reports Rosuvastatin did not produce significant reduction in the lipid parameters. The present study results were in line with a previous study from Japan [15]. The probable reasons could be due to varying sample size in each group and may also be related to variation in drug response associated with ethnic groups. Interethnic differences in statin efficacy in terms of differential LDL-C response to statin therapy have been documented in several pharmacologic investigations carried out among African-Americans, American Indians, Whites Hispanics and South Asians[16,17]. An international study from the Middle East region evaluating the frequency of lipid abnormalities in patients receiving statin treatment for long duration showed that almost two-thirds of statin-treated patients in the United Arab Emirates, Saudi Arabia, Lebanon and Jordan had inadequately controlled lipid levels[18] In this study the strongest variables associated with lipid abnormalities were current tobacco smoking and sedentary lifestyle[18].

Statins and updated hypercholesterolemia treatment guidelines

In the most recent update in treatment of hypercholesterolemia is the publication of The American College of Cardiology and American Heart Association (ACC/AHA) guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. According to this guideline LDL-Cholesterol levels is no more considered as a major risk factor for coronary events. This guideline identifies four major groups of patients for whom cholesterol-lowering statins, have the greatest chance of preventing cardiovascular and cerebrovascular events. Patients with any form of clinical cardiovascular disease, LDL-C levels of 190 mg per dl, patients 40 to 75 years of age who have diabetes and finally patients 40 to 75 years of age who do not have diabetes but who do have an estimated 10-year ASCVD risk of 7.5% or greater[19].

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Conclusion:

This was a three arm head to head comparison study of Simvastatin, Atorvastatin and Rosuvastatin among the Middle East population with newly diagnosed dyslipidemia. This study revealed significant reduction in lipid levels (total cholesterol, and LDL) within the three treatment groups but no significant difference in the reduction of lipid levels observed between Simvastatin, Atorvastatin or Rosuvastatin after 12 weeks of treatment.

Limitations of the study:

In the present study, the patient adherence to statin therapy was not confirmed by patient diary or pill count. Life style modification adopted by the patients was not assessed in the study which could impact the overall benefit with treatment.

Future scope of the study:

Further studies can be conducted in accordance with the latest ACC/AHA guidelines which would provide useful information and explore the pharmacogenetic variation in response to statins.

Author's contribution:

LJJ designed the study, conducted literature review, interpreted the results, drafted the manuscript, edited and reviewed the manuscript. EMFE participated in the designing of the study, acquired the data, edited and reviewed the manuscript. MAMF participated in the designing of the study, and acquired the data. JD participated in the designing of the study statistical analysis, interpreted the data, and revised the manuscript. JK planned the study with LJJ, interpreted the data, drafted the manuscript, and revised it. AK participated in concept design and report preparation. NS participated in concept design and manuscript editing. All the authors approved the final document.

Conflict of interest:

There is no conflict of interest among authors arising from the study.

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