

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

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### ABSTRACT

**Objective:** 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.

**Materials 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. 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

## INTRODUCTION

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<sup>1</sup>. Prevalence of hypercholesterolemia in Arab world ranges from 2.7-51.6%<sup>2</sup>. In the United Arab Emirates, the prevalence of hypercholesterolemia is estimated to be around 39.6%<sup>3</sup>.

Statins are now the established first-line cholesterol-lowering drugs due to their effectiveness and safety<sup>4</sup>. Treatment with statins has shown reduction in the recurrence of cardiovascular events, cardiovascular death and all-cause mortality in patients with hypercholesterolemia<sup>5</sup>. 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<sup>6</sup>.

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<sup>7</sup>. 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<sup>6,8,9</sup>. However, limited studies on Statin therapies in hypercholesterolemia have been published from the Middle East. This study compared the effectiveness of atorvastatin, simvastatin and Rosuvastatin in the treatment of newly diagnosed dyslipidemia among patients reporting to the Department of Cardiology of a tertiary care center in Ajman, UAE.

## MATERIALS AND METHODS

A non-interventional study was carried out among adult patients with newly diagnosed dyslipidemia reporting to the Department of Cardiology from January 2012. Patients receiving 20 mg of Simvastatin, Atorvastatin or Rosuvastatin were followed up after three months of initiating treatment to assess the efficacy. Ethical review board approval was obtained for the study and all patients provided written informed consent.

The patients of both gender, age above 20 years, newly diagnosed dyslipidemia and willing to participate in the research were included. A Case Record Forms (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. 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).

## RESULTS

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

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

Simvastatin, Atorvastatin and Rosuvastatin reduced total cholesterol by 36%, 49% and 38% and LDL-cholesterol levels by 34%, 48% and 35% respectively and this reduction within each group was statistically significant ( $p < 0.01$ ). All the three groups 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.

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	36	<0.01
	Triglycerides	139.5	12	NS
	LDL	140	34	<0.01
	HDL	43.79	-0.3	NS
Atorvastatin (n=40)	Total cholesterol	236.8	49	<0.001
	Triglycerides	154.75	18	NS
	LDL	161.8	48	<0.001
	HDL	44.2	-2.3	<0.05

Rosuvastatin (n=16)	Total cholesterol	241.1	38	<0.001
	Triglycerides	139.4	13	NS
	LDL	167.4	35	<0.001
	HDL	46	-0.4	NS

NS- Not significant

## DISCUSSION

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<sup>8,10</sup>. Binbrek AS et al documented greater reductions in LDL-C levels with a starting dose (10 mg) of Rosuvastatin compared with atorvastatin 10 mg<sup>11</sup>. Studies from Qatar, Pakistan and Greece also reported similar findings of significant reduction in low-density lipoprotein cholesterol and total cholesterol levels with Rosuvastatin<sup>12-14</sup>.

In comparison to prior reports Rosuvastatin did not produce significant reduction in the lipid parameters. 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<sup>15,16</sup>. 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<sup>17</sup>. In this study the strongest variables associated with lipid abnormalities were current tobacco smoking as well as a sedentary lifestyle<sup>17</sup>.

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<sup>18</sup>.

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<sup>8,10-14</sup>.

There have been a few limitations in our study e.g. a) small sample size; b) patient adherence to statin therapy was not confirmed by patient diary or pill count; and c) life style modification was not assessed in the present study which could impact the overall benefit with treatment which. However, the strength of the study includes three arm head to head comparisons of commonly prescribed statins among the Middle East population.

In conclusion, there was no significant difference in the reduction of lipid levels between Simvastatin, Atorvastatin or Rosuvastatin among patients with newly diagnosed dyslipidemia. However, further studies with larger number of patients conducted in accordance to the latest ACC/AHA guidelines can provide useful information.

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