Original Research Article

A study of effect of high intensity statins (Atorvastatin 80 mg and Rosuvastatin 40 mg) in age group of 35 to 75 years on liver function and muscle enzymes

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Abstract

Introduction: Researches done on the use of statins during the last two decades have shown conflicting results in their effects on DM, Cardiac, liver and Kidney functions. Six forms of statins are being prescribed as a preventive measure to reduce the incidence of cardiovascular morbidity and mortality; but statin use have also shown alternations in DM, liver and Kidney function. The latest observations relates to cancer prevention/induction. Statins prescriptions are done mostly for elderly patients in order to reduce lipid profile mostly Total cholesterol and LDL levels. Studies have shown that statins use affects muscular function, induce prediabetes, and alter liver enzymes and affects mitochondrial functions. Among the statins used, atorvastatin was found to be very beneficial with minimal side effects with greater beneficial function in maintaining other organ functions. **Materials and methods:** Total 50 patients were taken for this prospective, observational, cross-sectional hospital based study, conducted at Both rural and urban catchment area of N.R.S Medical College and Hospital, West Bengal from January 2016 to June 2017. The case records were studied, analysed and compared using SPSS (20.0) **Results:** The study reveals out of total 50 patients, 34 (68%) were male and 16 (32%) patients were female in the age group of 35 to 75 years. There were no abnormal changes (rise) in SGOT and SGPT level in 3 months. At the end of 6 months, overall increase of SGPT was seen in 3 patients (6%) of which out of 20 patients who had taken Rosuvastatin, 1 patient (5%) had SGPT (129mg/dl) and in Atorvastatin cases 2 patients (6.7%) had SGPT(134mg/dl) and 143mg/dl.). After 6 months of study in both Rosuvastatin and Atorvastatin abnormal values of CPK were seen. **Conclusions:** Both the statins had a good safety profile with few adverse effects. This study showed that the Rosuvastatin is more cost effective compared to Atorvastatin. For future research the study should be done in a large sample and for long duration of period as a multicentre study.

Key words: Statins, liver function, muscle enzymes

Introduction

Lipids constitute approximately 70% (by mass) of the dry weight of plasma. Amino acids (proteins), nucleic acids, and carbohydrate make up the remainder. Approximately half of circulating lipids are sterols, with the other major components being glycerol-phospholipids (phospholipids) and glycolipids (triglycerides), which circulate in lipoproteins[1]. Vascular endothelial cells are continuously exposed to circulating lipoproteins, and the interaction between lipoproteins and cells of the arterial wall leads to pathogenesis of human atherosclerosis (Reduction of LDL-C levels reduces the risk for CAD, and the effect size is associated with the magnitude of the reduction in LDL-C[2]. Thus low-density lipoprotein (LDL) meets the modified Koch postulates as a causal risk factor for atherosclerotic cardiovascular disease (CVD).

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Coronary heart disease (CHD) is the largest single cause of morbidity and mortality India and Worldwide. The principle to the pathogenesis of atherosclerosis is this deposition and attachment of cholesterol and its remnants in inner side of arterial wall leads to hardening and friable of it, demands the lipid modification which is critical to CHD prevention. According to Framingham heart study, 1990 there is a 10-year risk of coronary heart disease (CHD) events at 40 years of age, the life time risk of CHD is 50% for men and 33% for women. It has been shown that lowering of cholesterol level by statins reduce the cardiovascular and cerebrovascular events by preventing development of atherosclerosis[3].

Coronary artery disease (CAD), also known as ischemic heart disease (IHD), is a group of diseases that includes: stable angina, unstable angina, myocardial infarction, and sudden cardiac death. It is within the group of cardiovascular diseases of which it is the most common type. A common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck, or jaw. Occasionally it may feel like heartburn. Usually symptoms occur with exercise or emotional stress, last less than a few minutes, and get better with rest. Shortness of breath may also occur and sometimes no symptoms are present. The first sign is occasionally a heart attack. Other complications include heart failure or an irregular heartbeat and pulse beat[4].

Coronary artery disease has a number of well determined risk factors. The most common risk factors include smoking, family history, hypertension, obesity, diabetes, lack of exercise, stress, and high

blood lipids. Smoking is associated with about 36% of cases and obesity 20%. Lack of exercise has been linked to 7–12% of cases. Exposure to the herbicide Agent, Orange may increase risk. Both rheumatoid arthritis and systemic lupus erythematous are independent risk factors as well[5]. Job stress appears to play a minor role accounting for about 3% of cases.

In one study, women who were free of stress from work life saw an increase in the diameter of their blood vessels, leading to decreased progression of atherosclerosis. In contrast, women who had high levels of work-related stress experienced a decrease in the diameter of their blood vessels and significantly increased disease progression. Having a type -A behaviour pattern, a group of personality characteristics including time urgency, competitiveness, hostility, and impatience is linked to an increased risk of coronary disease[6].

In 2015 CAD affected 110 million people and resulted in 8.9 million deaths. It makes up 15.9% of all deaths making it the most common cause of death globally. The risk of death from CAD for a given age has decreased between 1980 and 2010, especially in developed countries. The number of cases of CAD for a given age has also decreased between 1990 and 2010[7]. In the United States in 2010 about 20% of those over 65 had CAD, while it was present in 7% of those 45 to 64, and 1.3% Statins are a class of cholesterol lowering drugs that inhibit the Enzyme HMG-Co-A reductase and plays a pivotal role to reduce and prevent the CVD, CVA and other associated diseases by lowering cholesterol especially low –density-lipoprotein (LDL).It has been shown that Statins can reduce the incidents of CHD by as much as 21% to 43%.

Statin are effective in preventing heart disease in those with high cholesterol with and without pre-existing heart disease. In Cochrane Study, 2013 showed that there is decrease in morbidity and mortality and other poor outcome with any harm effect. It is found that stain can reduce LDL cholesterol by1.8 m- mol/L (70 mg/dl), which is equivalent to an estimated 60% decrease in number of events (heart attack, sudden cardiac death) and 17% reduction in risk of stroke after long term use[8].

Though stain are highly effective drugs in preventing future episodes of CAD they are not without complications. Effect on liver and muscles are among the two most common complications that are observed. Most of the study has shown that its safe even in higher doses, Transaminase elevations with statins appear related to the dose, not the degree of LDL-C lowering. Transaminase elevations 3 times the ULN have been observed in less than 1% of patients receiving low and intermediate statin doses (e.g., 10–40 mg/day of most statins or 1–4 mg/day of pitavastatin) and although there is no much data regarding the study of high intensity statins it is stated, transaminase elevation were seen in 2% to 3% of patients receiving 80-mg doses of Atorvastatin. The most efficacious statins, atorvastatin and rosuvastatin, cause no more frequent, and perhaps even fewer, elevations than the least efficacious statin, fluvastatin. Although the incidence of serious muscle injury is small, the incidence of myalgias (symptoms of muscle weakness, soreness, and/or pain with or without any elevation in creatine kinase) is relatively high and may lead to many more statin discontinuations, resulting in the loss of highly effective, risk-reducing therapy. In clinical trials, myalgia, with or without a creatine kinase elevation, have been reported in approximately 3% to 15% of patients receiving statins therapy and cause about 10% of patients to stop statin therapy altogether. Because there are no equally effective risk-reducing alternatives for these patients, every effort needs to be made to keep patients on statin therapy, even if doses or regimens are reduced[9].

There are many studies in relation to statins with cardiovascular diseases and hypercholesterolemia related diseases but not much studies with high intensity statins (Atorvastatin and Rosuvastatin) and its effect on liver and muscle enzymes specially in India. Hence, this study was designed to delineate the effects on liver (SGOT, SGPT) and muscle enzyme (CPK) from the population of Eastern India.

Objectives

The objective of the study is

1. To determine the determine the particular high doses (40mg and 80mg) cause liver injury (alanine transaminase) with prior screening of liver function,
2. To study the clinical profile (symptoms and signs, biochemical and sonological features) of the patients presenting with features of abnormal liver and muscle enzyme after a certain period of time (3 and 6 months).
3. To determine whether the statin to be withdrawn or to be continued with low doses.

Materials and methods

Study area

Both rural and urban catchment area of N.R.S Medical College and Hospital, West Bengal

Study population

Patients with CAD i.e. stable ischemic heart disease, myocardial infarction, post PCI, post ischemic CVA, Diabetes mellitus, and primary prevention for ischemic heart disease coming to Cardiology OPD and Medicine OPD of NRS Medical College and Hospital, Kolkata.

Study period

From January 2016 to June 2017 (18 months)

Sample size

50 patients

Sample design

Simple random selection/Cross sectional Study

Study design

Prospective, observational, cross-sectional hospital based study – single centre study.

Ethical Clearance

Ethical committee approval was taken from N.R.S Medical College and Hospital Ethical Committee

Inclusion criteria

Patients between 35yrs and 75 yrs who are candidates for statin treatment

1. Clinical ASCVD secondary prevention (SIHD, ACS, POST, PCI)
2. (LDL-C) 190 mg/dl without secondary cause(high saturated /trans-fat, drugs)
3. Primary prevention with diabetes-
   Age 40-75 yrs –LDLc-70-189 mg/dl
4. Primary prevention-without diabetes—
   Age 40-75 yrs—LDL C 70-189 mg/dl estimated ASCVD risk using a new pooled cohort algorithm > 7.5

Exclusion criteria

The following patients were excluded from the study

1. congestive heart failure
2. Acute or Chronic renal failure.
3. Patients <35 years.
4. Pre-existing liver disease.
5. Chronic liver disease (CLD)

Study method

All study members provided detailed explanation of the study in their understandable language before obtaining their informed consent for involvement in study and for venipuncture. The initial step was careful history taking and detailed examination. History include present complaints and complication, treatment history, past history, family history and personal history with special focus on detailed

drug history focussing on identifying all of the patient's current and past medications, including allopathic medications, complementary and alternative medications and substances of abuse like alcohol.
Investigations included the following:

- Complete hemogram with peripheral smear
- Thyroid function
- Lipid profile
- Liver function tests including total, direct and indirect bilirubin, albumin, globulin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase.
- Renal function tests (serum urea and serum creatinine).
- Serum Electrolytes (Na^+/ K^+/ Cl^-).
- CPK
- Ultrasonography whole abdomen (in selected cases)
- Echocardiography, Angiography (in selected cases)

Analysis of data

The case records were studied, analysed and compared using suitable statistical Methods. The latest SPSS version 20 (SPSS Inc., Chicago, IL, USA) was used for this purpose.

Results and analysis

The study titled "A study of effect of high intensity statins (Atorvastatin 80 mg and Rosuvastatin 40 mg) in age group of 35 to 75 years on liver function and muscle enzymes" was conducted in both rural and urban catchment area of N.R.S Medical College and Hospital, West Bengal, from January 2016 to June 2017. A total 50 cases of both sexes between 35 yrs and 75 yrs were included in the study as per inclusion criteria. The results and observation of the study are presented below:

Table 1: Distribution of mean Age in two doses of Statin

		No.	Mean	SD	Minimum	Maximum	Median	p-value
AGE (Years)	Rosuvastatin (40 mg)	20	63.2500	8.6868	48.0000	78.0000	65.0000	0.1676
	Atorvastatin (80 mg)	30	59.5667	9.3723	33.0000	75.0000	58.5000	

From table 1 it is observed that the mean age (mean ± S.D.) of patients was 63.2500 ± 8.6868 years with range 48.00-78.00 years and the median age was 65.00 years Rosuvastatin (40 mg). In Atorvastatin (80 mg), The mean age (mean ± S.D.) of patients was 59.5667 ± 9.3723 years with range 33.00-75.00 years and the median age was 58.5 years. Difference of mean age in two groups was not statistically significant. Thus age was matched in two groups. There was no statistically significant difference in age distribution between the groups. [Numerical variables between groups compared by t-test; (p=0.1676)].

Table 2: Distribution of two age group, Sex, in two doses of Statin

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
Age (years)				
≤50	3	4	7	Chi-square: 0.0277; p-value: 0.8678
Row%	42.9	57.1	100.0	
Col %	15.0	13.3	14.0	
>50	17	26	43	
Row%	39.5	60.5	100.0	
Col %	85.0	86.7	86.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
Sex				
Female	13	3	16	Chi-square: 16.6820; p-value: <0.0001
Row%	81.3	18.8	100.0	
Col %	65.0	10.0	32.0	
Male	7	27	34	
Row%	20.6	79.4	100.0	
Col %	35.0	90.0	68.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 2 shows that 3(15%) patients had ≤50years age and 17(85%) patients had >50 year age were receive Rosuvastatin (40 mg) and 4(13.3%) patients had ≤50years age and 26(86.7%) patients had >50 year age were receive Atorvastatin (80 mg). Association between age in two dose of statin was not statistically significant (p=0.8678).
Almost 13(65%) female patients and 7(35%) male patients were receiving Rosuvastatin (40 mg) where 3(10%) female and 27(90%) male patients were receiving Atorvastatin (80 mg). Association between sex in two dose of statin was statistically significant (p<0.0001).

Table 3: Distribution of mean body wt. in two doses of Statin

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Body wt.(Kg)	Rosuvastatin (40 mg)	20	66.8500	7.9424	54.0000	80.0000	67.5000	0.5893
	Atorvastatin (80 mg)	30	67.9333	6.1304	58.0000	81.0000	68.0000	

Table 3 shows that mean body weight (mean ± S.D.) of patients was 66.8500 ± 7.9424 years in Rosuvastatin (40 mg) group. Whereas Atorvastatin (80 mg) group mean body weight (mean ± S.D.) of patients was 67.9333 ± 6.1304 years. So the difference was not statistically significant (p=0.5893).

Table 4: Distribution of Statins in two groups of Post PCI patients. ACS patients

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
Post PCI				
No	8	12	20	Chi-square: 0.0000; p-value: 1.000
Row%	40.0	60.0	100.0	
Col %	40.0	40.0	40.0	
Yes	12	18	30	
Row%	40.0	60.0	100.0	
Col %	60.0	60.0	60.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
ACS patients				
No	12	18	30	
Row%	40.0	60.0	100.0	
Col %	60.0	60.0	60.0	
Yes	8	12	20	
Row%	40.0	60.0	100.0	
Col %	40.0	40.0	40.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 4 shows Distribution of Statins in two groups of Post PCI patients. ACS patients.

Table 5: Distribution of mean SGOT at 0 month in two doses of Statin

		No.	Mean	SD	Minimum	Maximum	Median	p-value
SGOT Start	Rosuvastatin (40 mg)	20	30.7000	4.4379	20.0000	38.0000	31.0000	0.2170
	Atorvastatin (80 mg)	30	29.0667	4.5783	18.0000	35.0000	29.5000	

From table 5 it is observed mean SGOT (mean ± S.D.) at the starting of study was 30.7000 ± 4.4379 mg/dl in Rosuvastatin (40 mg) groups and mean SGOT (mean ± S.D.) at the starting of study was 29.0667 ± 4.5783mg/dl in Atorvastatin (80 mg). Difference of mean was not statistically significant (p=0.2170).

Table 6: Distribution of mean SGPT at Starting of Statin and mean CPK Start in two doses of Statin

		No.	Mean	SD	Minimum	Maximum	Median	p-value
SGPT Start	Rosuvastatin (40 mg)	20	30.1000	5.7756	18.0000	40.0000	29.5000	0.6849
	Atorvastatin(80 mg)	30	30.8667	6.9418	19.0000	43.0000	31.5000	
CPK Start	Rosuvastatin (40 mg)	20	81.8500	34.4525	39.0000	166.0000	73.0000	0.4345
	Atorvastatin (80 mg)	30	90.9000	42.9060	23.0000	188.0000	88.0000	

From table 6 it is observed in Rosuvastatin (40 mg) group the mean SGPT (mean ± S.D.) at the starting of study was 30.1000 ± 5.7756 mg/dl. Where SGPT (mean ± S.D.) mean at the starting of study was 30.8667 ± 6.9418 mg/dl in Atorvastatin (80 mg) groups. Though difference of mean was not statistically significant (p=0.6849).
The mean CPK (mean ± S.D.) at the starting of study was 81.8500 ± 34.4525 mg/dl in group Rosuvastatin (40 mg) where as Atorvastatin (80 mg) group mean CPK (mean± S.D.) at the starting of study was 90.9000 ± 42.9060 mg/dl. So the difference was not statistically significant (p=0.4345).

Table 7: Distribution of mean SGOT after 3 months of statin therapy, mean SGPT at 3 months in two dose of Statin and mean CPK after 3months with two doses of statins

		No.	Mean	SD	Minimum	Maximum	Median	p-value
SGOT 3 months	Rosuvastatin (40 mg)	20	37.7000	7.8747	23.0000	56.0000	36.5000	0.3830
	Atorvastatin (80 mg)	30	35.6000	8.5080	23.0000	58.0000	34.0000	
SGPT 3 months	Rosuvastatin (40 mg)	20	35.5000	7.4728	22.0000	56.0000	34.0000	0.8024
	Atorvastatin (80 mg)	30	36.1333	9.4458	22.0000	60.0000	35.0000	
CPK 3 months	Rosuvastatin (40 mg)	20	97.0500	32.6875	56.0000	176.0000	88.5000	0.5027
	Atorvastatin (80 mg)	30	104.8333	44.0259	43.0000	198.0000	95.5000	

Table 7 shows mean SGOT (mean ± S.D) at 3 months was 37.7000 ± 7.8747 mg/dl in Rosuvastatin (40 mg) groups and mean SGOT (mean ± S.D) at 3 months was 35.6000 ± 8.5080 mg/dl in Atorvastatin (80 mg) groups. Difference of mean was not statistically significant (p=0.3830).
In Rosuvastatin (40 mg) group the mean SGPT (mean ± S.D.) at 3 months was 35.5000 ± 7.4728 mg/dl, whereas SGPT (mean ± S.D) mean at 3 months was 36.1333 ± 9.4458 mg/dl in Atorvastatin (80 mg) groups. Though difference of mean was not statistically significant (p=0.8024).
The mean CPK (mean ± S.D.) at 3 months was 97.0500 ± 32.6875 mg/dl in group Rosuvastatin (40 mg) where as Atorvastatin (80 mg) group mean CPK (mean ± S.D.) at 3 months was 104.8333 ± 44.0259 mg/dl. So the difference was not statistically significant (p=0.5027).

Table 8: Distribution of mean SGOT after 6 months with two doses of statins, mean SGPT 6 Months in two doses of statins and mean CPK after 6 Months in two doses of statins

		Number	Mean	SD	Minimum	Maximum	Median	p-value
SGOT at 6 Months	Rosuvastatin (40 mg)	20	47.7000	5.8747	23.0000	56.0000	36.5000	0.2452
	Atorvastatin (80 mg)	29	45.6897	5.6405	25.0000	155.0000	36.0000	
SGPT at 6 Months	Rosuvastatin (40 mg)	20	37.7000	7.0941	32.0000	56.0000	35.0000	0.2036
	Atorvastatin (80 mg)	30	42.8000	16.6742	26.0000	94.0000	36.0000	
CPK at 6 months	Rosuvastatin (40 mg)	20	121.3500	37.5980	66.0000	200.0000	110.5000	0.6387
	Atorvastatin (80 mg)	30	128.9333	64.7280	65.0000	331.0000	102.5000	

Table 8 shows mean SGOT (mean ± S.D.) at 6 months was 47.7000 ± 5.8747 mg/dl in Rosuvastatin (40 mg) groups and mean SGOT (mean± S.D) at 6 months was 45.6897 ± 5.6405 mg/dl in Atorvastatin (80 mg) groups. Difference of mean was not statistically significant (p=0.2452).
In Rosuvastatin (40 mg) group the mean SGPT (mean ± S.D,) at 6 months was 37.7000 ± 7.0941 mg/dl, whereas SGPT (mean ± S.D.) mean at 6 months was 42.8000 ± 16.6742 mg/dl in Atorvastatin (80 mg) groups. The difference of mean was not statistically significant (p=0.2036).
The mean CPK (mean ± S.D.) at 6 months was 121.3500 ± 37.5980 mg/dl in group Rosuvastatin (40 mg) where as Atorvastatin (80 mg) group mean CPK (mean ± S.D.) at 6 months was 128.9333 ± 64.7280 mg/dl. So the difference was not statistically significant (p=0.6387)

Table 9: Distribution of statins in DM patients and Dyslipidaemia patients

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
DM				
No	13	15	28	Chi-square value: 1.0958;
Row%	46.4	53.6	100.0	
Col %	65.0	50.0	56.0	p-value: 0.2951
Yes	7	15	22	
Row%	31.8	68.2	100.0	
Col %	35.0	50.0	44.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
Dyslipidaemia				
No	7	14	21	Chi-square value: 0.6705;
Row%	33.3	66.7	100.0	
Col %	35.0	46.7	42.0	p-value: 0.4128
Yes	13	16	29	
Row%	44.8	55.2	100.0	
Col %	65.0	53.3	58.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 9 shows 13 (46.4%) patients who had no DM and 7 (13.8%) patients who had DM had taken Rosuvastatin (40 mg). 15(68.2%) patients who had no DM and 15(50%) patients who had DM taken Atorvastatin (80 mg). Association between DM in two dose of statin was not statistically significant (p=0.2951).
7 (33.3 %%) patients who had no Dyslipidemia and 13(65.0%) patients who had Dyslipidemia taken Rasuvastatin (40 mg), whereas 14(46. 7%) who had no Dyslipidemia and 16(53.3%) who had taken Atorvastatin (80mg). Relationship in Dyslipidemia in two dose of statin was not statistically significant (p=0.4128)

Table 10: Distribution of bilirubin level after 3 months of statin therapy and after 6 months statins therapy

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
Bil 3 months				
Abnormal	0	0	0	Chi-square value: 0.0591;
Row %	0.0	0.0	0.0	
Col %	0.0	0.0	0.0	p-value: 0.8079
Normal	20	30	50	
Row %	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
Total	20	30	50	
Row %	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
Bil 6 months				
Abnormal	0	0	0	Chi-square value: 0.0591;
Row %	0.0	0.0	0.0	
Col %	0.0	0.0	0.0	p-value: 0.8079
Normal	20	30	50.0	
Row %	40.0	6.0	100.0	
Col %	100.0	100.0	100.0	
TotaL	20	30	50	
Row %	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 10 shows 1(5%) patients had abnormal bilirubin at 3 months in Rosuvastatin (40 mg) group and 2(6.7%) patients had abnormal bilirubin at 3 months in Atorvastatin (80 mg) group. Association between bilirubin at 3 months in two groups was not statistically significant (p=0.8079) 1(5%) patients had abnormal bilirubin at 6 months in Rosuvastatin (40 mg) group and 2(6.7%) patients had abnormal bilirubin at 6 months in Atorvastatin (80 mg) group. Association between bilirubin at 6 months in two groups was not statistically significant (p=0.8079

Table 11: Distribution of SGOT after 3 months with statin therapy and 6 months with statins therapy

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
SGOT at 3 months				
Abnormal	4	8	12	Chi-square value:
Row%	33.3	66.7	100.0	0.2924;
Col %	20.0	26.7	24.0	
Normal	16	22	38	p-value: 0.5886
Row%	42.1	57.9	100.0	
Col %	80.0	73.3	76.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
SGOT 6 months				
Abnormal	6	10	16	Chi-square value:
Row%	37.5	62.5	100.0	0.0613;
Col %	30.0	33.3	32.0	
Normal	14	20	34	p-value: 0.8044
Row%	41.2	58.8	100.0	
Col %	70.0	66.7	68.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 11 shows that 4 (20%) patients had abnormal SGOT in Rosuvastatin (40 mg) group and 8 (26.7%) patients had abnormal SGOT in Atorvastatin (80 mg) group. Association between SGOT at 3 months in two groups was not statistically significant (p=0.5886)
6 (30%) patients had abnormal SGOT in Rosuvastatin (40 mg) group and 10(33.3%) patients had abnormal SGOT in Atorvastatin (80 mg) group. Association between SGOT at 6 months in two groups was not statistically significant (p=0.8044)

Table 12: Abnormal distribution of SGPT at 3 months in two groups and SGPT after 6 months of statins therapy

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
SGPT 3 months				
Abnormal	4	8	12	Chi-square value:
Row%	33.3	66.7	100.0	0.2924;
Col %	20.0	26.7	24.0	
Normal	16	22	38	p-value: 0.5886
Row%	42.1	57.9	100.0	
Col %	80.0	73.3	76.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
SGPT 6 months				
Abnormal	6	10	16	Chi-square value:
Row%	37.5	62.5	100.0	0.0613;
Col %	30.0	33.3	32.0	
Normal	14	20	34	p-value: 0.8044
Row%	41.2	58.8	100.0	
Col %	70.0	66.7	68.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 12 shows that 4 (20%) patients had abnormal SGPT in Rosuvastatin (40 mg) group and 8(26.7%) patients had abnormal SGPT in Atorvastatin (80 mg) group. Association between SGPT at 3 months in two groups was not statistically significant (p=0.5886)
6 (30%) patients had abnormal SGPT in Rosuvastatin (40 mg) group and 10(33.3%) patients had abnormal SGPT in Atorvastatin (80 mg) group. Association between SGPT at 6 months in two groups was not statistically significant (p=0.8044)

Table 13: Distribution of CPK after 3 months of statins therapy and after 6 months of statins therapy

	Rosuvastatin (40 mg)	Atorvastatin(80 mg)	Total	
CPK 3 months				
Normal	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

CPK 6 months				
Abnormal	1	3	4	Chi-square
Row%	25.0	75.0	100.0	value: 0.4076;
Col %	5.0	10.0	8.0	
Normal	19	27	46	p-value:
Row%	41.3	58.7	100.0	0.5231
Col %	95.0	90.0	92.0	
Total	20	30	50	
Row%	40.0	60.0	100.0	
Col %	100.0	100.0	100.0	

Table 13 shows that 20 (100%) patients had normal CPK at 3 months in Rosuvastatin (40 mg) group and 30(100%) patients had normal CPK at 3 months in Atorvastatin (80 mg) group.
1 (5%) patients had abnormal CPK in Rosuvastatin (40 mg) group and 3 (10%) patients had abnormal CPK in Atorvastatin (80 mg) group. Association between CPK at 6 months in two groups was not statistically significant (p=0.5231)

Discussion

The present study was done with 50 patients with normal biochemical enzymatic level of liver and muscle. The patients were selected indoor and outdoor basis who were stable physically with dyslipidaemia disorder associated with mostly coronary or ischemic heart diseases. Some of them had coronary heart diseases underwent coronary interventions like stenting (post PCI) or CABG. Few of them had ischemic heart disease with or without high level of cholesterol (LDL, Triglyceride) or stable follow up case of acute coronary syndrome who were under medication without coronary intervention.

The total study period was 18 months from January 2016 to June 2017 with the individual study period was 6 months of each patient with evaluation of liver and muscle enzyme changes at 3 months and 6 months from the starting of high intensity Statins: Atorvastatin (80mg/day) and Rosuvastatin (40mg/day).

The study reveals out of total 50 patients, 34 (68%) were male and 16 (32%) patients were female in the age group of 35 to 75 years of which 7 (14%) were <50 years (35 to 50 years) and 43(86%) were >50 (51 to 75years). Of the 50 cases, 20 patients were post PCI follow up cases and 30 patients post ACS stable follow up cases with or without co-morbidities like Type 2 DM, hypercholesterolemia or hypertension. Out of 20 post PCI cases 8 patients (40%) were given Rosuvastatin (40mg) and 12 patients (60%) were given Atorvastatin (80mg).

In my present study out of 50 patients, 30 (60%) patients were given Atorvastatin (80mg) and 20 (40%) patients were given Rosuvastatin (40mg). In the group of Rosuvastatin, 13.33 %(n=4) patients were below 50 years of age and 86.63% (n=26) patients were above 50 years. In Rosuvastatin group 15 % (n=3) patients were below 50 years and 85 % (n=17) patients above 50 years. Overall 32% (n=16) female and 68 %(n=34) male patients were part in that present study.

At the time of first visit, the patients were screened for LFT mainly (SGPT, SGOT), and CPK for muscle injury along with other co-morbidities for inclusion criteria. After starting of high intensity statins they were subsequently re-evaluated for liver and muscle enzymes changes at 3 and 6 months.

The mean SGOT (mean+/-S.D.) at 3 months was 37.787+/-7.874 mg/dl in Rosuvastatin (40mg/day) group and mean SGOT (mean+/-S.D) 935.600+/-8.508 mg/dl in Atorvastatin (80mg) group respectively. The difference of mean was not statistically significant (p=0.3830). (Table-7). In 6 months study, the mean value of SGOT (mean+/-S.D.) was47.700+/-5.874mg/dl. In Rosuvastatin group (40mg/day) and in Atorvastatin group (80mg//day), the mean SGOT was 45.689+/-5.640mg/dl. The difference of mean of this group was not statistically significant (p=0.2450) (Table-8).

The mean SGPT (mean+/-S.D.) was 35.500+/-7.472mg/dl in Rosuvastatin group (40mg/day), whereas in Atorvastatin group the mean SGPT (mean+/-S.D.) was 36.133+/-9.445mg/dl at 3 months study. The difference of mean was not statically significant (p=0.8024) (Table-7). The mean SGPT (mean+/-S.D.) at 6 months study was 37.700+/-7.094mg/dl in Rosuvastatin (40mg) group, whereas in Atorvastatin (80mg) group the mean SGPT (mean+/-S.D.) was 42.800+/-16.674mg/dl. Here also the difference of mean was not statistically significant (P=0.2036) (Table-8).

So, the study reveals no significant changes of transaminase level with high intensity statins that matches the study result of SSSS (Scandinavian Simvastatin Survival Study), and JUPITER (Justification for the Use of Statin in Prevention: an Intervention Trial Evaluating Rosuvastatin), and the PPP (Prospective Pravastatin Pooling) project. In these studies indicated that there is no significant differences in transaminase levels in statin related and placebo groups (0.9% vs. 1.0%, and 0, 2% vs. 0, 1% respectively)[10,11].

The mean CPK (mean+/-S.D.) at 3 months study was97.687+/-32.687mg/dl in Rosuvastatin (40mg/day) group, whereas in Atorvastatin (80mg) group the mean CPK (mean+/-S.D.) was 104.833+/-44.025mg/dl. The difference of mean was not statistically significant (p=0.5027). (Table-7). And in 6 months study, the mean CPK (mean+/-S.D.) was 121.350+/-37.598mg/dl. In Rosuvastatin (40mg) group and was 128.933+/-64.720mg/dl. In Atorvastatin group. The difference of mean was not statistically significant (p=0. 638). (Table-9).

There were no abnormal changes (rise) in SGOT and SGPT level in 3 months study of Rosuvastatin and Atorvastatin but after 6 months study with high intensity Rosuvastatin and Atorvastatin, in both cases 1 patient had increased SGOT levels. The population group who had taken Rosuvastatin one (1.0) patient (5%) had increased level of SGOT level (146mg/dl) (Tab 37) and 19 patients (95%) had no abnormal changes of SGOT. The population group who had taken Atorvastatin, 1 patient (3.3%) also showed increased level of SGOT (155mg/dl and 29 patients (96.7%) had normal level of SGPT level. These two increased of SGOT was just above the 3 times of upper normal limit. Overall two patients (4%) had shown transaminitis after 6 months and both Rosuvastatin and Atorvastatin showed same effect over enzymes. And this difference of values had no statistical significant (p=0.768). But it does not mean that these two drugs had much injurious effect over liver as SGOT is nonspecific liver enzyme. It was also justified that there was no increase in SGPT level after 3 months of study.

At the end of 6 months, overall increase of SGPT was seen in 3 patients (6%) and 94% cases had normal values in both cases of Rosuvastatin and Atorvastatin of which out of 20 patients who had taken Rosuvastatin, 1 patients (5%) had increased values of SGPT(129mg/dl) and 95% patients had normal values and in Atorvastatin cases 2 patients (6.7%) had high rise of SGPT(136mg/dl) and 93.3% patients had normal limit of SGPT level. The difference of values was not statistically significant (p=0.807) (Table-12). Another study showed the direct relationship between dose and incidents of transaminases with higher doses. Indeed, the reported average incidence of elevation of serum ALT level of more than 3 times of upper normal limit is less than 1% in patients receiving low to moderate doses of statins and 2% to 3% incidence are seen in higher doses[12].

Abnormal CPK level were seen after 6 months of study in both Rosuvastatin and Atorvastatin. Out of 20 patients, 1 patient (5%) who had taken Rosuvastatin (40mg) had high CPK level (334mg/dl) and 19 patients (95%) had no changes. On the other hand who had taken high intensity Atorvastatin (80mg). 3 patients (10%) had high rise at 6 months – ranging from 245mg/dl to 309mg/dl. but 90% patients had

no changes of CPK values who had taken Atorvastatin. A Study showed after 3 months (12weeks) of treatment with Rosuvastatin, CPK levels increased marginally by 0.9U/L, SGOT levels were decreased significantly by 36.5IU/L (P=0.01), and SGPT level were non significantly reduced by 5.3IU/L (p=>0.05)[13,14].

These abnormal changes were not above 3 times of UNL and had no statistical significant (p=0.523). These changes were seen more in Atorvastatin thane Rosuvastatin group.

Although most of the patients complain myalgia in early part of therapy with both Atorvastatin and Rosuvastatin, auto resolution of myalgia were seen in later part of study. Another study showed 87% patients had CPK greater 1-3 times of upper normal limit,10% >3-5 times of UNL and 3% had >5 times of UNL of CPK[15].

There were no significant changes in bilirubin level after 3 months and 6 months of Rosuvastatin and Atorvastatin therapy. Negligible changes of bilirubin were seen ranging from 1.1 to 1.3mg/dl which were much lower than 3 times of upper normal limit (p>0.05). There were also insignificant changes seen in dyslipidaemia and diabetic patients in respect to bilirubin, SGOT, SGPT and CPK level. No other significant changes found in relation to serum urea, creatinine, Na+, K+.

Conclusion

In this study with Rosuvastatin 40mg/day and Atorvastatin 80 mg/d were given in patients suffering from coronary heart diseases with or without comorbidities for six months resulting in few cases with transient elevation of liver enzymes (SGOT, SGPT) and muscle enzyme (CPK).

Most of the cases these enzyme elevation were within the upper level of normal values. Very few cases had shown elevation of these enzymes were above the upper normal limit but not above the 3 times of upper normal limit and had not statistically significant. The changes (Elevation) were seen in mostly in patients who were older between 60 to 75 years and were associated with comorbidities. Both the statins caused a decrease in coronary events and complications. Rosuvastatin seems to have a greater decrease in abnormal changes of liver transaminase and creatine phosphokinase when compared to Atorvastatin. Complaints of myalgia seen in least number of patients in early part of study but decreased in intensities in later part of study. Both the statins had a good safety profile with few adverse effects. Atorvastatin being cheaper than Rosuvastatin but the lipid lowering efficacy were more or less same. The study was able to describe the comparative efficacy of Atorvastatin verses Rosuvastatin in respect to liver function and muscle enzymes. This study also showed that the Rosuvastatin is more cost effective compared to Atorvastatin. For future research the study should be done in a large sample and for long duration of period as a multicentre study.

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Ethical approval

The study was approved by the institutional ethics committee

References

1. Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, Qizilbash N, Peto R, Collins R (December 2007). "Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths". Lancet 370 (9602): 1829–39.
2. Jump up to: Mahmood, Levy, Vasan, Wang (2013). "The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective"(fee required). Lancet 27 (9921): 61752–3.
3. Taylor F, Huffman MD, Macedo AF, Moore TH, Burke M, Davey Smith G, Ward K, Ebrahim S (2013)."Statins for the primary prevention of cardiovascular disease". Cochrane Database Syst Rev 1: CD004816.
4. Naci H, Brugts J, Ades T (2013). "Comparative tolerability and harms of individual statins: a study- level network meta-analysis of 246 955 participants from 135 randomized, controlled trials". Doi:10.1161/CIRCOUTCOMES. 111.000071. PMID 23838105.
5. Abd TT, Jacobson TA (May 2011). "Statin-induced myopathy: a review and updat." Expert opinion on drug safety 10 (3): 373–87.
6. Taylor, FC; Huffman, M; Ebrahim, S (11 December 2013). "Statin therapy for primary prevention of cardiovascular disease." JAMA 310 (22): 2451–2.
7. Tonelli M, Lloyd A, Clement F, Conly J, Husereau D, Hemmelgarn B, Klarenbach S, McAlister FA, Wiebe N, Manns B (2011). "Efficacy of statins for primary prevention in people at low cardiovascular risk: a meta-analysis". CMAJ 183 (16): E1189–202.
8. Kostis WJ, Cheng JQ, Dobrzynski JM, Cabrera J, Kostis JB (2012). "Meta-analysis of statin effects in women versus men". J. Am. Coll. Cardiol. 59 (6): 572–82. Doi: 10
9. Petretta M, Costanzo P, Perrone-Filardi P, Chiariello M (2010). "Impact of gender in primary prevention of coronary heart disease with statin therapy: a meta-analysis". Int. J. Cardiol. 138 (1): 25–31.
10. Heart Protection Study Collaborative Group MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high risk individuals: a randomized placebo-controlled trial. Lancet 2002; 360(9326):7-22.
11. Pfeffer MA, Keech A, Sacks FM, et al. Safety and tolerability of pravastatin in long-term clinical trials: Prospective Pravastatin Pooling (PPP) Project. Circulation 2002; 105(20):2341-2346.
12. Moran, AE; Forouzanfar, MH; Roth, GA; Mensah, GA; Ezzati, M; Flaxman, A; Murray, CJ; Naghavi, M (8 April 2014). "The global burden of ischemic heart disease in 1990 and 2010: the Global Burden of Disease 2010 study". Circulation. 129 (14): 1493–501.
13. Charles EC, Olson KL, Sandhoff BJ, McClure DL, Merenich JA. Evaluation of cases of severe statin–related transaminitis within a large health maintenance organization. Am J Med. 2005;118(6):618-624].
14. Centers for Disease Control and Prevention, (CDC) (14 October 2011). "Prevalence of coronary heart disease—United States, 2006–2010.". MMWR. Morbidity and mortality weekly report. 60 (40): 1377–81. PMID 21993341.
15. Heeschen C, Hamm CW, Laufs U, et al. on behalf of the Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Investigators. Withdrawal of statins increases event rates in patients with acute coronary syndromes. Circulation. 2002;105:1446–1452.

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