WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 15, 1310-1338. Research Article ISSN 2277– 7105

A STUDY ON COMPARATIVE LIPID LOWERING, EFFICACY AND SAFETY OF ATORVASTATIN VERSUS ROSUVASTATIN IN HYPERLIPIDEMIA

Prasanth Vas Sahu*, B.A. Vishwanath, Bharathi Kalyanam, Phool Kumari Shah, Pravin Rajbanshi, Praveen Kumar and Brunda M.S

Department of Clinical Pharmacy, Aditya Bangalore Institute of Pharmacy Education and Research, Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka.

Article Received on
02 October 2017,
Revised on 23 Oct. 2017,
Accepted on 13 Nov. 2017
DOI: 10.20959/wjpr201715-9722

***Corresponding Author**
Prasanth Vas Sahu
Department of Clinical Pharmacy, Aditya Bangalore Institute of Pharmacy Education and Research, Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka.

ABSTRACT

Background: Elevated levels of blood lipids are well documented risk factors for cardiovascular disease. Current classification schemes and treatment levels for hyperlipidemia are based on the National Cholesterol Education Panel's (NCEP) Adult Treatment Program-3 (ATP-III) guidelines. Globally, a third of ischaemic heart disease is attributable to high cholesterol. Overall, raised cholesterol is estimated to cause 2.6 million deaths (4.5% of total) and 29.7 million disability adjusted life years (DALYS), or 2.0% of total DALYS. Raised total cholesterol is a major cause of disease burden in both the developed and developing world as a risk factor for Ischemic heart disease and stroke. Statins are the preferred class of drugs to lower elevated low density lipoprotein cholesterol (LDL-C). New guidelines from ATP-IV are expected to be released in the near future, but in the meantime physicians are faced with uncertainty about how low to target LDL-C, whether to pharmacologically treat high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) levels and how best to achieve target goals. Study on drug use evaluation on a tertiary care hospital was conducted. **Objectives:** The comparison of Hyperlipidemic drugs such as ATORVASTATIN and ROSUVASTATIN by analysing the appropriateness of prescription with special reference to:

- Selection of antihyperlipidemic drugs (ATORVASTATIN and ROSUVASTATIN) in various clinical conditions
- Concomitant drugs used

- Switched therapy
- Frequency of administration
- Drug-wise distribution
- Lab data collection

Methods and Methodology: comparison of antihyperlipidemic drugs in a tertiary care hospital is a retrospective and prospective study, patients who were satisfying the inclusion criteria was enrolled into the study conducted for the period of 6 months. Data collection form and other relevant source from Medical Record department are used as source of data and materials. **Results:** 150 hyperlipidemic cases were examined and 59% were male and 41 % female. Where ATORVASTATIN 50.66% and ROSUVASTATIN 49.33% were used, according to age wise distribution hyperlipidemic patients was found as following, 31-40 years 7.33%, 41-40 years 14%, 51-60 years 25.33%, 61-70 years 36%, 71-80 years 10.66%, 81-90 years 6.66%. where we found age between 61-70 years were more hyperlipidemic patients. Comparison between two drugs we found lipid lowering data which shows the effectiveness of the drugs where 5mg of ROSUVASTATIN shows 41% LDL-C reduction whereas ATORVASTATIN 10mg shows 38% LDL-C reduction, similarly 10mg ROSUVASTATIN shows 47% LDL-C reduction and atorvastatin 20mg shows 41% LDL-C reduction, 20mg ROSUVASTATIN shows 55% LDL-C reduction and 40mg ATORVASTATIN shows 47% LDL-C reduction, 40mg ROSUVASTATIN shows 63% and 80mg ATORVASTATIN shows 55% LDL-C reduction. Which shows ROSUVASTATIN is more effective than ATORVASTATIN. Comparison between two drugs we got p-value of ROSUVASTATIN is 0.021178 and ATORVASTATIN is 0.44964. which shows the effectiveness of the drugs, as per our study we found ROSUVASTATIN is more effective than ATORVASTATIN. **Conclusion:** To conclude, although this study had a small sample size it gave us an overall idea about the comparative study on lipid lowering efficacy and safety profile of ATORVASTATIN versus ROSUVASTATIN in hyperlipidemia in a Tertiary Care Hospital. Despite of the fact that patient with Renal Impairment were contraindicated to use ROSUVASTATIN. The current study revealed that although ATORVASTATIN was prescribed more frequently than ROSUVASATIN but effectiveness of ROSUVASTAIN was more than that compared to ATORVASTATIN. Most of the patient who reported with Hyperlipidemia to the hospital were prescribed ATORVASTATIN.

KEYWORDS: Comparison, efficacy, and lipid lowering.

OBJECTIVE OF THE STUDY

PRIMARY OBJECTIVE: To compare the lipid lowering and efficacy of atorvastatin and rosuvastatin in hyperlipidemia condition.

SECONDARY OBJECTIVE

- To evaluate the efficacy of atorvastatin based on
  - Frequency of administration
  - Duration of therapy
  - Drug wise distribution
  - Disease wise distribution
  - Switched-therapy
  - Reason for switching

- To evaluate the efficacy of rosuvastatin based on
  - Frequency of administration
  - Duration of therapy
  - Drug wise distribution
  - Disease wise distribution
  - Switched-therapy
  - Reason for switching

- To compare the efficacy of both drugs

INTRODUCTION

Hyperlipidemia refers to increased levels of lipids (fats) in the blood, including cholesterol and triglycerides. Although hyperlipidemia does not cause symptoms, it can significantly increase your risk of developing cardiovascular disease, including disease of blood vessels supplying the heart (coronary artery disease), brain (cerebrovascular disease), and limbs (peripheral vascular disease). These conditions can in turn lead to chest pain, heart attacks, strokes, and other problems. Because of these risks, treatment is often recommended for people with hyperlipidemia.

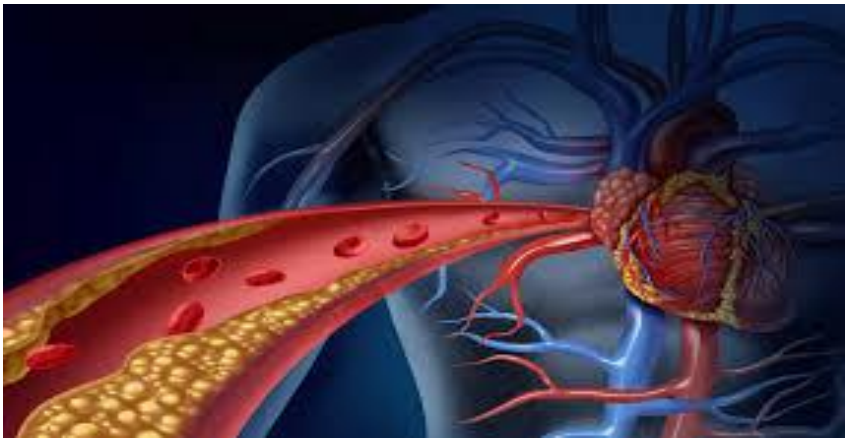
Hyperlipidemia is a mouthful, but it's really just a fancy word for too many lipids – or fats – in the blood. That can cover many conditions, but for most people, it comes down to two well-known terms: high cholesterol and high triglycerides. Our bodies make and use a certain

amount of cholesterol every day, but sometimes that system gets out of whack, either through genetics or diet. Higher levels of the “good" HDL cholesterol are associated with decreased risk of heart disease and stroke. HDL helps by removing cholesterol from your arteries, which slows the development of plaque. The “bad” LDL cholesterol, on the other hand, can lead to blockages if there’s too much in the body.

A cholesterol test generally determines the 4 distinct numbers: Total Cholesterol, HDL, LDL, Triglycerides (TG).

High-density lipoprotein (HDL) is the good cholesterol that benefits your heart. This cholesterol works by transporting damaging low-density lipoprotein and very-low-density lipoprotein to your liver, where they are broken down, allowing your body to eliminate them. High-density lipoprotein is the only type of cholesterol that needs to be above, versus below, a certain level. Ideally, HDL cholesterol should be over 60 milligrams per deciliter.

Low-density lipoprotein (LDL) is very damaging to your cardiovascular system. It builds up on arterial walls, making them stiff and causing blood clots. As heart works harder to push blood through your clogged blood vessels, your blood pressure goes up. Over time, the extra wear and tear on heart makes heart muscle weak, elevating your risk of heart disease. Low-density lipoprotein needs to stay below 100 milligrams per deciliter.



TOTAL CHOLESTEROL = HDL + LDL + (0.2*TRIGLYCERIDES)

According to the National Cholesterol Education Program(NCEP), if a person has no other risk factors, an LDL-C level can be evaluated as follows: Less than 100 mg/dL (2.59 mmol/L) — Optimal. 100-129 mg/dL (2.59-3.34 mmol/L) — Near optimal, above optimal. 130-159 mg/dL (3.37-4.12 mmol/L) — Borderline high.

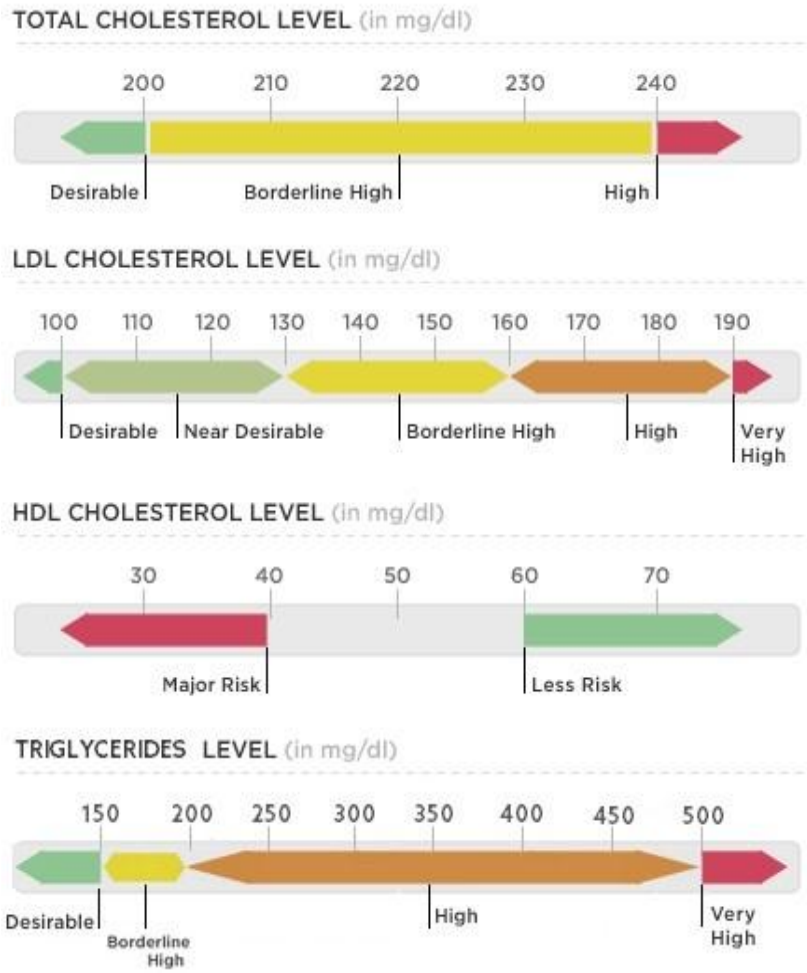
A typical level of HDL-C is between 40-50 mg/dL (1.0-1.3 mmol/L) for men and between 50-59 mg/dl (1.3-1.5 mmol/L) for women and is associated with average risk of heart disease. Based on many epidemiologic studies, HDL-C of 60 mg/dL (1.55 mmol/L) or higher is associated with a less than average risk of heart disease.

A simple blood test can reveal whether your triglycerides fall into a healthy range. Normal — Less than 150 milligrams per deciliter (mg/dL), or less than 1.7 millimoles per liter (mmol/L)
Borderline high — 150 to 199 mg/dL (1.8 to 2.2 mmol/L)
High — 200 to 499 mg/dL (2.3 to 5.6 mmol/L)

Total Cholesterol Level	Category
Less than 200mg/dL	Desirable
200-239 mg/dL	Borderline high
240mg/dL and above	High

LDL (Bad) Cholesterol Level	LDL Cholesterol Category
Less than 100mg/dL	Optimal
100-129mg/dL	Near optimal/above optimal
130-159 mg/dL	Borderline high
160-189 mg/dL	High
190 mg/dL and above	Very High

HDL (Good) Cholesterol Level	HDL Cholesterol Category
Less than 40 mg/dL	A major risk factor for heart disease
40—59 mg/dL	The higher, the better
60 mg/dL and higher	Considered protective against heart disease



Causes

Cholesterol, a waxy substance, is a type of fat your body makes. It can also come from what you eat. Foods that have cholesterol, saturated fat, and trans fats can raise your blood cholesterol level. These include:

1. Cheese
2. Egg yolks
3. Fried and processed foods
4. Ice cream
5. Pastries
6. Red meat

Don't exercise much? That can lead to putting on extra pounds, which can raise your cholesterol.

As you get older, your cholesterol levels often creep up, too.

Hyperlipidemia can run in families. People who inherit the condition can get very high cholesterol. That means they have a much greater chance of having a heart attack, even when they're young.

Primary causes of Cholesterol Elevation

1. eating a diet high in saturated fat
2. not being physically active
3. being overweight or obese
4. smoking
5. having a large waist circumference.

Secondary causes

1. type 2 diabetes
2. underactive thyroid gland (hypothyroid)
3. kidney problems
4. liver problems
5. alcohol intake

High cholesterol can be inherited

If one of your parents, a brother or a sister has high cholesterol you might too.

There are over 100 genes that can affect blood fats and how these are metabolised in the body.

1. Familial* Hypercholesterolaemia (FH)
2. Familial* Combined Hyperlipidaemia (FCH)
3. Type 3 Hyperlipidaemia
4. Polygenic Hypercholesterolaemia
5. Lysosomal Acid Lipase Deficiency (LALD)

Symptoms and Risks

Most people with hyperlipidemia can't tell that they have it at first. It's not something you can feel, but you'll notice the effects of it someday.

Cholesterol, along with triglycerides and other fats, can build up inside your arteries. This makes the blood vessels narrower and makes it more difficult for blood to get through. Your blood pressure could go up.

The buildup can also cause a blood clot to form. If a blood clot breaks off and travels to your heart, it causes a heart attack. If it goes to brain, it can cause a stroke.

Statins are a class of drugs often prescribed by doctors to help lower cholesterol levels in the blood. By lowering the levels, they help prevent heart attacks and stroke. Studies show that, in certain people, statins reduce the risk of heart attack, stroke, and even death from heart disease by about 25% to 35%. Studies also show that statins can reduce the chances of recurrent strokes or heart attacks by about 40%.

Statin drugs work by blocking the action of the liver enzyme that is responsible for producing cholesterol. Too much cholesterol in the blood can cause a buildup of plaque on the walls of the arteries. That buildup can eventually cause the arteries to narrow or harden. Sudden blood clots in these narrowed arteries can cause a heart attack or stroke.

Statins lower LDL cholesterol and total cholesterol levels. At the same time, they lower triglycerides and raise HDL cholesterol levels. Statins may also help to stabilize plaques in the arteries. That makes heart attacks less likely.

Statins, also known as HMG-CoA reductase inhibitors, are a class of lipid-lowering medications. Statins have been found to reduce cardiovascular disease (CVD) and mortality in those who are at high risk. The evidence is strong that statins are effective for treating CVD in the early stages of a disease (secondary prevention) and in those at elevated risk but without CVD (primary prevention).

They act by inhibiting the enzyme HMG CoA reductase, which controls synthesis of cholesterol in the liver. Most manufacturers of statins recommend that they **are taken at night**, on the basis of physiological studies which show that most cholesterol is synthesised when dietary intake is at its lowest.

Statins are widely prescribed for the primary and secondary prevention of coronary artery disease. They act by inhibiting the enzyme HMG CoA reductase, which controls synthesis of cholesterol in the liver. Most manufacturers of statins recommend that they are taken at night, on the basis of physiological studies which show that most cholesterol is synthesised when dietary intake is at its lowest. One small clinical trial found that taking smaller doses of simvastatin than are used in treatment, in the morning, was less efficient. However, a trial

using atorvastatin found no significant difference in cholesterol concentrations between patients taking the statin in the morning and those taking it in the evening.

HMG-CoA reductase (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase, officially abbreviated HMGCR) is the rate-controlling enzyme of the mevalonate pathway, the metabolic pathway that produces cholesterol and other isoprenoids.

HMG-CoA reductase is the rate-limiting enzyme for cholesterol synthesis and is regulated via a negative feedback mechanism mediated by sterols and non-sterol metabolites derived from mevalonate, the product of the reaction catalyzed by reductase. Normally in mammalian cells this enzyme is suppressed by cholesterol derived from the internalization and degradation of low density lipoprotein (LDL) via the LDL receptor. Competitive inhibitors of the reductase induce the expression of LDL receptors in the liver, which in turn increases the catabolism of plasma LDL and lowers the plasma concentration of cholesterol, an important determinant of atherosclerosis. Alternatively spliced transcript variants encoding different isoforms have been found for this gene.

People with CVD — Several large trials have demonstrated that aggressive lipid lowering is beneficial in people with coronary heart disease. Many healthcare providers recommend treating all patients with CVD with high-dose statin therapy. People who have a heart attack (myocardial infarction or MI) are started on cholesterol-lowering medication while in the hospital and are advised to make lifestyle changes, regardless of their low-density lipoprotein (LDL) cholesterol level (see "Patient education: Heart attack recovery (Beyond the Basics)"). In addition to simply placing a patient on statin therapy, some healthcare providers recommend that lipid lowering treatment achieve specific goals in patients with known CVD:

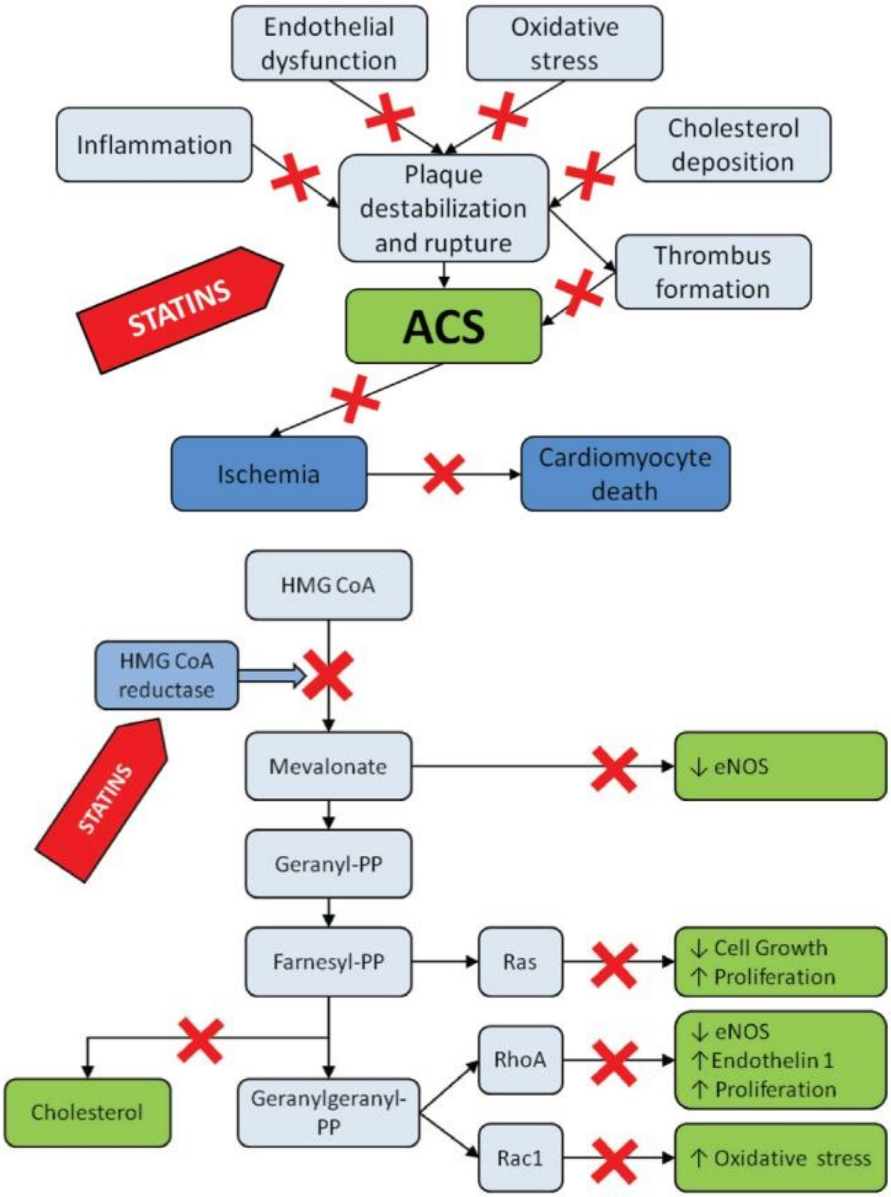
- A target LDL cholesterol level below 70 to 80 mg/dL (1.81 to 2.07 mmol/L) is recommended for people who have CVD and have multiple major risk factors (eg, people with diabetes or who smoke).
- A target LDL cholesterol level less than 100 mg/dL (2.59 mmol/L) is recommended for people who have CVD but do not have many additional risk factors. Lifestyle changes as well as nonstatin medications may be recommended when LDL cholesterol levels are higher than 100 mg/dL (2.59 mmol/L).

Why statins as first line drug therapy?

It has repeatedly been shown that statins decrease morbidity and mortality in patients with atherosclerosis, thus supporting their use for the primary and secondary prevention of ischemic heart disease. Different pathological pathways that are triggered in the setting of acute coronary syndrome (ACS), such as endothelial dysfunction, activation of inflammatory and coagulation cascades, and thrombus formation, are known to be inhibited by statins, thereby justifying the use of these agents in patients with ACS. Several recent prospective controlled clinical trials have demonstrated the safety and, in some cases, the efficacy of statins when administered early after ACS. An increasing number of publications have reported, however, that statins may confer a beneficial effect not only in early secondary prevention, but also in the direct treatment of ACS (ie, when statins are administered as first-line treatment in clinically unstable patients). This therapeutic option is supported by the following: numerous experimental studies demonstrating a protective effect of statins under conditions of acute ischemia; analysis of different registries and trials, which has demonstrated a more favourable prognosis for statin-treated patients at the time of acute myocardial ischemia; and small clinical trials reporting a lower periprocedural infarction rate during coronary intervention or lower levels of several prognostic biomarkers, in addition to a lower incidence of cardiovascular events associated with statin therapy. Nevertheless, confirmation of this hypothesis in large prospective controlled clinical trials will be necessary before the implementation of statins as first-line therapy in unstable patients with ACS, irrespective of blood cholesterol levels.

Statins that are approved for use in the U.S. include:

- Atorvastatin (Lipitor),
- Fluvastatin (Lescol, Lescol XL),
- Lovastatin (Mevacor, Altoprev),
- Pravastatin (Pravachol),
- Rosuvastatin (Crestor),
- Simvastatin (Zocor), and
- Pitavastatin (Livalo).



Among all the above used Statins Drug therapy the most frequently used are Rosuvastatin & Atorvastatin.

Atorvastatin is in a group of drugs called 3-hydoxy-3 methylglutaryl coenzyme (HMG CoA) reductase inhibitors, or "statins." Atorvastatin reduces levels of "bad" cholesterol (low-density lipoprotein, or LDL) and triglycerides in the blood, while increasing levels of "good" cholesterol (high-density lipoprotein, or HDL).

Atorvastatin are available in strength(s): 10 mg; 20 mg; 40 mg; 80 mg.

Rosuvastatin is an HMG-CoA reductase inhibitor, also known as a "statin." It works by reducing the production of certain fatty substances in the body, including cholesterol.

Loweringhigh cholesterol and triglycerides in certain patients. It also increases high-density lipoprotein (HDL) ("good") cholesterol levels. It is used to slow atherosclerosis (narrowing of the arteries) in patients with high blood cholesterol levels. It is used in certain patients to reduce the risk of heart attack or stroke. It is also used in certain patients to reduce the need for medical procedures to open blocked heart vessels.

Rosuvastatin are available in strength(s): 5 mg; 10 mg; 20 mg; 40 mg.

METHODOLOGY

➢ Duration of Study

The study was conducted for a period of 6 month.

➢ Site of the Study

Study was conducted in a tertiary care hospital.

➢ Study Design

A hospital based comparative study.

➢ Sources of Data and Materials

- Patient case sheet (inpatient).
- Medication/treatment chart.
- Laboratory data report.
- Suitable design documentation form.

➢ Study Criteria

Inclusion criteria

- Department of Cardiology

Exclusion criteria

- Department of Pediatrics
- Department of Neurology

➢ Method of Data Collection

- Data collection form

➢ Stastistical analysis

- Chi-squre test

STUDY PROCEDURE

This is a comparative study, the patients who were satisfying the inclusion criteria will be enrolled into the study with the help of patient consent form. The clinical pharmacist will review the patient case notes, medication chart, laboratory data and other prevalent data.

A suitable designed data collection form will be used to record all the necessary data including patient demographic details, patient medication history, and reason for admission, any allergic reaction, medication details and lab investigation.

Drug related problem (DRPs) will be identified and evaluated by referring Micromedex and standard text books and finding will be discusses with the physicians to reduce DRPs.

LIMITATION

- The study was done for a short term period of 6 months.
- A longer term study with a larger group of patients can be carried out in cardiology department with more number of follow –ups.

RESULTS AND INTERPRETATION

Table 1: Gender Wise Categorization

S.N	Gender	No. of Patients	Percentage
1.	Male	88	58.66%
2.	Female	62	41.33%

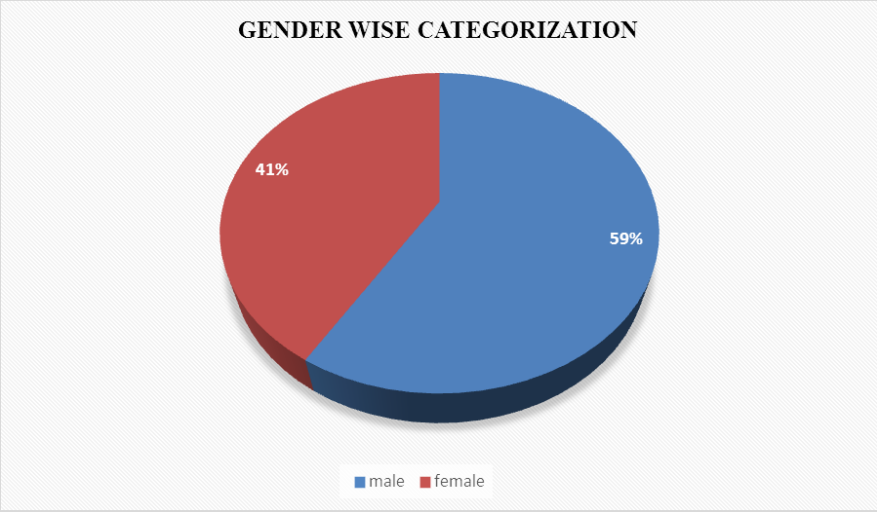


Figure 1: Gender categorization.

During the course of the study, the total number of subjects were 150 and out of these population, 88 were Males and 62 were Females which resembles the 59 % of Male and 41% of Female Patients out of the counter Sample (100%).

Table 2: Drug wise categorization.

S.N	DRUGS	NO.OF PATIENTS	PERCENTAGE
1.	ATORVASTATIN	76	50.66%
2.	ROSUVASTATIN	74	49.33%

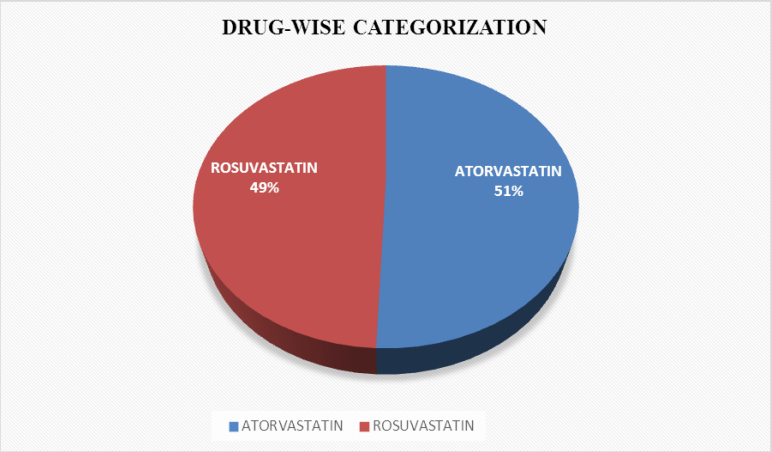


Figure 2: Drug categorization.

During the course of study of 150 patients, as compared among the concerned drugs, it has been observed that ATORVASTATIN (50.66%) was prescribed more than the ROSUVASTATIN (49.34%) for the effectiveness of Hyperlipidemia.

Table 3: Drug wise categorization in male and female.

S.N	DRUGS	GENDER	NO.OF PATIENTS	PERCENTAGE
1.	ATORVASTATIN	MALE	45	51.13%
2.	ATORVASTATIN	FEMALE	31	50%
3.	ROSUVASTATIN	MALE	43	48.86%
4.	ROSUVASTATIN	FEMALE	31	50%

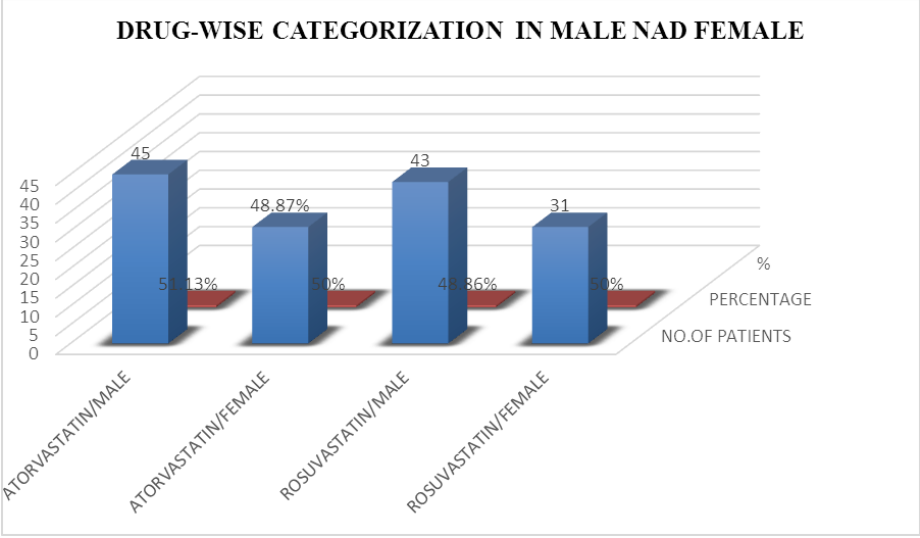


Figure 3: Drug categorization in male and female.

During the study done in 150 subjects, from the above table as mentioned we found that the ATORVASTATIN in Male subjects was prescribed more compared to ROSUVASTATIN (51% & 49%) respectively but in case of Female subjects ATORVASTATIN & ROSUVASTATIN were prescribed equally (50 % - 50%).

Table 4: Age Wise Distribution.

S.N	AGE GROUP(YEARS)	NO.OF PATIENTS	% OF PATIENTS
1.	31-40	11	7.33%
2.	41-50	21	14%
3.	51-60	38	25.33%
4.	61-70	54	36%
5.	71-80	16	10.66%
6.	81-90	10	6.66%

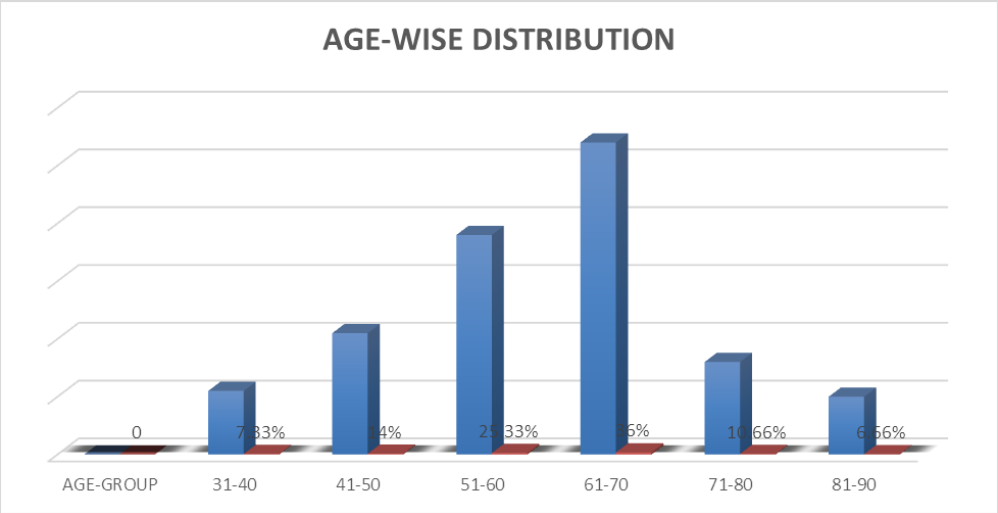


Figure 4: Age Wise Distribution.

During the course of the study in among the 150 subjects, it has been observed that Patient aged 61-70 Years with Hyperlipidemia (36% out of the counter sample) were more in number compared to the other aged group Patients.

Table 5: Atorvastatin Switched To Rosuvastatin.

S.N	DRUGS	NO.OF PATIENTS	PERCENTAGE
1.	ATORVASTATIN	47	31.33%
2.	ATORVASTATIN TO ROSUVASTATIN	29	19.34%
3.	ROSUVASTATIN	74	49.33%

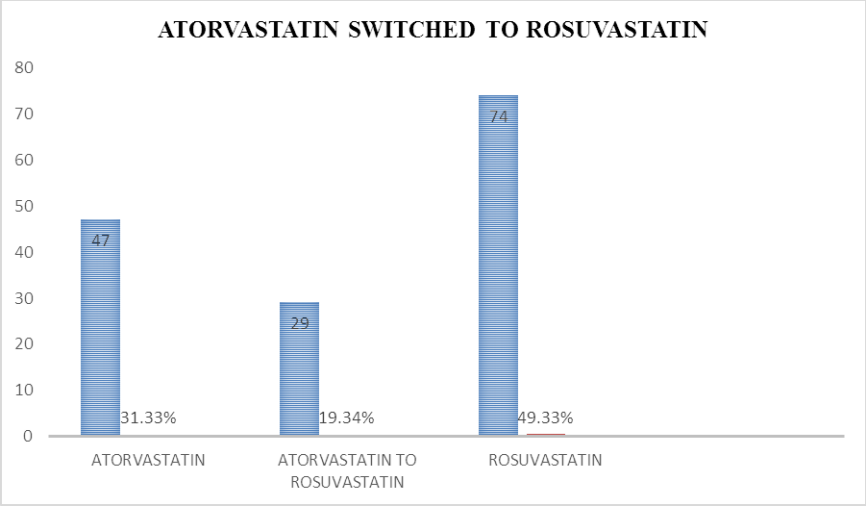


Figure 5: Atorvastatin switched to Rosuvastatin.

Among all the prescriptions during the course of the study, the patient earlier taking ATORVASTATIN switched to ROSUVASTATIN was found to be 19.34%.

Table 6: Comparison of lipid lowering effects between hyperlipidemic drugs, atorvastatin and rosuvastatin.

IN ATORVASTATIN

CLASS INTERVAL	31-40	41-50	51-60	61-70	71-80	81-90
FREQUENCY	9	8	25	22	6	6

CLASS INTERVAL	MID VALUE (X)	FREQUENCY (F)	FX	DEVIATION (d) (x-x̄)	Frequency deviaton (Fd)
31-40	35.5	9	319.5	-23.5	-211.5
41-50	45.5	8	364	-13.5	-108
51-60	55.5	25	1387.5	-3.5	-87.5
61-70	65.5	22	1441	6.5	143
71-80	75.5	6	453	16.5	99
81-90	85.5	6	513	26.5	159
	∑X=363	∑F=76	∑FX=4478	∑(x-x̄) =9	∑|Fd|= -6

Arithmetic mean (x̄) = ∑FX/∑F

= 4478/76

= 59

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

SD = √∑(9)^2/6-1

= √81/5 = 4.02

P value- 0.044964, significant

IN ROSUVASTATIN

CLASS INTERVAL	31-40	41-50	51-60	61-70	71-80	81-90
FREQUENCY	2	13	13	32	10	4

CLASS INTERVAL	MID VALUE (X)	FREQUENCY (F)	FX	DEVIATION (d) (x-x̄)	Frequency deviaton (Fd)
31-40	35.5	2	71	-26.35	-52.7
41-50	45.5	13	591.5	-16.35	-212.55
51-60	55.5	13	721.5	-6.35	-82.55
61-70	65.5	32	2096	3.65	116.8
71-80	75.5	10	755	13.65	136.5
81-90	85.5	4	342	23.65	94.6
	∑X=363	∑F=74	∑FX=4577	∑(x-x̄) =11.9	∑|Fd|=0.1

Arithmetic mean (x̄) = ∑FX/∑F

= 4577/74

= 61.84

$$s = \sqrt{\frac{\sum(x - \bar{x})^2}{n - 1}}$$

SD = √∑(11.9)^2/6-1

= √141.61/5 = 5.321

P value- 0.021178, significant

Table 6: comparison of lipid lowering effects between hyperlipidemic drugs, atorvastatin and rosuvastatin.

DRUGS	STANDARD DEVIATION	P-VALUE
ATORVASTATIN	4.02	0.044964
ROSUVASTATIN	5.321	0.021178

The P value for ROSUVASTATIN is 0.021178 and ATORVASTATIN is 0.044964 which shows ROSUVASTATIN is more effective in LIPID lowering as there is 2% probability difference exists while ATORVASTATIN shows 4% probability difference exists.

Table 7: Lipid Lowering Data.

ROSUVASTATIN	ATORVASTATIN	MEAN LDL-C (mg/dL)	DECREASED LDL-C BY ROSUVASTATIN (mg/dL)	DECREASED LDL-C BY ATORVASTATIN (mg/dL)
5MG	10MG	140	57.5	54
10MG	20MG	140	66	58
20MG	40MG	140	77	67
40MG	80MG	140	88	77

Figure 7: Lipid lowering data.

In the above table as per 6 weeks review after the patient had been asked for lipid tests, it has been observed that ROSUVASTATIN 5 MG and ATORVASTATIN 10 MG reduced 57.5 mg/dL whereas 54 mg/dL respectively and it also concludes that being ROSUVASTATIN half the strength of ATORVASTATIN-10 it was more effective to reduce the levels of lipid.

Table 8: Effectiveness of the Drugs.

ROSUVASTATIN	ATORVASTATIN	%DECREASED LDL-C BY ROSUVASTATIN	%DECREASED LDL-C BY ATORVASTATIN
5MG	10MG	41%	38%
10MG	20MG	47%	41%
20MG	40MG	55%	47%
40MG	80MG	63%	55%

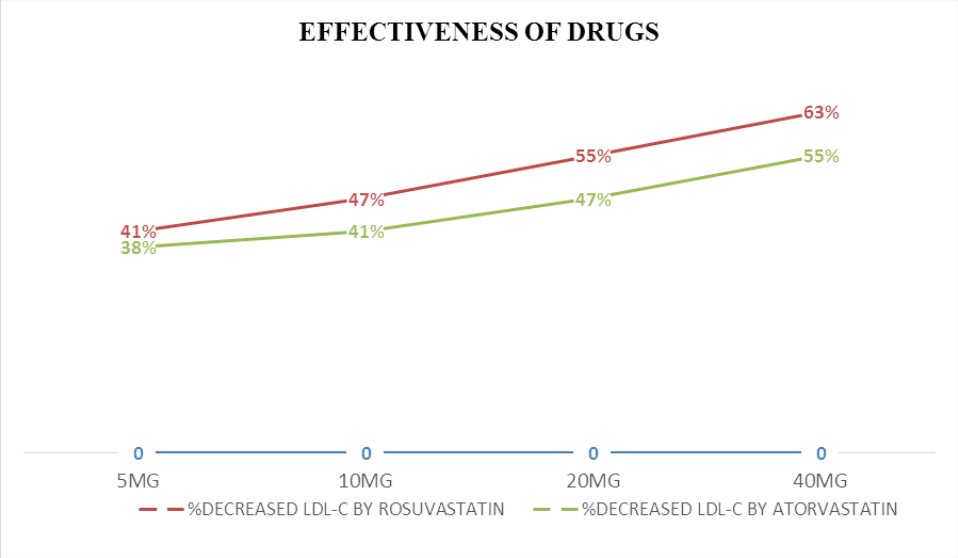


Figure 8: Effectiveness of the Drugs.

From the above data ROSUVASTATIN 5mg shows 41% decreased LDL-C in other hand ATORVASTATIN 10mg shows 38% decreased LDL-C which shows the effectiveness of the drugs. So it is believed that although ROSUVASTATIN being with low dose of 5 mg showed more effectiveness than ATORVASTATIN being taken 10 mg which means with double the strength of ROSUVASTATIN-5 mg i.e 10 mg (5mg*2 =10 mg) and even with this dose showing the 7.31% less effectiveness compared to the ROSUVASTATIN.

Table 9: Patients on Statins Therapy under Concomitant Conditions.

DISEASE	ATORVASTATIN		ROSUVASTATIN	
	NO.OF PATIENTS	PERCENTAGE	NO.OF PATIENTS	PERCENTAGE
CVD	67	34%	65	35%
DM	40	20%	41	21%
HTN	56	28%	49	26%
CKD	12	6%	9	5%
OTHERS	24	12%	24	13%

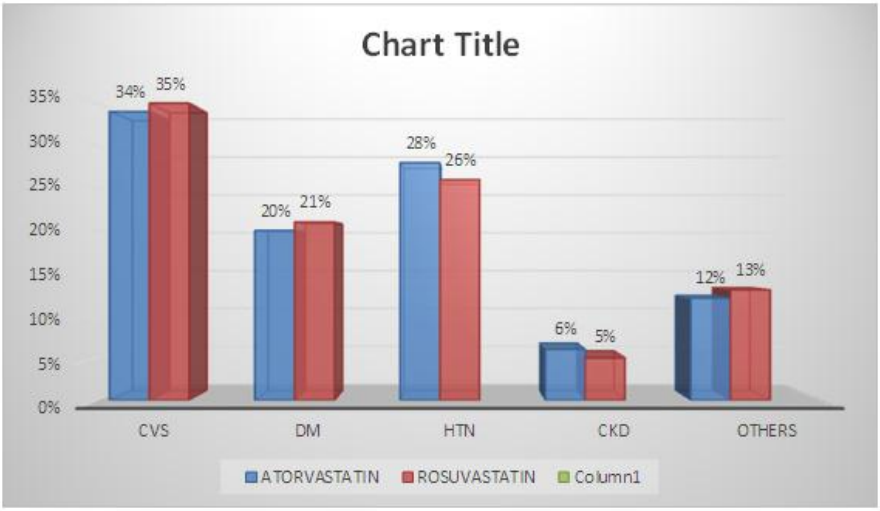


Figure 9: Patients on statins therapy under concomitant conditions.

In the above table as per concomitant therapy conditions of statins usage, the use of ATORVASTATIN & ROSUVASATIN was more in Cardiovascular Disease(CVD) compared to the usage of statins in the concomitant therapy of DM, HTN, CKD & others.

Table 10: Comparison number of patients with Adverse drug reaction.

Adverse drug reaction	Atorvastatin	Rosuvastatin
Headache	3	2
Drowsiness	2	1
Constipation	1	2
myalgia	1	0
Renal failure	0	1
total	7	6

Figure 11: Comparison number of patients with Adverse drug reaction.

In 150 patients, we found adverse drug reaction with ATORVASTATIN total 7 number of patients and wih ROSUVASTATIN total 6 number of patients, which shows both the drugs are not much harmful for patients. According to our data ATORVASTATIN is more safe in renal disease condition than ROSUVASTATIN.

Teble 11: Reason for switching from atorvastatin to rosuvastatin.

REASON FOR SWITCHING	NO.OF PATIENTS	PERCENTAGE
DIABETES MELLITUS	12	41%
HYPERTENSION	9	31%
CVD	8	28%
TOTAL	29	100%

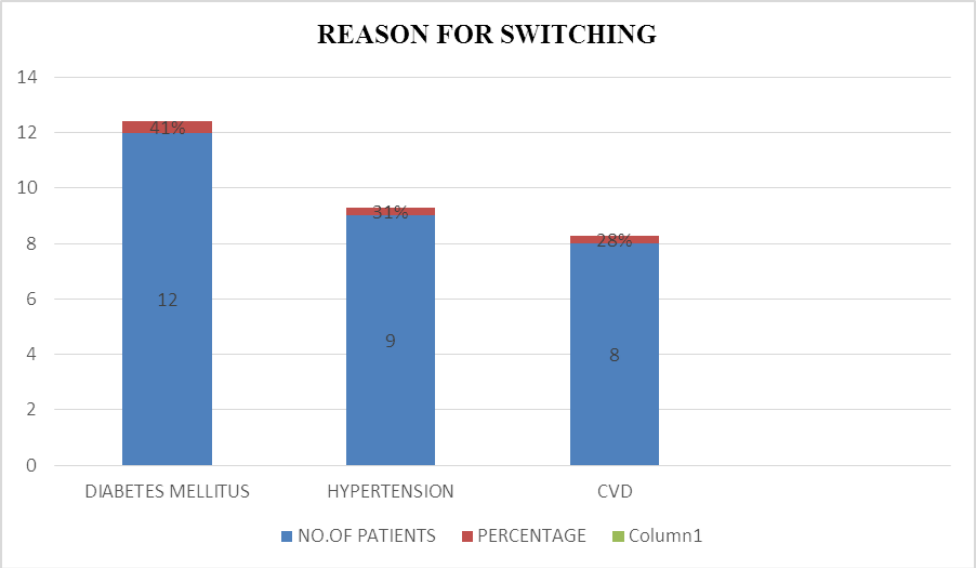


Figure-12.

DISCUSSION

Hyperlipidemia an abnormal increase in the levels of fats (lipids), including cholesterol, in the blood. This may be of dietary origin or may be due to PANCREATITIS or bile system disorder or may be a dangerous familial disorder of dominant inheritance. Most people with familial hyperlipidemia develop serious coronary artery disease before the age of 50.

Hyperlipidemia results in CHD or atherosclerosis at other sites, symptoms may include chest pain (angina), heart attack, or stroke. Hyperlipidemia itself does not produce symptoms. When levels are exceedingly high, cholesterol may be deposited (xanthomas) in tendons or just beneath the skin under the eyes. Very high triglyceride levels may result in the formation of nodules on the elbows or knees, or the appearance of multiple, pimple-sized, yellowish skin eruptions. The skin deposits fats or xanthomas. Swelling of organs such as the liver, spleen, or pancreas (pancreatitis). Blockage of blood vessels in brain and heart.

Hyperlipidemia can be inherited and increases the risk of disease of the blood vessels leading to stroke and cardiovascular diseases. Statins are the mainstay in the management of

dyslipidemia. Outcome trials of statins have proved conclusively that these drugs decrease LDL-C levels, resulting in a significant reduction of cardiovascular events in many high-risk patients. ROSUVASTATIN has been considered superior in achieving greater LDL-C level reductions as compared to ATORVASTATIN.

A recent study published by the *New England Journal of Medicine* pitted two of the top statins against each other to see which is more effective ATORVASTATIN and ROSUVASTATIN.

Over 1,000 patients with heart disease participated in this study — half of whom took the maximum daily dose of atorvastatin (80 mg) while the other half were prescribed the maximum daily dose of ROSUVASTATIN (40 mg). After following participants for more than two years, researchers found that ROSUVASTATIN was more effective in lowering "bad cholesterol" and raising "good cholesterol." However, maximal doses of both drugs were equally effective in helping to reverse heart disease by clearing about 1% of plaque from the arteries, and resulted in similar rates of side effects and cardiac events among patients.

Based on findings, ATORVASTATIN and ROSUVASTATIN are equally as safe and effective in lowering cholesterol and possibly reversing plaque build-up with aggressive treatment. And although rosuvastatin may help decrease LDL cholesterol better than atorvastatin.

In our study elevated Lipid Levels compared Across doses to ROSUVASTATIN (5-40mg) and ATORVASTATIN (10-80mg), showed ROSUVASTATIN (5mg shows 41% reduction in LDL-C) was more effective in lowering "bad cholesterol", than ATORVASTATIN (10mg shows 38% reduction in LDL-C).

FIGURE 1*:* TABLE 1-GENDER WISE CATEGORIZATION

During the course of the study, the total number of subjects were 150 and out of these population, 88 were Males and 62 were Females which resembles the 59 % of Male and 41% of Female Patients out of the counter Sample (100%).

TABLE 2: DRUG WISE CATEGORIZATION

During the course of study of 150 patients, as compared among the concerned drugs, it has been observed that ATORVASTATIN (50.66%) was prescribed more than the ROSUVASTATIN (49.34%) for the effectiveness of Hyperlipidemia.

TABLE 3: DRUG WISE CATEGORIZATION IN MALE AND FEMALE

During the study done in 150 subjects, from the above table as mentioned we found that the ATORVASTATIN in Male subjects was prescribed more compared to ROSUVASTATIN (51% & 49%) respectively but in case of Female subjects ATORVASTATIN & ROSUVASTATIN were prescribed equally (50 % - 50%).

TABLE 4: AGE WISE DISTRIBUTION

During the course of the study in among the 150 subjects, it has been observed that Patient aged 61-70 Years with Hyperlipidemia (36% out of the counter sample) were more in number compared to the other aged group Patients.

TABLE 5: ATORVASTATIN switched to ROSUVASTATIN

Among all the prescriptions during the course of the study, the patient earlier taking ATORVASTATIN switched to ROSUVASTATIN was found to be 19.34%.

TABLE 6: COMPARISON OF LIPID LOWERING EFFECTS BETWEEN HYPERLIPIDEMIC DRUGS, ATORVASTATIN AND ROSUVASTATIN

As per our study and the understanding from the literature it has been found that ROSUVASTATIN is more effective in lowering the lipid levels compared to the ATORVASTATIN therapy so has been proved from the P value calculated from the above table. The P value for ROSUVASTATIN is 0.021178 and ATORVASTATIN is 0.044964 which shows ROSUVASTATIN is more effective in LIPID lowering as there is 2% probability difference exists while ATORVASTATIN shows 4% probability difference exists.

TABLE 7: LIPID LOWERING DATA

In the above table as per 6 weeks review after the patient had been asked for lipid tests, it has been observed that ROSUVASTATIN 5 MG and ATORVASTATIN 10 MG reduced 57.5 mg/dL whereas 54 mg/dL respectively and it also concludes that being ROSUVASTATIN half the strength of ATORVASTATIN it was more effective to reduce the levels of lipid**.**

TABLE 8: EFFECTIVENESS OF THE DRUGS

From the above data ROSUVASTATIN 5mg shows 41% decreased LDL-C in other hand ATORVASTATIN 10mg shows 38% decreased LDL-C which shows the effectiveness of the drugs. So it is believed that although ROSUVASTATIN being with low dose of 5 mg showed more effectiveness than ATORVASTATIN being taken 10 mg which means with double the strength of ROSUVASTATIN-5 mg i.e 10 mg (5mg*2 =10 mg) and even with this dose showing the 7.31% less effectiveness compared to the ROSUVASTATIN.

TABLE 9: PATIENTS ON STATINS THERAPY UNDER CONCOMITANT CONDITIONS

In the above table as per concomitant therapy conditions of statins usage, the use of ATORVASTATIN & ROSUVASATIN was more in Cardiovascular Disease(CVD) compared to the usage of statins in the concomitant therapy of DM, HTN, CKD & others.

TABLE 10: COMPARISON NUMBER OF PATIENTS WITH ADVERSE DRUG REACTION

Out of 150 patients, thirteen patients complained adverse drug reaction. In present study we found, ATORVASTATIN only contributed in four number of all reported adverse effects including headache, drowsiness, myalgia and constipation, whereas ROSUVASTATIN found to be reason for six number of adverse effects including renal impairment, drowsiness, headache and constipation.

FUTURE PLAN

- The study can be designed to determine the long term effects of medicines, LDL-C level can control on quality of life of patients in hyperlipidemic disease condition.
- The study can be carried out for long term patients follow-up to identify effect of ATORVASTATIN and ROSUVASTATIN in hyperlipidemic patients.

ACKNOWLEDGEMENTS

“If any of you lack wisdom, let him ask of God, who gives to all liberally and reproach, and it will be given to him.”

We are deeply indebted to the Almighty **GOD**, for enabling us to complete this project work in a fine manner.W e owe a great deal of thanks to many people who supported us with their time and encouragement throughout this enormous project work.

We are very grateful to **RGUHS** for granting us permission to do this work.

The present study has been undertaken and completed under the expert guidance and encouragement of **Mrs. Bharathi Kalyanam, M.Pharm** Guide, department of Clinical Pharmacy, ABIPER.

We are very grateful to the HOD **Mr.** for his unending help and support throughout our project.

We express our deepest sense of gratitude to **Mr. Ram Kumar, Principal of ABIPER** , for his sincere gratitude and support.

Our sincere thanks to **Dr. Praveen Kumar, Dr. Ritty Sara Cherian, Dr. Nagalatha** and other teachers for providing their support to accomplish this wonderful work.

We would like to express our deep sense of love and affection to our **colleagues** for their kind help, co-ordination and support throughout our graduation. You all are the one who made everything beautiful, funny and happy.

At this moment we would love to express our thanks to our **Juniors, non-teaching staffs** for supporting us throughout our work in their own way.

We take this opportunity to thank the **Liberian** for extending library facilities throughout tis study.

We are grately indebated to our beloved parents **Mr.Ramprasad shah, Mrs. Sabitri Devi Shah, Mr. Tulasi Das Sahu, Mrs. Puspa Latha Sahu and Mr.Pitambar Rajbanshi, Mrs. Shyama Kumari Rajbanshi** for their unending Prayers, Love, Faith, Encouragement and Support throughout this wonderful journey. We are sure about experiencing such sweetest love and care in our future ahead too.

We express our deepest and sincere thanks to the **Cardiology department** (Dr.Mahadev D.Dixit, Dr.Pradeep Kumar.D, Dr.Raghu.B and Dr.Sanjay Bhat), **other Doctors, Management ,Lab technician, Nurses** of Tertiary Care Hospital for allowing us to collect all the primary informations required for the study. We are grateful to you all.

We extend our special thanks to computer operator, printers and binders for their technical assistance and preparation of this manuscript on time.

Last but not the least, we extend our thanks to all those who have been directly or indirectly associated with our study.

CONCLUSION

To conclude, although this study had a small sample size it gave us an overall idea about the comparative study on lipid lowering efficacy and safety profile of ATORVASTATIN versus ROSUVASTATIN in hyperlipidemia in a Tertiary Care Hospital. Despite of the fact that patient with Renal Impairment were contraindicated to use ROSUVASTATIN. The current study revealed that although ATORVASTATIN was prescribed more frequently than ROSUVASATIN but effectiveness of ROSUVASTAIN was more than that compared to ATORVASTATIN. Most of the patient who reported with Hyperlipidemia to the hospital were prescribed ATORVASTATIN.

The present study revealed that polypharmacy and prescription by brand names were common. Use of generic name in the prescriptions need to be promoted and encouraged.

REFERENCE

1. Brunzell JD Failor RA. Diagnosis and Treatment of dyslipidemia. In: Dale DC, Federman DD. ACP MEDICINE. 3rd ed. New York: WebMD Inc, 2007; 729-47.
2. Talbert RL. Dyslipidemia. In: Diprio JT, editor. Pharmacotherapy-A Pathophysiological Approach. 8th ed. New York: McGraw-Hill, 2008; 365-88.
3. Brewer HB Jr. New features of the National Cholesterol Education Program Adult Treatment Panel III lipid-lowering guidelines. ClinCardiol, 2003; 26(S3): 19-24.
4. Farnier M, Picard S. Diabetes: Statins, fibrates, or both. CurrAtheroscler Rep, 2001; 3(1): 19-28.
5. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panal III).Final report. Circulation, 2002; 106(25): 3143-421.
6. Goodmamgillman. Drug therapy for hyperlipidemia and dyslipidemia. In: Laurence L, Bruton, Bruce A, chabner, BjornC, Knollmann. The pharmacological basis of therapeutics. New York, 2012; 824-845.

7. Kumar T, Kapoor A. Premature coronary artery disease in North Indians: An angiography study of 1971 patients. Indian Heart J, 2005; 57: 311-8.
8. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart, 2008; 94: 16-26.[PubMed].
9. Lanca A J. Hyperlipidemia and cardiovascular disease. CME resource, 2010; 136(2): 66 [5] Li J-J, Lu Z-L, Kou W-R, Chen Z, Wu Y-F, Yu X-H, et al. Impact of Xuezhikang on coronary events in hypertensive patients with previous myocardial infarction from China Coronary Secondary Prevention Study (CCSPS). Ann Med, 2010; 42: 231–40.
10. Nicholls SJ, Tuzcu EM, Sipachi I, Schoenhagen P, Hazen SL, Ntanios F, et al. Effects of obesity on lipid-lowering, anti-inflammatory, and anti- atherosclerotic benefits of atorvastatin or pravastatin in patients with coronary artery disease (from the REVERSAL study). Am J Cardiol, 2006; 97: 1553–7.
11. Parks Text Book of Preventional and Social Medicine, 18th Edition, Ch., 6: 286-287.
12. Editorial, Cardiology Today: Nove-Dec 1997-Vol-1, Vol-2.
13. Jacobe, N.J., Van Demark, P.J. (1960) Arch Biochem. Biophys. 88,250. [4] Trinder, P (1960) Amn. Clin. Biochem., 6.24 [5] Bucolo G., David M.Clin. Chem, 1973; 19: 476.
14. Ravi GR, Pradeepa R, Mohan V. Hyperlipidemia and coronary artery disease. An Update. Indian Heart J, 2004; 56: 21-6.
15. Kumar T, Kapoor A. Premature coronary artery disease in North Indians: An angiography study of 1971 patients. Indian Heart J, 2005; 57: 311-8.
16. Wierzbicki AS, Lumb PJ, Semra Y, Chik G, Christ ER, Crook MA. Atorvastatin compared with simvastatin based therapies in the management of severe familial hyperlipidemia. QJM, 1999; 92: 387-94.
17. Fleg JL, Mete M, Howard BV, Umans JG, Roman MJ, Ratner RE, et al. Effect of statins alone versus statins plus ezetimibe on carotid atherosclerosis in type 2 diabetes: The SANDS (Stop Atherosclerosis in Native Diabetics Study) trial. J Am CollCardiol, 2008; 52: 2198-205.
18. Josan K, Majundar SR, Mcalister FA. The efficacy and safety of intensive statin therapy: A meta analysis randomized trials. CMAJ, 2008; 176: 576-83.
19. Miettinen TA. Diurnal variation of LDL and HDL cholesterol. Ann Clin Res, 1980; 12: 295-8.
20. Saito Y, Yoshida S, Nakaya N, Hata Y, Goto Y. Comparison between morning and evening doses of simvastatin in hyperlipidemic subjects: a double-blind comparative study. Arterioscler Thromb, 1991; 11: 816-26.

21. Cilla DD, Gibson DM, Whitfield LR, Sedman AJ. Pharmacodynamic effects of atorvastatin after administration to normocholesterolaemic patients in the morning and evening. J Clin Pharmacol, 1996; 36: 604-9.
22. Bandolier. Cholesterol fairy home to roost. *Bandolier,* 2001; 88: 7. www.jr2.ox.ac.uk/bandolier/band88/b88-7.html (accessed 15 Aug 2003).
23. Kiortsis DN, Giral P, Bruckert E, Turpin G. Factors associated with low compliance with lipid-lowering drugs in hyperlipidemic patients. J Clin Pharm Ther, 2000; 25: 445-51.
24. Comparison of the efficacy of rosuvastatin versus atorvastatin in achieving lipid goals: results from the STELLAR trial. McKenney JM1, Jones PH, Adamczyk MA, Cain VA, Bryzinski BS, Blasetto JW; STELLAR Study Group.
25. Comparative Study of Atorvastatin and Rosuvastatin in Combination with Fenofibrate in mixed Hyperlipidemia Rohit Dixit and Shankar Jagan, Department of Pharmacology, Navodaya Medical College, INDIA, Medical Review Safety Physician, Accenture, Chennai, INDIA.
26. Journal of Lipids Volume 2014 (2014), Article ID 875907, 5 pages http://dx.doi.org/10.1155/2014/875907 Research Article, Comparison of Low-Dose Rosuvastatin with Atorvastatin in Lipid-Lowering Efficacy and Safety in a High-Risk Pakistani Cohort: An Open-Label Randomized Trial.
27. Jones PH1, Hunninghake DB, Ferdinand KC, Stein EA, Gold A, Caplan RJ, Blasetto JW; Statin Therapies for Elevated Lipid Levels Compared Across Doses to Rosuvastatin Study Group. Erratum in Clin Ther, 2005 Jan; 27(1): 142.
28. Am J Manag Care. 2007 Dec;13 Suppl 10:S270-5 Fox KM1, Gandhi SK, Ohsfeldt RL, Davidson MH.S.
29. Effect of rosuvastatin compared with other statins on lipid levels and National Cholesterol Education Program goal attainment for low-density lipoprotein cholesterol in a usual care setting. Bullano MF1, Wertz DA, Yang GW, Kamat S, Borok GM, Gandhi S, McDonough KL, Willey VJ.
30. Guidelines for lowering lipids to reduce coronary artery disease risk: a comparison of rosuvastatin with atorvastatin, pravastatin, and simvastatin for achieving lipid-lowering goals. Shepherd J1, Hunninghake DB, Barter P, McKenney JM, Hutchinson HG.
31. Atorvastatin vs. Rosuvastatin Study shows both cholesterol-lowering drugs are equally safe and effective. BY AMERICAN COLLEGE OF CARDIOLOGY.

32. A Comparison of Statin Therapies in Hypercholesterolemia in Women: A Subgroup Analysis of the STELLAR Study. Welty, Francine K.; Lewis, Sandra J.; Friday, Karen E.; Cain, Valerie A.; Anzalone, Deborah.
33. Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. JAMA, 1998; 280: 605–613.
34. Mora S, Glynn RJ, Hsia J, et al. Statins for the primary prevention of cardiovascular events in women with elevated high-sensitivity C-reactive protein or dyslipidemia: Results from the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) and meta-analysis of women from primary prevention trials. Circulation, 2010; 121: 1069–1077.
35. Igase M, Kohara K, Tabara Y, et al. Low-dose rosuvastatin improves the functional and morphological markers of atherosclerosis in asymptomatic postmenopausal women with dyslipidemia. Menopause, 2012; 19: 1294–1299.
36. Pasternak RC, Smith SC, Jr, Bairey-Merz CN, et al. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. J Am Coll Cardiol, 2002; 40: 567–572.
37. McKenney JM, Davidson MH, Jacobson TA, Guyton JR. Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. Am J Cardiol, 2006; 97: 89C–94C.
38. Singh RB, Rastogi SS, Rastogi V, Niaz MA, Madhu SV, Chen M, Shoumin Z. 1997. Blood pressure trends, plasma insulin levels and risk factors in rural and urban elderly populations of north India.Coron Artery Dis, 8: 463-468.
39. Downs JR, Clearfield M, Weis S, Whitney E, Shapiro DR, Beere PA, Langendorfer A, Stein EA, Kruyer W, Gotto AM, Jr. 1998. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA 279: 1615-1622.
40. Grundy SM, Cleeman JI, Merz CN, Brewer HB, Jr., Clark LT, Hunninghake DB, Pasternak RC, Smith SC, Jr., Stone NJ. 2004. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation, 110: 227-239.

41. Hill JS, Hayden MR, Frohlich J, Pritchard PH. 1991. Genetic and environmental factors affecting the incidence of coronary artery disease in heterozygous familial hypercholesterolemia. Arterioscler Thromb, 11: 290-297.
42. Chen Z, Peto R, Collins R, MacMahon S, Lu J, Li W. 1991. Serum cholesterol concentration and coronary heart disease in population with low cholesterol concentrations. BMJ, 303: 276-282.
43. Khoo KL, Tan H, Liew YM, Deslypere JP, Janus E. 2003. Lipids and coronary heart disease in Asia. Atherosclerosis, 169: 1-10.
44. Khoo KL, Tan H, Liew YM. 1997. Serum lipids and their relationship with other coronary risk factors in healthy subjects in a city clinic.Med J Malaysia, 52: 38-52.
45. Rafidah HM, Azizi A, Noriah MN. 2008. Blood pressure variability and arterial elasticity in hyperlipidaemic subjects.Singapore Med J, 49: 297-303.
46. Bhatt DL, Steg PG, Ohman EM, Hirsch AT, Ikeda Y, Mas JL, Goto S, Liau CS, Richard AJ, Rother J, Wilson PW. 2006. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. Jama, 295: 180-189.
47. WHO. 1999. 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension. Guidelines Subcommittee. J Hypertens.
48. Scheuner MT, Whitworth WC, McGruder H, Yoon PW, Khoury MJ. 2006. Expanding the definition of a positive family history for early-onset coronary heart disease.Genet Med, 8: 491-501.
49. 2009. Standards of medical care in diabetes--2009. Diabetes Care, 32(Suppl 1): S13-61.
50. NCEP. 2001. Executive Summary of The Third Report of The National Cholesterol.