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Assessment of Lipid Profile and Serum Creatinine Kinase in Subjects with Hyperlipidemia on Moderate Intensity Statin Therapy Attending a Postgraduate Teaching Hospital in South India

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Authors' contributions

This work was carried out in collaboration among all authors. Author TKMM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors RTS and KGR supervised the study. All authors read and approved the final manuscript.

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ABSTRACT

Atherosclerosis of large and medium sized arteries are believed to be the major reason behind the development of Coronary Artery Diseases and Hyperlipidemia has been found to be one of the most important contributing factors. Appropriate lifestyle changes along with proper drug therapy lead to a considerable reduction in mortality rate due to coronary artery disease. Reduction of LDL Cholesterol is the primary goal of cholesterol-lowering therapy, but most of the patients are usually unable to achieve the treatment goals with lifestyle modifications alone; and in such situations, drug therapy is essential to prevent the disease progression and further future complications. The aim of the study was to demonstrate impact of three moderate intensity statins on lipid profile and biomarker representing muscle toxicity. It was a prospective observational study conducted in a tertiary care teaching hospital in south India. Patients of both gender falling the age group between 30 and 70 years with newly diagnosed Hyperlipidemia attending the Department of Medicine OPD,

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were enrolled in the study. Total 229 participants were enrolled in study and all the drug treatment were found to be effective in achieving the treatment goal; at the same time Rosuvastatin 10 mg treatment group exhibited better efficacy along with minimal muscle toxicity.

Keywords: Atherosclerosis; cardiovascular diseases; lipid profile; serum creatinine kinase; statin therapy.

1. INTRODUCTION

Cardiovascular diseases (CVD) are those abnormal conditions related with the heart and blood vessels, which is considered as one of the leading causes of morbidities and mortalities worldwide [1]. The overall risk for CVD starts for an individual at their young age without a known risk for CVD, Coronary heart disease (CHD) accounts for approximately one-third to one-half of the total cases of CVD [2]. The most common CVDs are hypertension, coronary artery disease (CAD), cerebrovascular disease, and peripheral vascular disease [3]. Hypertension, hyperlipidemia, diabetes, obesity, sedentary lifestyle, improper diet, alcohol consumption and tobacco use are considered to be the modifiable risk factors leading to CVDs. Among them hyperlipidemia, diabetes, hypertension, obesity, and smoking are identified to be accountable for more than half of CVD mortality [4]. Cholesterol is an important parameter that frequently gets connected to the onset of CVD and the word itself has turned into a derogatory, widely considered as a next to a toxic substance that encompasses human blood vessels and produces unfortunate healthy situations. Cholesterol transportation in the body is made with the help of lipoproteins and there are two types of lipoproteins: LDL leads to an upsurge of cholesterol in arteries and HDL transports the cholesterol from various part of the body back to the liver [5].

The National Cholesterol Education Programme (NCEP) guidelines define Hyperlipidemia as a serum Total Cholesterol levels >200 mg/dl, serum Triglyceride level >150 mg/dl, Serum HDL cholesterol levels <40 mg/dl (for men) and <50 mg/dl (for women) and LDL cholesterol levels >130 mg/dl [6]. Hyperlipidemia is a disorder of lipoprotein metabolism, which includes a number of abnormalities such as hypercholesterolemia, hypertriglyceridemia and low levels of high-density lipoprotein cholesterol. Hyperlipidemia usually result from an inherited defect in lipoprotein metabolism or most commonly from a combination of genetic and lifestyle factors [7]. The cholesterol, fat, calcium and other substances found in the blood together develop form plaque in the intima of blood vessels including coronary arteries. Hyperlipidemia is believed to be the main contributing factor behind the plaque deposition and thus increased chance of developing CVD by obstructing the flow of blood to the heart [8]. Several studies in various population have demonstrated that the develop ment of hyperlipidemia positively correlated with the risk of heart disease. The elevated levels of total cholesterol, triglycerides and LDL are believed to increase the likelihood of heart disease, whereas high levels of HDL reduce the chance [9].

The physicians have relied on the standard lipid panel including total cholesterol, LDL, HDL, and triglycerides to assess their patients' risk for CVD since many years [10]. The risk status assessment of a standard lipid profile along with smoking, and family history are recommended as an integral component of approaches to cardiovascular risk prediction and appropriate drug therapy along with lifestyle modification might help to reduce the future complications [11]. Elevated LDL is the primary target for therapy and reduction of LDL is the primary goal of cholesterol-lowering therapy. Statins are the drug of choice for most of the clinicians and indications of statins have been greatly extended over the last several years [12]. Statin are HMG CoA Reductase Inhibitors and they reduce the plasma cholesterol by inhibiting the de-novo synthesis of cholesterol and increase the LDL catabolism. They also decrease the triglyceride levels and may increase HDL cholesterol levels [13]. Various studies conducted in different populations demonstrated the effectiveness of the moderate intensity statin therapy in Hyperlipidemia and it was found to be beneficial in reducing the Low Density Lipoprotein Cholesterol level. The dose dependent, mild and transient adverse effects are usually observed with statin therapy; they include gastrointestinal symptoms, altered liver function tests and muscle aches. Myopathy and disintegration of skeletal muscle have been rarely reported with statin therapy [14]. Before starting statin therapy Liver

function tests are normally advised in patients with hepatic insufficiency and serum creatine kinase levels is evaluated in patients with muscle complaints. The aim of the study was to assess the impact of moderate intensity statin therapy (Atorvastatin 10 mg, Atorvastatin 20 mg and Rosuvastatin 10 mg) on lipid profile and serum creatinine kinase in newly diagnosed Hyperlipidemia patients attending a teaching hospital in south India.

2. METHODOLOGY

It was a prospective observational study conducted at the Department of Medicine, MES Medical College Hospital Perinthalmanna; a super specialty teaching hospital under MES academy of Medical sciences, Perinthalmanna located in South India. The new patients with suspected Hyperlipidemia attending the Department of Medicine OPD, during the study period were considered for the study. Male and female patients with age between 30 and 70 years with newly diagnosed Hyperlipidemia as per National Cholesterol Education Programme (NCEP) guidelines were enrolled in the study. Participants with comorbidities including Hypertension, Diabetes Mellitus or both were also included in the study. Pregnant & lactating women, patients with renal or hepatic diseases, patients with history of use of lipid lowering medicines, Patients with hypothyroidism, malignancy or myopathy, patients who had undergone bypass surgery and those who taking Immunosuppressant medications, Azole antifungal agents, Protease inhibitors were excluded from the study. After the detailed clinical examination, the drug therapy with suitable statin of appropriate dose was prescribed by the treating Physician. The details of the diagnosis and drug therapy were well explained and written informed consent in vernacular language was obtained from each participant before enrolment. After conducting direct patient interview, the demographic details and anthropometric parameters of the participants were collected from the Medical Record Department after discussions with treating clinicians. Also the baseline values of lipid profile and serum creatinine kinase were collected. Total 229 subjects were enrolled and they were categorised to different treatment groups based on the drug and strength prescribed to Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10. Participants were followed up until their 1 year of treatment and changes in lipid profile and biochemical parameters related with muscle toxicity were recorded and statistically evaluated.

3. RESULTS AND DISCUSSION

Participants of different age group are distributed in all treatment groups; Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10. The age wise distribution of treatment group is given in Graph 1. The number of younger Hyperlipidemic patients found very less in number; whereas patients in the age group of 50 to 60 years found higher in number. Rosuvastatin found to be prescribed large in number for patients falling age group of 50 to 70 years.

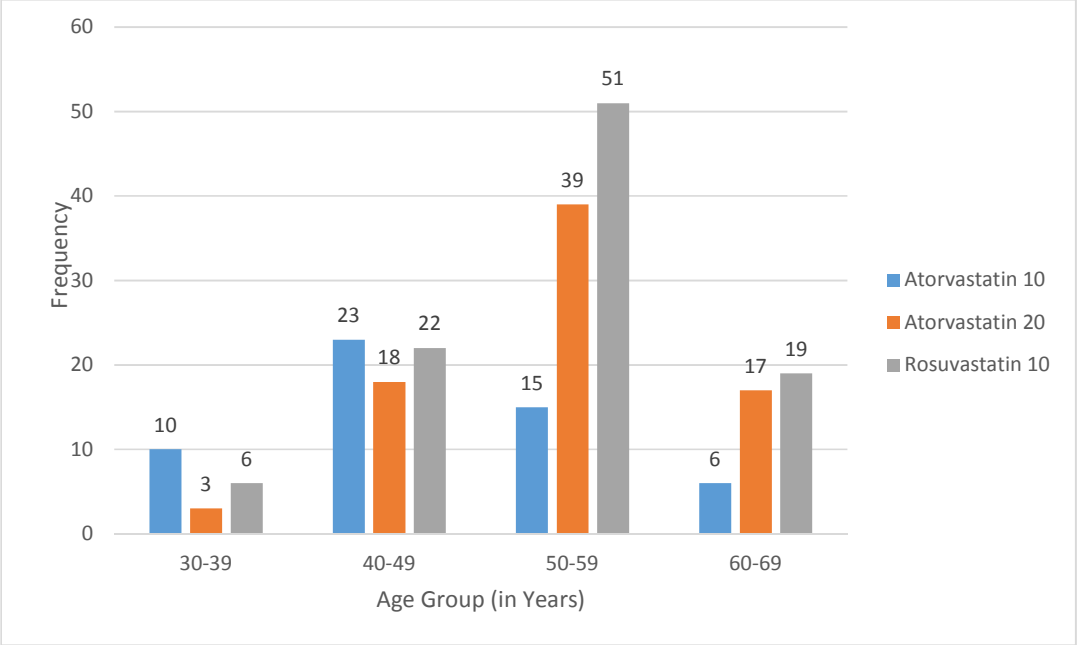
Among 229 total participants number of male patients found higher. The gender wise distribution of treatment group is given in Graph 2. The contribution of female participants point to the less prevalence of hyperlipidemia in female popular might be due to their hormonal protection in fertile age. The Rosuvastatin 10 mg was found prescribe more for both gender when compare with other drugs.

All the three drugs were found prescribed for participants of all BMI category. The distribution of subjects enrolled in different treatment group based on the Body Mass Index are given Graph 3. Atorvastatin 10 mg was prescribed more for participants of normal body weight. It was found that maximum patients are enrolled with BMI of overweight category and Rosuvastatin 10 mg was found to be more prescribed in overweight and obese patients. The obese participants were prescribed with Atorvastatin 20 mg and Rosuvastatin 10 mg only.

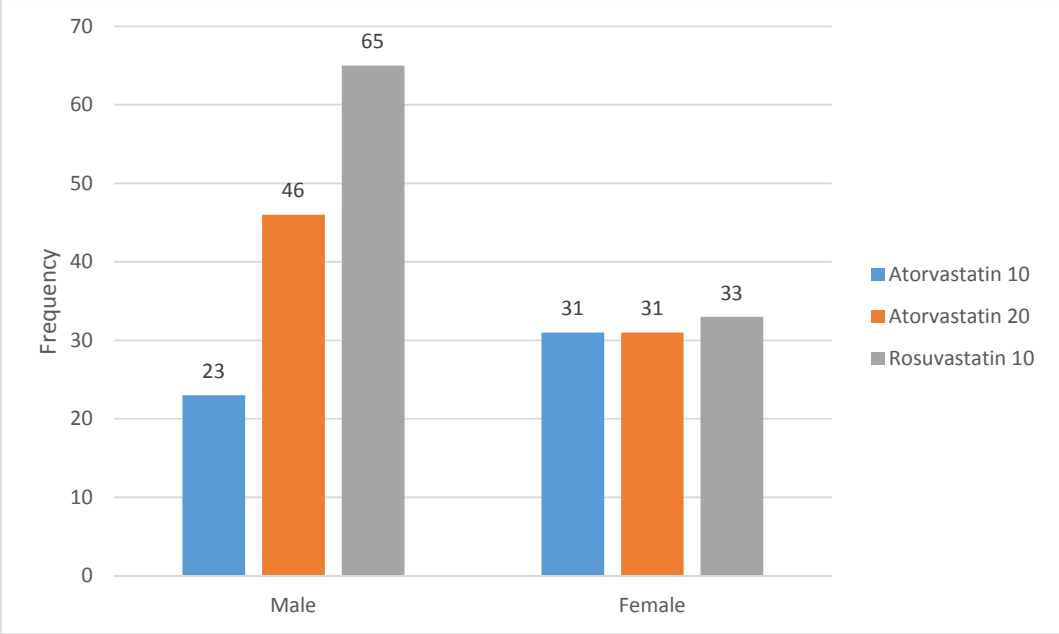
Among 229 participants enrolled 108 were found with normal waist circumference, whereas 121 participants found with abnormal waist circumference. This point to the association of abnormal waist circumference and prevalence of hyperlipidemia. The distribution of subjects in different treatment group based on the waist circumference are given Graph 4. Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10 were found prescribed for participants of both category of waist circumference, but Rosuvastatin 10 mg found dominated in number.

The distribution of subjects in different treatment group based on the risk factors of hyperlipidemia are given Graph 5. The main risk factors of Hyperlipidemia includes family history, comorbidity and smoking status were observed in all treatment groups. Majority of participants

has family history of Hyperlipidemia and it shows the association with future development of Hyperlipidemia. It is observed that the subjects with no comorbidities and never had a habit of cigarate smoking also contributed Hyperlipidemia. Participants of different risk factors were prescribed with Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10 and Rosuvastatin 10 mg was found prescribed higher in number.



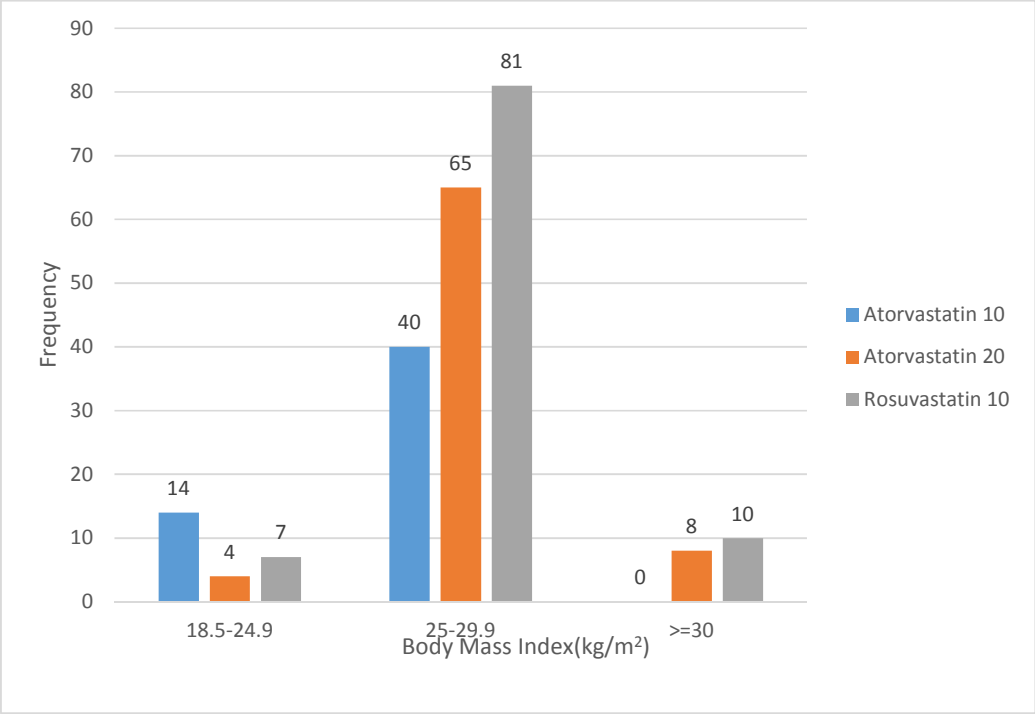
Graph 1. Distribution of subjects based on age group



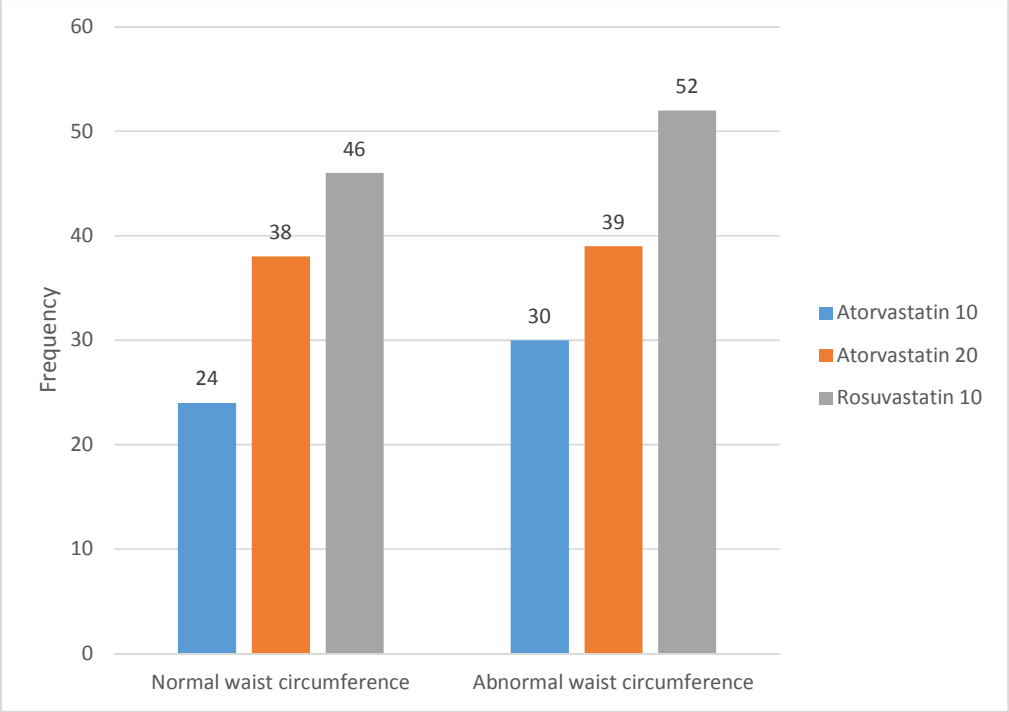
Graph 2. Distribution of treatment groups based on gender

The effectiveness of Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10 on hyperlipidemia are given in Table 1 and Graph 6. It is observed that all drug treatments made satisfactory result in achieving goal of the drug therapy; Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10 caused a significant reduction in lipid profile. Atorvastatin 10 treatment caused lowest reduction in lipid profile when compare with other treatment groups. . Atorvastatin 20 mg caused the higher reduction in total cholesterol with 37.89% followed by Rosuvastatin 10 mg with a median reduction of 36.70% total cholesterol. With Rosuvastatin 10 mg treatment caused a highest reduction (43.08%) in Triglyceride level in patients with hyperlipidemia followed by Atorvastatin 20 mg caused a median reduction of 38.64%. Rosuvastatin 10 mg was found highest effective in enhancing the level of good Cholesterol HDL with a median increase of 5.33% followed by Atorvastatin 20 mg with a median reduction of 4.88% and Atorvastatin 10 mg showed the lowest increase in HDL. The primary goal with moderate intensity statin therapy was LDL reduction and Atorvastatin 20 mg treatment group showed the median reduction in LDL level by 48.02%, followed by Rosuvastatin made 44.84% and Atorvastatin 10 mg also found achieved the goal of the drug therapy. The mean change of TC, TG, HDL and LDL were significantly different in the three groups (P< 0.01). The result from the current study indicates the prominent role of Atorvastatin 20 mg among moderate intensity statin drugs in management of Hyperlipidemia.

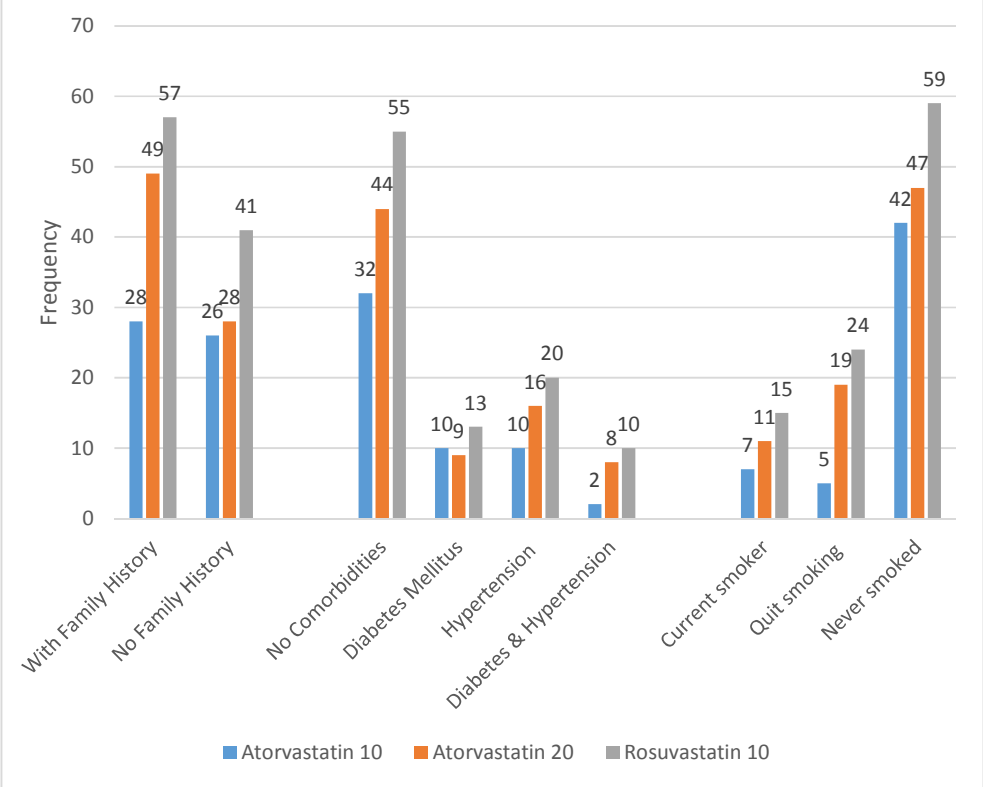
The impact of drug therapy with Atorvastatin 10, Atorvastatin 20 and Rosuvastatin 10 for duration of 1 year on serum creatinine kinase of hyperlipidemic patients are detailed in Table 2 and graph 7. All treatment groups showed increase in serum Creatinine Kinase enzyme level; whereas Rosuvastatin caused the lowest change in serum creatinine Kinase with a median elevation of 115.25% and Atorvastatin 20 mg showed the maximum muscle toxicity with median elevation of Creatinine Kinase by 182.35%. Atorvastatin 10 mg also showed a median increase in Creatinine Kinase enzyme by 122.97%. As Rosuvastatin 10 mg treatment caused the lowest muscle toxicity, the result obtained from the study suggest that Rosuvastatin 10 mg may be prescribed for Hyperlipidemia patients of all age group and those with body ache.



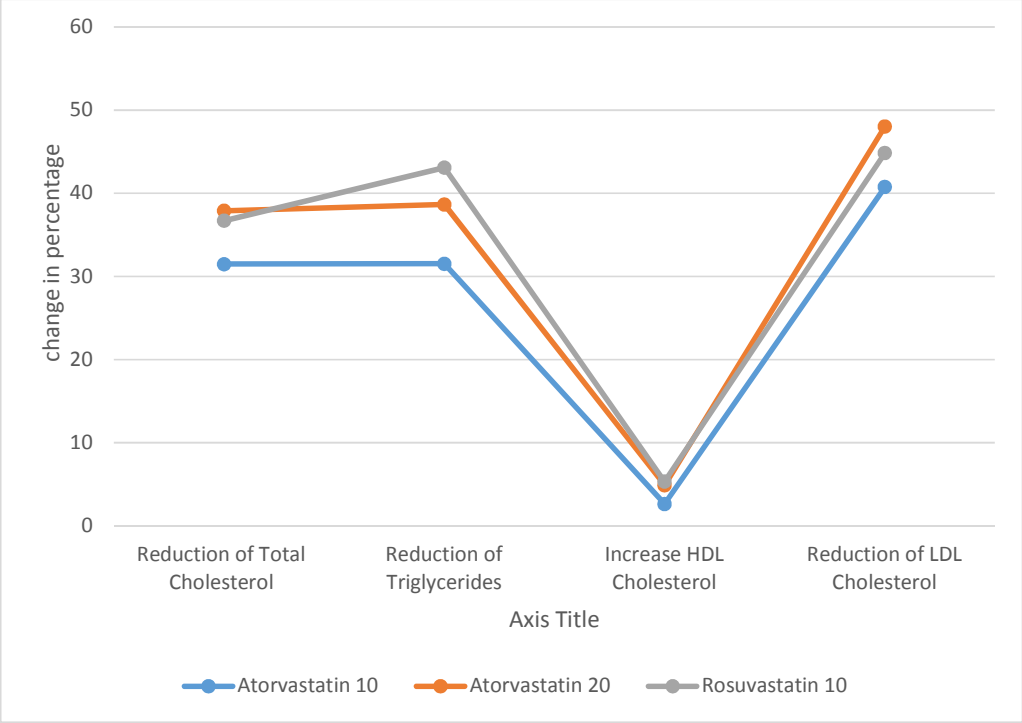
Graph 3. Distribution of treatment groups based on body mass index



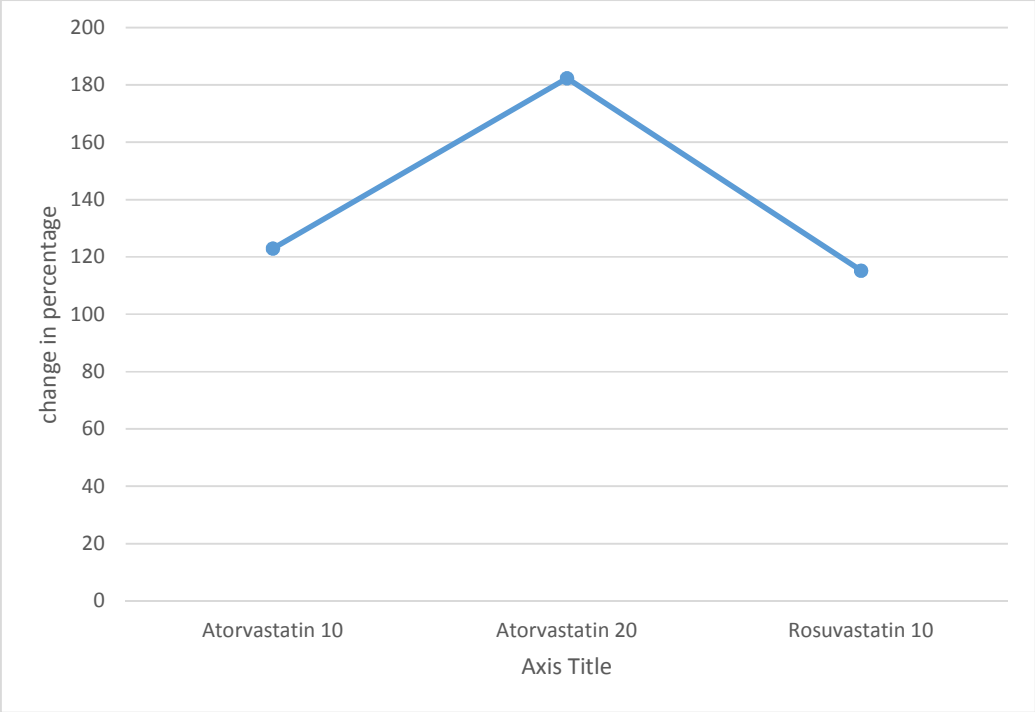
Graph 4. Distribution of treatment group based on waist circumference



Graph 5. Distribution of treatment groups based on risk factors



Graph 6. Effect of different drug treatment on lipid profile in subjects with Hyperlipidemia



Graph 7. Effect of different drug treatment on serum creatinine kinase in subjects with hyperlipidemia

Table 1. Effect of different drug treatment on lipid profile in subjects with Hyperlipidemia

Lipid Profile Parameters	Atorvastatin 10 (N=54)		Atorvastatin 20 (N=77)		Rosuvastatin 10 (N=98)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Baseline Total Cholesterol (mg/dl)	252.33	6.08	265.99	8.83	263.47	8.58	<0.001
End of the treatment Total Cholesterol (mg/dl)	172.20	5.78	165.52	6.72	166.86	7.50	
Median Reduction of Total Cholesterol (%)	31.46		37.89		36.70		
Baseline Triglycerides (mg/dl)	199.72	24.99	202.20	21.33	206.01	19.84	<0.001
End of the treatment Triglycerides (mg/dl)	133.98	9.36	124.99	14.02	117.92	12.72	
Median Reduction of Triglycerides (%)	31.51		38.64		43.08		
Baseline HDL Cholesterol (mg/dl)	43.35	5.18	43.35	4.90	41.68	4.01	<0.001
End of the treatment HDL Cholesterol (mg/dl)	44.72	5.03	45.42	5.02	44.06	3.99	
Median Increase in Cholesterol (%)	2.63		4.88		5.33		
Baseline LDL Cholesterol (mg/dl)	169.04	7.72	182.20	9.01	180.58	8.04	<0.001
End LDL Cholesterol (mg/dl)	100.59	6.97	95.11	8.32	99.21	6.80	
Median Reduction in LDL Cholesterol (%)	40.76		48.02		44.84		

Table 2. Effect of different drug treatment on serum creatinine kinase in subjects with hyperlipidemia

	Atorvastatin 10 (N=54)		Atorvastatin 20 (N=77)		Rosuvastatin 10 (N=98)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Baseline Creatinine Kinase (U/L)	35.46	5.67	39.99	6.06	37.27	5.45	<0.001
End of the treatment Creatinine Kinase (U/L)	78.57	10.35	112.26	19.21	79.24	11.65	
Median Increase of Creatinine Kinase %	122.97		182.35		115.25		

4. CONCLUSION

The present study was aimed to assess the impact of moderate intensity statin therapy on lipid profile and creatinine kinase in newly diagnosed hyperlipidemia patients. All the three drug treatment were found to be effective in achieving the treatment goal; whereas Atorvastatin 20 mg caused the highest reduction in LDL level with a highest elevation in serum Creatinine kinase level. Rosuvastatin 10 mg treatment exhibited a significant reduction in LDL level along with an appreciable decrease in Total Cholesterol and Triglycerides. Also Rosuvastatin 10 mg caused a considerable increase in HDL level and minimal elevation in biochemical marker of muscle toxicity. The result obtained from this study points to the importance of Rosuvastatin 10 mg in pharmacotherapy of hyperlipidemia due to its ability to produce better efficacy along with minimal adverse effect.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

The details of the diagnosis and drug therapy were well explained and written informed consent in vernacular language was obtained from each participant before enrolment.

ETHICAL APPROVAL

The Institutional Ethics Committee (IEC) of MES Academy of Medical Sciences, Perinthalmanna had approved the research proposal and permission had been given to conduct the research work at Department of medicine as per letter No: IEC/MES/07/2018.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bastien M, Poirier P, Lemieux I, Després JP. Overview of epidemiology and contri bution of obesity to cardiovascular disease. Progress in cardiovascular diseases. 2014; 56(4):369-81.
2. Yazdanyar A, Newman AB. The burden of cardiovascular disease in the elderly: Mor bidity, mortality and costs. Clinics in Geriatric Medicine. 2009;25(4):563-77.
3. Cacoub PP, Abola MT, Baumgartner I, Bhatt DL, Creager MA, Liau CS et al. REACH Registry Investigators. Cardio vascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Conti nued Health (REACH) Registry. Athero sclerosis. 2009;204(2):e86-92.
4. Michas G, Karvelas G, Trikas A. Cardio vascular disease in Greece; the latest evidence on risk factors. Hellenic Journal of Cardiology. 2019;60(5):271-5.
5. Jia L, Betters JL, Yu L. Niemann-pick C1-like 1 (NPC1L1) protein in intestinal and hepatic cholesterol transport. Annual review of physiology. 2011;73:239-59.
6. Tóth PP, Potter D, Ming EE. Prevalence of lipid abnormalities in the united states: The national health and nutrition examination survey 2003–2006. Journal of clinical lipido logy. 2012;6(4):325-30.
7. Bays H, Blonde L, Rosenson R. Adipo sopathy: how do diet, exercise and weight loss drug therapies improve meta bolic disease in overweight patients?. Ex pert review of cardiovascular therapy. 2006;4(6):871-95.
8. Milutinović A, Šuput D, Zorc-Pleskovič R. Pathogenesis of atherosclerosis in the tunica intima, media, and adventitia of coronary arteries: An updated review. Bos

nian journal of basic medical sciences. 2020; 20(1):21.
9. Arsenault BJ, Rana JS, Stroes ES, Després JP, Shah PK, Kastelein JJ, Wareham NJ et al. Beyond low-density lipo protein cholesterol: Respective contribu tions of non–high-density lipopro tein cholesterol levels, triglycerides and the total cholesterol/high-density lipoprotein cholesterol ratio to coronary heart disease risk in apparently healthy men and women. Journal of the American College of Cardio logy. 2009;55(1):35-41.
10. Lemieux I, Lamarche B, Couillard C, Pas cot A, Cantin B, Bergeron J, Dagenais GR, Després JP. Total cholesterol/HDL choles terol ratio vs LDL cholesterol/HDL choles terol ratio as indices of ischemic heart disease risk in men: The Quebec Cardiovascular Study. Archives of internal medicine. 2001;161(22):2685-92.
11. Anderson TJ, Grégoire J, Hegele RA, Couture P, Mancini GJ, Mc Pherson R et al. 2012 update of the Canadian Cardio vascular Society guidelines for the diag nosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. Canadian Journal of Cardiology. 2013; 29(2):151-67.
12. Newman CB, Preiss D, Tobert JA, Jacobson TA, Page RL, Goldstein LB et al. Statin safety and associated adverse events: A scientific statement from the American Heart Association. Arterioscle rosis, thrombosis and vascular biology. 2019;39(2):e38-81.
13. Schonewille M, de Boer JF, Mele L, Wolters H, Bloks VW, Wolters JC et al. Statins increase hepatic cholesterol synthe sis and stimulate fecal cholesterol elimination in mice. Journal of lipid resear ch. 2016;57(8):1455-64.
14. Thompson PD, Panza G, Zaleski A, Taylor B. Statin-associated side effects. Journal of the American College of Cardiology. 2016;67(20):2395-410.

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