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CLINICAL STUDY OF ATORVASTATIN AND ATORVASTATIN WITH VITAMIN D3 ON LIPID PROFILE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

Pharmacology

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ABSTRACT

Dyslipidaemia is an independent risk factor for cardiovascular diseases (CVD). There is a strong relationship between elevated levels of plasma cholesterol and atherosclerotic vascular disease. By reducing the total cholesterol and LDL cholesterol to below critical levels, there is a marked reduction in cardiovascular mortality. Hence this clinical study was undertaken to compare efficacy of the fixed dose combination of Atorvastatin with vitamin D and Atorvastatin alone on lipid profile in patients with chronic kidney disease .

METHODS: 60 patients with dyslipedemia and chronic kidney disease were selected and divided into two groups of 30 each atorvastatin and atorvastatin with vitamin D3 The treatment efficacy was monitored by doing lipid profile at first, third and sixth month of therapy.

RESULTS: At the end of sixth month the mean total cholesterol was significantly reduced in atorvastatin vitamin D3 group than in atorvastatin group with 'p' value <0.001. The mean LDL-C, TG, VLDL were significantly reduced in atorvastatin vitamin D3 group than in atorvastatin group with 'p' value <0.001. The Atorvastatin and vitamin D3 treated group showed good response compared to atorvastatin treated group.

KEYWORDS

Dyslipidaemia, Chronic Kidney Disease Atorvastatin, Vitamin D3, Lipid Profile

1.INTRODUCTION

Dyslipidaemia and atherosclerosis are closely linked to cardiovascular diseases like hypertension, coronary artery disease[1]. Dyslipidaemia is an independent risk factor for cardiovascular diseases (CVD). In India the most common cause of morbidity and mortality includes CVD[2]. Dyslipidaemia is a disorder of lipoprotein metabolism. This includes either lipoprotein overproduction or deficiency[3]. Dyslipidaemia can be diagnosed by doing plasma lipid profile. This is manifested by elevation of the total cholesterol, the low-density lipoprotein (LDL) cholesterol and the triglyceride concentrations, and a reduction in the high-density lipoprotein (HDL) cholesterol concentration in the blood[3]. A large proportion of individuals in the society have dyslipidaemia, often associated with modifiable risk factors. The global prevalence of hypercholesterolemia among adults in the year 2008 was 39% (37% males-37% and females- 37%). The most common lipid abnormalities observed in Tamilnadu as per the ICMR-INDIAB study are hypercholesterolemia-18.3%, high LDL-15.8%, low HDL-72.3%[4].

The risk factors for dyslipidaemia include diabetes, hypertension, chronic kidney disease, physical inactivity. The prevalence of dyslipidaemia in India is increasing, that calls for urgent lifestyle modification strategies. This is aimed to prevent and manage this important cardiovascular risk factors. Vitamin D deficiency affects more than one billion population worldwide[5]. This pandemic of vitamin D deficiency can mainly be attributed to lifestyle changes (for example reduced physical activity, fast food) and environmental factors(air pollution due to various causes) .This result in inadequate exposure to sunlight. Ultraviolet –B (UVB) rays in the sunlight induce vitamin D synthesis in the skin. The increasing prevalence of vitamin D deficiency is an important health problem in the community. Vitamin D deficiency is an independent risk factor for mortality in general population[6]. Various research supporting the role of vitamin D against many diseases including heart disease, hypertension, dyslipidaemia, type 2 diabetes ,autoimmune diseases, tuberculosis, cancer and mental illness. It is also observed that there is a strong correlation between low vitamin D level and fibromyalgia[7] Many physicians have suggested oral supplementation of vitamin D -1000 IU/day[8]. Adequate vitamin D levels are necessary for good vascular health[9]. Vitamin D deficiency is associated increased incidence of CVD[10]. Seasonal variation in vitamin D levels - deficiency in winter leads to peripheral insulin resistance in type 2 diabetes mellitus patients which in turn alters the lipid profile contributing to metabolic syndrome[11]. Serum levels of vitamin D are inversely correlated with very low density lipoprotein and triglyceride levels. Low serum 25 (OH) vitamin D levels are associated with reversible myalgia in statin treated patients. Normalization of low serum 25 (OH) vitamin D by oral vitamin D supplementation reverses myalgia, which otherwise might cause satin intolerance. Atorvastatin is the most effective drug for treating Dyslipidaemia. Atorvastatin acts by inhibiting HMG-CoA reductase enzyme. This enzyme involved in rate limiting step in biosynthesis of cholesterol in the body. Atorvastatin is effective in reducing high LDL-C levels in patients with dyslipidaemia. It is also effective in reducing triglyceride levels. There is a strong relationship between elevated levels of plasma cholesterol and atherosclerotic vascular disease. By reducing the total cholesterol and LDL cholesterol to below critical levels, there is a marked reduction in cardiovascular mortality. Hence this clinical study was undertaken to compare efficacy of the fixed dose combination of Atorvastatin with vitamin D and Atorvastatin alone on lipid profile in patients with chronic kidney disease

2.AIM To compare the effect of Atorvastatin and vitamin D3 combination with Atorvastatin on lipid profile in Patients with chronic kidney disease

3.MATERIALS AND METHODS

STUDY CENTRE: The study was carried out in the outpatient department of General Medicine and Department of Nephrology, Government Rajaji Hospital, Madurai after obtaining clearance from Institutional Ethical Committee , Government Rajaji Hospital, Madurai.

STUDY POPULATION: Patients attending the Outpatient department of Medicine and Nephrology , Government Rajaji Hospital, Madurai

SAMPLE SIZE: Total sample was 60 cases, those who satisfied the inclusion and exclusion criteria.

STUDY DESIGN: It was a single centre, open labeled, prospective, interventional study in patients with Dyslipidemia.

STUDY MATERIALS Drugs 1.Atorvastatin 10 mg 2. Atorvastatin 10 mg and Vitamin D3 1000 IU

ETHICAL APPROVAL: Ethical clearance was obtained from Institutional ethical Committee, Government Rajaji Hospital, Madurai. Ref.Letter No .990/E4/3/2012.

INCLUSION CRITERIA

1. Age – from 30 yrs to 60 yrs
2. Sex-both male and female
3. Patient with chronic kidney disease with hypercholesterolemia
4. Subjects willing for the study

EXCLUSION CRITERIA

1. Patients with liver disease
2. Patients with hypothyroidism
3. Patients with history of allergy / hypersensitivity to the drugs
4. Patients with H/o Excessive alcohol intake
5. Patient who are already on Atorvastatin
6. Pregnancy
7. Lactation
8. Children
9. Previous participation

DISCONTINUATION

1. Patients were given the freedom to quit the study at any time.
2. Subjects were withdrawn from the study, if they develop any adverse effects to drugs.

METHODOLOGY

60 patients with Dyslipidemia were taken into the study. The patients were diagnosed to have Dyslipidemia as per laboratory data. Out of 60 patients, 30 patients were treated with atorvastatin 10 mg/day orally and the remaining 30 patients were treated with atorvastatin 10mg and vitamin D3 1000IU/day orally. In atorvastatin group 30 had chronic kidney disease (CKD). In atorvastatin vitamin D3 group 30 had CKD. Patients satisfying the eligibility criteria were included in this study. Patients were informed both verbally and in writing by the investigator about the nature, significance, implications and the risks of study prior to enrollment. These were explained by the investigator in a language and terms that were easy to understand by the patient. Informed consent was obtained from all the patients personally, dated and signed both by the patient and the investigator. The details of the investigator (name, phone number and contact address) were given to each and every patient, to enable them to contact for any ailments at any time during the study period.The socio- demographic data, age, sex, address, educational qualifications, smoking and alcohol intake were collected at initial visit. Clinical examination and lab investigations were done. Patients attended the medicine and nephrology OPD fortnightly to procure drugs. During these visits, compliance was checked by counting empty drug packs and patients with poor compliance were given counseling to adhere to therapy. Adverse drug reactions to drugs were assessed.The treatment efficacy was monitored by doing lipid profile at first, third and sixth month of therapy. Other biochemical parameters like liver function tests ,thyroid function test , complete hemogram, blood sugar, renal function test and urine test were also monitored during their visits. The results were tabulated and analyzed statistically.

Statistical analysis Data were entered in Microsoft excel sheet and analyzed by paired t test and independent t test.

4.RESULTS

60 patients were recruited for the study. All the patients were followed up till the end of the study. There were no dropouts

Efficacy parameters

Lipid profile – total cholesterol, LDL, HDL, TG, VLDL were evaluated at the base line, third month and 6th month.

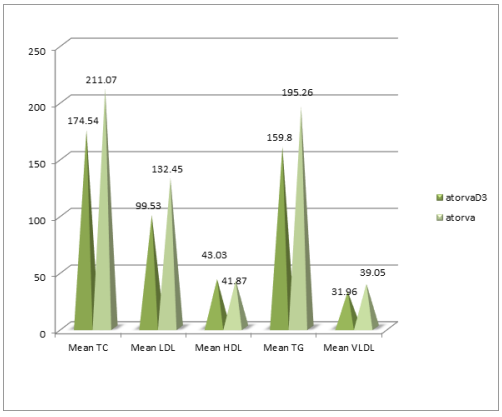
TABLE NO: 1 Comparing Atorvastatin And Vitamin D3 Combination With Atorvastatin On Lipid Profile In Chronic Kidney Disease Patients

Lipid profile	Atorvastatin and vitamin D3 (N=30)		Atorvastatin (N=30)		t test	df
	Mean	SD	Mean	SD		
Total cholesterol	174.54	9.472	211.07	17.509	10.052	58
LDL	99.53	8.046	132.45	11.043	13.196	58
HDL	43.03	1.426	41.87	1.224	-3.400	58
TG	159.80	19.324	195.26	24.517	6.221	58
VLDL	31.96	3.865	39.05	4.906	6.218	58

P<0.05

In order to compare the effect of Atorvastatin and vitamin D3 combination with Atorvastatin on lipid profile in patients with Chronic Kidney Disease an independent-samples t-test was conducted.

FIGURE- 1: Comparing Atorvastatin And Vitamin D3 Combination With Atorvastatin On Lipid Profile In Chronic Kidney Disease Patients



5.DISCUSSION & CONCLUSION

Dyslipidemia is an important predictor of cardiovascular disease. Dyslipidemia represents the elevation of plasma cholesterol and /or triglycerides or a low level of HDL. Multiple genetic abnormalities and environmental factors are involved in clinical lipid abnormalities and routinely used laboratory measurements do not define the underlying abnormalities. Most patients with Dyslipidemia are asymptomatic for many years. It can be diagnosed on the basis of measurement of fasting lipid profile. Initial therapy for Dyslipidemia is therapeutic life style changes with restricted intake of total and saturated fat along with regular physical activity. This is followed by pharmacological therapy. Lipid lowering drugs should be selected on the basis of specific lipoprotein disorder and plasma concentration of each lipoprotein. Statins are the most potent and effective drug for the treatment of Dyslipidemia. Statins are the drug of choice for the management of Dyslipidemia because of their proven efficacy and safety profile. They also have a role in managing cardiovascular risk in patients with relatively normal levels of plasma cholesterol. They are highly efficacious at lowering LDL-C, with reduction ranges from 20%- 55%[12]. Atorvastatin acts by inhibiting HMG-CoA redutase enzyme which is the rate limiting step for cholesterol biosynthesis. Vitamin D3 has favorable effects on plasma lipid profile. It has TG lowering effects especially in patients with CKD. Two mechanisms have been proposed for TG lowering effect of vitamin D. First, vitamin D may reduce serum TG by reducing hepatic TG formation and secretion via an effect on hepatocellular calcium. Second, vitamin D has suppressive effect on serum parathyroid hormone (PTH) levels. The reduction in serum PTH may decrease serum TG via increased peripheral removal. It also has pleiotropic effect. Many physicians have increased their recommendations for vitamin D3 supplem entation to at least 1000IU. Meta analytical studies from various sites have substantiated that supplementation with vitamin D has markedly reduced the mortality. Statin and vitamin D have synergistic actions in preventing CVD. Addition of vitamin D3 improved statin tolerance by reducing the incidence of myalgia. Hence the study was undertaken to explore the effects of atorvastatin vitamin D3 combination on lipid profile in chronic kidney disease patient population.After the institutional ethical clearance and informed consent, a single blind open label, comparative trial was attempted among 60 patients with Dyslipidaemia.60 patients with Dyslipidaemia were selected from outpatient department of general medicine and Nephrology. Their socio demographic, clinical and lab data were collected. They were explained about the study and were given the drugs orally. Fasting plasma lipid profile, liver function tests were done before starting drug therapy. Treatment efficacy in both groups was assessed at the end of third and sixth month. At the end of sixth month the mean total cholesterol was significantly reduced in atorvastatin vitamin D3 group than in atorvastatin group with 'p' value <0.001. The mean LDL-C, TG, VLDL were significantly reduced in atorvastatin vitamin D3 group than in atorvastatin group with 'p' value <0.001. The mean HDL-C in atorvastatin vitamin D3 group was- 45.32 and in atorvastatin group was-44.28 with 'p' value <0.001. The significant reduction in total cholesterol, TG, LDL, VLDL could be due to reduction in hepatic TG formation and suppressive effect on parathyroid hormone levels.Fasting plasma lipid profile improved significantly in both groups. However the improvement was very high in the atorvastatin vitamin D3 group and also Myalgia was less

common in atorvastatin vitaminD3 treated group compared to atorvastatin treated group[13]

60 patients with Dyslipidaemia were selected from outpatient department of general medicine and Nephrology. Out of 60 patients, 30 patients were treated with atorvastatin 10 mg/day orally and the remaining 30 patients were treated with atorvastatin 10mg and vitamin D3 1000IU/day orally.Both groups were followed for a period of 6 months. The compliance was checked and efficacy was monitored by doing lipid profile.The Atorvastatin and vitamin D3 treated group showed good response compared to atorvastatin treated group.

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