Original research article

A Comparative Study of Efficacy of Atorvastatin and Atorvastatin with Omega-3 Fatty Acids Combination in Dyslipidemic Patients

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Abstract

Background and Objectives: Hyperlipidaemia refers to elevated levels of lipids in the blood. Lipids such as cholesterol and triglycerides are insoluble in plasma. Circulating lipid is carried in lipoproteins that transport the lipid to various tissues for energy use, lipid deposition, steroid hormone production, and bile acid formation. To compare the efficacy of Atorvastatin alone with Atorvastatin plus Omega- 3 fatty acids combination in management of hyperlipidaemia. **Methods:** The study was a comparative, prospective, randomized and open label study. Patients with history of recent MI or post MI, attending the out patients / in patients, Department of General Medicine, DMCH, Darbhanga. Study duration of Two years. **Conclusion:** The efficacy of combination therapy i.e., Atorvastatin plus Omega-3 fatty acids showed statistically significant rise in HDL cholesterol with mean percentage difference of 3.7% when compared to monotherapy with Atorvastatin.

Keywords: Hyperlipidaemia, Atorvastatin, HDL, LDL, VLDL.

Introduction

Hyperlipidaemia refers to elevated levels of lipids in the blood. Lipids such as cholesterol and triglycerides are insoluble in plasma. Circulating lipid is carried in lipoproteins that transport the lipid to various tissues for energy use, lipid deposition, steroid hormone production, and bile acid formation. Most people who have hyperlipidaemia experience no symptoms. Abnormalities in lipoprotein metabolism are a major predisposing factor to atherosclerosis, increasing risk for CHD. Cardiovascular disease (CVD) due to atherosclerosis of the arterial vessel wall and to thrombosis is the foremost cause of pre-mature mortality and of disability-adjusted life years (DALYs), and is also increasingly common in developing countries. The main clinical entities are coronary artery disease, ischaemic stroke, and peripheral arterial disease. [1] Hyperlipidaemia characterized by increased levels of total cholesterol, LDL-C and triglycerides, is a major modifiable risk factor in primary and secondary prevention of

coronary artery disease. However the term dyslipidaemia is preferred to hyperlipidaemia because low levels of plasma HDL-C levels can be harmful. [2] Coronary heart disease (CHD) is the most common cause of death worldwide. According to WHO, an estimated 7.2 million people died from CHD in 2008, representing approximately 12% of deaths worldwide, while in the year 2030 it is estimated that 23.6 million people will die from cardiovascular disease.[3] World health organization has drawn attention to the fact that coronary heart disease as our modern EPIDEMIC i.e., a disease that affects population not an unavoidable attribute of aging. In India, the burden of ischemic heart disease is increasing every year, because of consequence of exposure to risk factors like inappropriate nutrition, sedentary life, smoking, obesity etc. It is expected to be the single most important cause of death in India by year 2015. [4] The rate of coronary heart disease has risen from 4% to 11% in past five decades.[5] Recently World Health Organization (WHO) has declared that by 2020, 60% of cardiovascular cases will be of Indian origin. [6] Hence control of hyperlipidaemia can prevent recurrent attack of this life threatening diseases. The drugs reduce blood cholesterol levels by 25-35% and cause a 35-45% reduction in risk of ischaemic heart disease.[7] The drug treatment of Hyperlipidaemia includes Statin, Fibric acid derivatives, Cholestyramine resins, Niacin, Ezetimibe & Omega 3 fatty acids [8]. Statins are the first line therapy for lowering lipid levels. Treatment of hyperlipidemia with statins has become an integral part of management of vascular diseases. [9] Statins reduce cardiovascular events and total mortality in persons at risk for and with coronary disease, but there remains a significant residual event rate, particularly in those with the atherogenic lipid phenotype that is characterized by a low high-density lipoprotein (HDL) cholesterol and increase in non-HDL cholesterol. The choices for therapies to supplement statins include niacin, fibrates, and omega-3 fatty acid. [10] Clinical trials of prescription omega-3 fatty acids as monotherapy or as an adjunct to statin therapy have supported its efficacy for improving the lipid profile (reducing triglycerides and triglyceride-rich lipoproteins and raising HDL-C) in individuals with hypertriglyceridemia or mixed dyslipidemia.

Objectives

***primary**
To compare the efficacy of Atorvastatin alone with Atorvastatin plus Omega- 3 fatty acids combination in management of hyperlipidaemia.
***secondary**
To note down any untoward effects with these drugs.

Material and Method

The study was a comparative, prospective, randomized and open label study. Patients with history of recent MI or post MI, attending the out patients / in patients, Department of General Medicine, Darbhanga Medical College and Hospital Darbhanga, Laheriasarai. Study duration of Two years.

Ethical clearance was obtained from the Institutional Ethics committee (IEC) of DMCH Darbhanga, before the start of study. A total of One Hundred (100) patients were selected for the study by applying Inclusion - Exclusion criteria. The patients were explained about the study details and a written / informed consent was taken from all the patients before subjecting them to the study. A detailed history of all registered patients was recorded. A thorough clinical examination was done for all patients and the required laboratory investigations respectively. These patients were divided randomly into two groups. One group was given Tab. Atorvastatin 10 mg once daily orally and another group was given Tab.

Atorvastatin (10mg/day) with Cap.Omega-3 fatty acids 300mg twice daily (600mg/day). The patients were given treatment for a period of 6 months and were followed up every month till the end of the study. Bellary. Omega-3 fatty acids were procured from outside. Clinical Efficacy was measured by assessing the change in parameters like reduction in Total cholesterol (TC), Triglycerides (TG's), LDL cholesterol levels and rise in HDL cholesterol in each group i.e., a group with Atorvastatin alone and a group with combination of Atorvastatin plus omega 3 fatty acids. The parameters were measured before the drug intervention and after drug intervention. The average of change in the each measurement between the groups is compared.

Inclusion criteria

Age 20 – 70 years

Sex: both males & females LDL Cholesterol > 100mg/dl HDL Cholesterol < 40mg/dl Triglycerides > 150mg/dl Total Cholesterol > 200mg/dl Serum creatinine < 1.2 mg/dl Normal liver function tests.

Exclusion criteria

Patients with Renal failure Patients with Hepatic failure Pregnant & lactating women Dropout patients are excluded.

All the patients included in the study are subjected to the following investigations.

Results

Age distribution

Out of 50 patients in the Atorvastatin group, 3 patients were in the 20–30yrs age group, 11 patients were in the 31–40yrs age groups, 14 were in the 41–50yrs age group and 16 were in 51-60yrs and only 6 patients were found in > 60yrs age group. Out of 50 patients in the Atorvastatin + Omega group, 1 patient was in the 20– 30yrs age group, 12 were in the 31–40yrs age group, 9 were in 41–50 age group, 20 were in the 51–60yrs age group and 8 patients were in > 60yrs age group.

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ex distribution

Out of 50 patients in the Atorvastatin group, 40 were males & 10 females.

Out of 50 patients in the Atorvastatin + Omega group, 42 were males & 8 were females. In total, out of 100 patients enrolled for the study, among them 82 were males & 18 were females. Among 100 patients, 4 patients were between 20-30 years age group, 22 patients were between 31-40 years, 23 patients between 41-50 years, 36 patients between 51 -60yrs and 14 were > 60yrs of age group. More number of patients were in the age group of 41-60 years (total of 59 patients).

*Total Cholesterol:

In Atorvastatin group (Group-A) the mean ± standard deviation (SD) of total cholesterol levels before treatment was 215.60±16.82 mg/dl and after treatment it was reduced to 187.80±12.47 mg/dl (P < 0.001). In Atorvastatin + Omega group (Group-B) the mean ± SD before treatment was 212.44±22.75 mg/dl and after treatment it was 184.54±13.58 mg/dl (P < 0.001). The percentage decrease of total cholesterol levels in Group-A was 12.66% and in Group B it was 12.54%.The difference in reduction being 0.12% between Group A and Group B.

*LDL-Cholesterol:

In Atorvastatin group (Group A) the mean ± standard deviation (SD) of LDL cholesterol levels before treatment was 140.24±16.83 mg/dl and after treatment it was reduced to

114.60±12.32mg/dl (P <0.001). In Atorvastatin + Omega group (Group-B) the mean ± SD before treatment was 136.50±22.48 mg/dl and after treatment it was 110.20 ± 13.36mg/dl (P < 0.001). The percentage decrease of LDL cholesterol levels in Group-A was 17.78% and in Group-B it was 17.71%.

*VLDL Cholesterol:

In Atorvastatin group (Group A) the mean ± standard deviation (SD) of VLDL cholesterol levels before treatment was 36.04 ± 3.38mg/dl and after treatment it reduced to 31.69 ± 1.44mg /dl (P < 0.001). In Atorvastatin + Omega group (Group B) the mean ± SD before treatment was 36.72 ± 4.08mg/dl and after treatment it was reduced to 31.55 ± 1.88mg/dl (P < 0.001). The percentage decrease in of VLDL-C levels in Group A was 11.57 % and in Group B it was 13.50%.The difference in decrease being 1.93% in between the two groups.

*Triglycerides:

In Atorvastatin group (Group A) the mean ± standard deviation (SD) of triglycerides levels before treatment was 180.10 ± 16.91 mg/dl and after treatment it was reduced to 158.48 ±7.24mg/dl (P < 0.001). In Atorvastatin + Omega group (Group B) the mean ± SD before treatment was 183.64±20.42 mg/dl and after treatment it was reduced to 157.78±9.44mg/dl (P < 0.001). The percentage decrease in of TG'S levels in Group-A was 11.5 % and in Group-B it was 13.5%.The difference in decrease being 2% in between the two groups.

*HDL Cholesterol: In Atorvastatin group (Group-A) the mean ± standard deviation (SD) of HDL cholesterol levels before treatment was 39.34 ± 1.77mg/dl and after treatment it increased to 41.50±1.67mg/dl (P < 0.001). In Atorvastatin + Omega group (Group-B) the mean ± SD before treatment was 39.20±2.60mg/dl and after treatment it was ± 2.08mg/dl (P < 0.001). The percentage increase in of HDL cholesterol levels in Group-A was 5.54% and in Group-B it was 9.27%.The difference in increase being 3.7% in between the two groups.

Post test analysis to compare between two groups:

*****Total Cholesterol: In Atorvastatin group (Group A) the mean reduction of total cholesterol levels was 27.80±12.88 and in combination group (Group-B) it was 27.90±15.91. In Atorvastatin group the mean ± standard deviation (SD) of total cholesterol levels after treatment was reduced to 187.80 ± 12.47mg/dl. In Atorvastatin + Omega group reduction was 184.54±13.58 mg/dl (p > 0.05).

*LDL Cholesterol: In Atorvastatin group the mean reduction of LDL-cholesterol levels was 25.63±13.19 and in combination group it was 26.30±15.79. In Atorvastatin group the mean ± standard deviation (SD) of LDL cholesterol levels after treatment was reduced 114.36 ± 12.46mg/dl. In Atorvastatin + Omega group the reduction was 110.20±13.36 mg/dl (p > 0.05).

*VLDL Cholesterol: In Atorvastatin group the mean reduction of VLDL-cholesterol levels was 4.34±2.51 and in combination group it was 5.16±2.62.

In Atorvastatin group the mean ± standard deviation (SD) of VLDL cholesterol levels after treatment was reduced to31.69 ± 1.44mg/dl. In Atorvastatin + Omega group it was 31.55±1.88 mg/dl (p > 0.05 HDL Cholesterol: In Atorvastatin group the mean increase in HDL - cholesterol levels was 2.16±1.01 and in combination group it was 3.57±1.26. In Atorvastatin group the mean ± standard deviation (SD) of HDL cholesterol levels after treatment was increased to 41.50 ± 1.67mg/dl. In Atorvastatin + Omega group increased to 42.78±2.08 mg/dl (p < 0.001). *Triglycerides: In Atorvastatin group the mean reduction triglycerides levels was 21.62±12.65 and in combination group it was 25.86±13.14 In Atorvastatin group the mean ± standard deviation (SD) of triglycerides levels after treatment was reduced to 158.48 ± 7.24mg/dl. In Atorvastatin + Omega group it reduced to 157.78±9.44 mg/dl (p > 0.05). In our study, there were no serious side effects seen during the treatment period. However 7 patients complained of constipation (4 in Group-A and 3

patients in Group-B). 6 patients complained of flatulence, and 2 patients complained of diarrhea in Atorvastatin + Omega group (Group-B).

Discussion

3 – hydroxyl – 3 – methylgluatryl – coenzyme-A reductase inhibitors (statins) are the most potent and frequently used drugs for the treatment of hypercholesterolemia. Statin therapy has been shown to reduce the rate of major vascular events in patients with established vascular disease, and is considered to be the first line therapy for the management of dyslipidaemia in such individuals.[11] When goal levels of LDL are achieved, but HDL is abnormally low, triglycerides abnormally high, and/or Lp(a) abnormally high, a second lipid lowering compound from a different class should be added to the regimen.[12] In a number of small studies, the combination of statins and Omega-3 fatty acids has been consistently shown to be an effective, safe, and well-tolerated treatment for combined dyslipidaemia.Omega-3 fatty acids provide additional lipid improvements without requiring additional laboratory tests and do not increase risk for adverse muscle or liver effects. Intakes of up to 250 mg/day, the relative risk of coronary heart disease mortality was 14.6% lower (95% CI, 8% to 21%) for each 100 mg/day of EPA/DHA.[13] In this context our study was undertaken with an aim to study and compare the efficacy of Atorvastatin alone and Atorvastatin plus Omega-3 fatty acids in patients diagnosed with dyslipidaemia and also to note down any untoward effects with these drugs during treatment, in the Department of medicine, DMCH Darbhanga, a tertiary care hospital. One hundred patients were recruited for our study by applying inclusion- exclusion criteria after obtaining their informed/written consent.

These patients were randomly divided into two groups of 50 patients each, with one group receiving Tab. Atorvastatin (10mg/day) and the other, Tab. Atorvastatin (10mg/day) plus Cap.Omega-3 fatty acids (300mg bid) for 6 months. Required investigations were performed at baseline and during subsequent follow ups. Efficacy was assessed by measuring change in lipid parameters. It is well-established that hypertension and dyslipidaemia are the two major contributing risk factors for CVD. Various epidemiological studies have shown the prevalence of the co-existence of hypertension and dyslipidaemia, in the range of 15 to 31%. The co-existence of the two risk factors has more than an additive adverse impact on the vascular endothelium, which results in enhanced atherosclerosis, leading to CVD.[14] In our study, in Atorvastatin group the difference between mean of HDL- cholesterol levels before and after treatment was 2.16± 1 and in combination group it was 3.5±1.29. When both the groups were compared the difference in the efficacy rate showed statistically significant results ($P < 0.001$). The percentage increase in of HDL cholesterol levels in Group-A was 5.54% and in Group-B it was 9.2%. The combination group improved the HDL-C levels very significantly with mean percentage difference of 3.7%. In our study, in Atorvastatin group the mean reduction of triglycerides levels was 21.62±12.65and in Atorvastatin + Omega group mean reduction was 25.86±13.14.The percentage decrease in TG'S levels in Group-A was 11.5 % and in Group-B it was 13.5%. The percentage of reduction was 2% high in Omega group compared to Atorvastatin alone group. However when both the groups were compared the difference in the efficacy was not that significant ($P > 0.05$).

In our study, in Atorvastatin group the mean reduction of VLDL cholesterol was 4.34±2.51 and mean percentage reduction was 11.57%. In Atorvastatin + Omega group the mean reduction was 5.16±2.62 and mean percentage reduction was 13.5%. The Omega group showed better efficacy in VLDL cholesterol reduction. However when both the groups were compared the difference in the efficacy was not statistically significant ($P > 0.05$). In our study, 4 patients complained of constipation and 2 patients complained of flatulence in

Atorvastatin group. In Omega group 3 patients complained of constipation, 6 patients complained of flatulence and 2 patients complained of diarrhea during 1st month which gradually subsided over a period time.

Conclusion

Hyperlipidaemia is a major cause of atherosclerosis and atherosclerosis- associated conditions, such as coronary heart disease (CHD), ischemic cerebrovascular disease, and peripheral vascular disease. These conditions still account for the majority of morbidity and mortality among middle-aged and older adults. The prevalence of hyperlipidaemia associated with coronary heart disease was higher among 41-60yrs age groups in both study groups, showing more vulnerable age group for CAD. The study also highlights that younger age group is at increased risk of hyperlipidaemia. Males were more in number as compared to females in both study groups.

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