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A Study of the Efficacy of Atorvastatin Alone and Its Combination with Omega-3 Fatty Acids in Patients with Hyperlipidemia

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Abstract: Atherosclerosis is one of the major causes of increased morbidity and mortality associated with coronary artery disease, cerebrovascular accidents, and peripheral vascular diseases. Dyslipidemia is one of the important causes that result in atherosclerosis. The incidence of atherosclerosis has been on the rising recently. Therefore prevention of dyslipidemia can decrease the development of atherosclerosis. Aims: The study was undertaken to determine the efficacy of atorvastatin alone and its combination with omega-3 fatty acids in the management of hyperlipidemia in patients attending a tertiary care hospital. Methods: This study was a cross-sectional prospective study conducted in the Department of Pharmacology and General Medicine, Kakatiya Medical College and Hospital, Warangal. The patients were selected from those visiting General Medicine OPD and diagnosed with hyperlipidemia. Sixty patients in the age group of 20 – 70 yrs, were recruited based on inclusion and exclusion criteria. They were divided into two groups. The Group I included the patients receiving Tab. Atorvastatin 10mg/day and Group II Atorvastatin 10mg/day plus Cap Omega-3 fatty acids 600mg/day for the duration of six months and follow up were done every month. Efficacy of treatment was assessed by the changes in laboratory parameters of Total cholesterol, Triglycerides, HDL-C, LDL-C, and VLDL-C. Results: The efficacy of combination therapy i.e., Atorvastatin plus Omega-3 fatty acids showed a statistically significant rise in HDL cholesterol with the mean percentage difference of 4.24% when compared to monotherapy with Atorvastatin. The efficacy of other parameters like total cholesterol (TC), LDL cholesterol, VLDL cholesterol, and triglycerides (TG'S) levels with the low dose of omega-3 fatty acids in combination therapy was not statistically significant and produced nearly identical alterations in serum lipoprotein levels when compared to monotherapy. Conclusion: Although statins are being used as first-line therapy for hyperlipidemia and in patients with elevated triglycerides. For patients with elevated LDL-C and low HDL-C combination therapy appears to be a better option. Thus omega-3 fatty acids may be a potential supplement for combination therapy apart from niacin and fibrates.
Keywords: Dyslipidemia, Atorvastatin**,** Omega-3 fatty acids.

INTRODUCTION

Hyperlipidemia is a condition characterized by abnormally increased levels of total cholesterol, LDL-C, and triglycerides is a major modifiable risk factor in the primary and secondary prevention of coronary artery disease. The term dyslipidemia is more preferable rather than hyperlipidemia because there is not only there is an increase in total cholesterol, LDL-C, and triglycerides but at the same time decrease in plasma HDL-C which may be harmful [1]. Most of the cases of hyperlipidemia experience no clinical symptoms. Circulating lipids are carried in lipoproteins that transport the lipid to various tissues for use to produce energy, lipid storage, steroid hormone production, and bile acid formation. Abnormalities in lipid and lipoprotein metabolism are the major predisposing factor for atherosclerosis, which increases the risk for CHD. Cardiovascular disease (CVD) due to atherosclerosis of the arterial vessel wall and formation of atheromatous plaque leading to thrombosis is the foremost cause of premature mortality and of disability-adjusted life years (DALYs) and is also increasingly common in developing countries. The main clinical entities are coronary artery disease, ischemic stroke, and peripheral arterial disease [2]. Coronary heart disease (CHD) is the most common cause of mortality worldwide. According to WHO, an estimated approximately 7.2 million people died from CHD in 2008, representing about 12% of deaths worldwide, while in the year 2030 it is estimated that 23.6 million people will die from cardiovascular disease [3].

WHO has considered coronary heart disease as a modern epidemic and it has drawn attention towards its management. One of the important causes for the development of coronary artery disease is aging of the

population. In India, the burden of IHD is increasing every year, because of the consequence of exposure to risk factors like inappropriate nutrition, sedentary life, smoking, obesity etc [4]. The rate of coronary heart disease has risen from 4% to 11% in past five decades [5]. Recently the World Health Organization (WHO) has declared that by 2020, 60% of cardiovascular disease cases will be of Indian origin [6]. Therefore the control and treatment of hyperlipidemia are increasing. The drugs that reduce blood cholesterol levels by 25-35% and cause a 35-45% reduction in risk of ischemic heart disease are being used in the treatment [7]. The main antihyperlipidemic drugs include statins, fibric acid derivatives, Cholestyramine Resins, Niacin, Exetimibe, and 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 the management of vascular diseases [9]. Large outcome trials designed to assess the value of combining statins with other agents has been of interest recently in order to target HDL cholesterol and non-HDL cholesterol. There is ample evidence for the clinician to consider combination therapy. The choices for therapies to supplement statins include niacin, fibrates, and omega-3 fatty acid [10]. Recent studies indicate that omega-3 fatty acids can improve plasma lipids in the dose-dependent manner in patients taking statins. This combination therapy may be preferable to drug combination for treatment of combined hyperlipidemia [11]. With this background we in the present study tried to compare the efficacy of Atorvastatin alone and Atorvastatin plus Omega-3 fatty acids in patients with hyperlipidemia at Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal.

MATERIALS AND METHODS

This cross-sectional prospective study was Department of General Medicine, Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, Warangal. The sources of patients were those visiting OPD of General Medicine with previously diagnosed hyperlipidemia having other comorbidities like diabetes mellitus, hypertension, and IHD. Institutional Ethical clearance was obtained from the Institutional Ethics committee (IEC) of Kakatiya Medical College, Warangal. The patients were explained about the study details in the local language and a written informed consent was taken from all the patients before subjecting them to the study. Only those voluntarily willing to participate in the study were included. A detailed history and clinical examination of the patients was done for all the patients and initial laboratory investigations were performed before the beginning of treatment. The patients were then divided into two groups randomly based on a computer-generated random number. A total of 60 patients were included in the study and they were divided into two groups. Group I received Tab. Atorvastatin 10 mg once daily orally and Group II received Tab. Atorvastatin (10mg/day) with Cap.Omega-3 fatty acids 300mg twice daily (600mg/day) the treatment was to continue for six months with monthly follow up till the end of the study. For estimation of lipid profile fasting blood samples were obtained in vacutainer and sent to Department of Biochemistry, Kakatiya Medical College and Mahatma Gandhi Memorial Hospital, Warangal. All the values were recorded and statistical analysis was done with SPSS version 17 on windows platform.

RESULTS

Out of 30 patients in the Atorvastatin group I, 3 patients was in the 21–30yrs age group, 6 patients were in the 31–40yrs age groups, 9 were in the 41–50yrs age group and 9 were in 51-60yrs and only 3 patients were found in > 60yrs age group. Out of 30 patients in the Atorvastatin + Omega group, 3 patients were in the 21– 30yrs age group, 3 were in the 31–40yrs age group, 6 were in 41–50 age group, 12 were in the 51–60yrs age group and 6 patients were in > 60yrs age group. Among 60 patients, 6 patients were between 20-30 years age group, 9 patients were between 31-40 years, 15 patients between 41-50 years, 21 patients between 51 -60yrs and 9 were > 60yrs of age group. A number of patients were in the age group of 41-60 years (total of 36 patients) table-1.

Table-1: Showing the distribution of the patients involved in the study

Age group in years	Group I (%)	Group II (%)	Total
21-30	3 (10%)	3 (10%)	6 (10%)
31-40	6 (20%)	3 (10%)	9 (15%)
41-50	9 (30%)	6 (20%)	15 (25%)
51-60	9 (30%)	12 (40%)	21 (35%)
>60	3 (10%)	6 (20%)	9 (15%)
Total	30 (100%)	30 (100%)	60 (100%)

Out of total 30 patients in the Atorvastatin group I, 24 (80%) were males and 6 (20%) were females and in the Atorvastatin + Omega group II, 27 (90%) were males and 3 (10%) were females. In Atorvastatin group (Group-I) the mean ± standard deviation (SD) of total cholesterol levels before treatment was 219.40±10.34 mg/dl and after treatment, it was reduced to 186.16±6.27 mg/dl ($P < 0.001$). The serum triglycerides levels before treatment were 165.53 ± 7.39 mg/dl and after treatment, it was reduced to 141.23 ±6.85mg/dl ($P < 0.001$) The LDL cholesterol levels before treatment was 129.56±15.57 mg/dl and

after treatment, it was reduced to 102.06±11.46mg/dl (P <0.001). The levels of VLDL cholesterol levels before treatment were 39.13 ± 2.10mg/dl and after treatment it reduced to 31.20 ± 0.94mg /dl (P < 0.001). HDL cholesterol levels before treatment was 37.16 ± 1.24mg/dl and after treatment it increased to 41.86±1.28mg/dl (P < 0.001) shown in table 2.

Table-2: Showing the mean values of parameters recorded in Group I (Atorvastatin) before and after the completion of the study.

Parameter	Before the start of the study Mean ± SD	At the end of the study Mean ± SD	P values
Total Cholesterol	219.40 ± 10.34	186.16 ± 6.27	< 0.001*
Triglycerides	165.53 ± 7.39	141.23 ±6.85	< 0.001*
LDL-C	129.56 ± 15.57	102.06±11.46	< 0.001*
VLDL-C	39.13 ± 2.10	31.20 ± 0.94	< 0.001*
HDL-C	37.16 ± 1.24	41.86±1.28	< 0.001*

* P values Significant

In Atorvastatin + Omega group (Group-II) the mean ± SD before treatment was 217.70±9.32 mg/dl and after treatment, it was 184.33±9.17 mg/dl (P < 0.001). the levels of triglycerides before the treatment was 166.70±7.94 mg/dl and after treatment, it was reduced to 140.43±7.54mg/dl (P < 0.001). The levels of LDL-C before treatment were 128.16±12.74 mg/dl and after treatment, it was 100.06 ± 10.61mg/dl (P < 0.001). The VLDL-C before treatment was 39.56 ± 2.13mg/dl and after treatment, it was reduced to 31.06 ± 0.96mg/dl (P < 0.001). The levels of HDL-C mean ± SD before treatment was 36.96±1.32mg/dl and after treatment, it was 43.20 ± 1.37mg/dl (P < 0.001) shown in table 3.

Table-3: Showing the mean values of parameters recorded in Group II (Atorvastatin + Omega 3 Fatty Acids) before and after the completion of the study

Parameter	Before the start of the study Mean ± SD	At the end of the study Mean ± SD	P values
Total Cholesterol	217.70 ± 9.32	184.33±9.17	< 0.001*
Triglycerides	166.70±7.94	140.43±7.54	< 0.001*
LDL-C	128.16±12.74	100.06 ± 10.61	< 0.001*
VLDL-C	39.56 ± 2.13	31.06 ± 0.96	< 0.001*
HDL-C	36.96±1.32	43.20 ± 1.37	< 0.001*

*P values Significant

The percentage decrease of total cholesterol levels in Group-I was 15.15% and in Group II it was 15.32%. The difference in reduction was 0.17% between Group I and Group II. The percentage decrease in of Triglycerides levels in Group-I was 14.68 % and in Group-II it was 15.75%. The difference in decrease was 1.07% reduction between the two groups. The percentage decrease of LDL cholesterol levels in Group-I was 21.22% and in Group-II it was 21.92%. The percentage decrease in of VLDL-C levels in Group I was 20.26 % and in Group II it was 21.48%. The difference in decrease was being 1.22% in between the two groups. The percentage increase in HDL cholesterol levels in Group-I was 12.64% and in Group-II it was 16.88%. The difference in the increase is 4.24% between the two groups shown in table-4.

Table-4: showing the comparison of mean values between two groups

Parameter	Mean Difference		Post-test analysis		P values
	Group I	Group II	Group I	Group II	
Total Cholesterol	33.24	33.37	186.16±6.27	184.33±9.17	> 0.1
Triglycerides	24.30	26.27	141.23±6.85	140.43±7.54	> 0.3
LDL-C	27.50	28.10	102.06±11.46	100.06±10.61	> 0.12
VLDL-C	7.93	8.50	31.20±0.94	31.06±0.96	> 0.05
HDL-C	4.70	6.24	41.86±1.28	43.20±1.37	<0.001*

* P values Significant

DISCUSSION

Hypertension and hyperlipidemia are the two major contributing risk factors for CVD. Epidemiological studies have shown the prevalence of the co-existence of hypertension and dyslipidemia, in the range of 15 to 31%. The co-existence of the two risk factors has an additive adverse impact on the vascular endothelium, which results in enhanced atherosclerosis,

leading to CVD [12]. In the present study, among the 60 patients included, 21 patients had hypertension (35%), 12 patients had diabetes mellitus (20%) and 6 patients had hypertension and diabetes (10%). The incidence of hyperlipidemia and CHD are 3-4 times more in men as compared to women especially in the age group of 40-60 years [13]. Shown in this study by the increase in the number of patients in this age group. Also, the numbers of male patients in our study were 51 were male patients and 9 were female patients out of the total 60 patients included in the study. Studies in India have shown the greater prevalence of hypertriglyceridemia in the age group of 31 - 40 years. And NCMH estimates there would be around 62 million patients with CAD by 2015 in India and of these, 23 million would be patients younger than 40 years of age [14]. In our study, in group I the mean reduction of VLDL cholesterol was 7.93 ± 0.71 and mean percentage reduction was 20.26%. In Atorvastatin + Omega group II the mean reduction was 8.50±0.92 and mean percentage reduction was 21.48%. The Omega group showed better efficacy in VLDL cholesterol reduction. However when both the groups were compared to the difference in the efficacy was not statistically significant ($P > 0.05$). The other parameters like total cholesterol and LDL-C levels showed less significant changes. The difference in the efficacy between two groups for total cholesterol and LDL cholesterol was not statistically significant ($P > 0.05$). Studies have found that a combination of statins and Omega-3 fatty acids has been consistently shown to be an effective, safe, and well-tolerated treatment for combined dyslipidemia. Omega-3 fatty acids provide additional lipid improvements. Intakes of up to 250 mg/day, the relative risk of coronary heart disease mortality were 14.6% lower (95% CI, 8% to 21%) for each 100 mg/day of EPA/DHA [15]. We in the study found the additional advantage of the addition of Omega 3 fatty acid was increased in HDL-C levels in the patients which has important beneficial effect as compared to statin alone treatment. Therefore it is recommended that when the goal is of achieving the decrease in the LDL-c as well as the increase in HDL-C combination of Atorvastatin with Omega 3 fatty acid shows better results. No particular adverse effects were noted in patients in both the groups however in Group II 3 patients suffered from constipation and 6 suffered from flatulence and 2 complained of diarrhea which gradually disappeared at the end of one month of treatment.

CONCLUSION

Within the limitations of the present study, it can be concluded that although statins are being used as first-line therapy for hyperlipidemia and in patients with elevated triglycerides. For patients with elevated LDL-C and low HDL-C combination therapy appears to be the better option. Thus omega-3 fatty acids may be a potential supplement for combination therapy apart from niacin and fibrates.

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