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A Study on Effect of Omega 3 Fatty Acids in Hypertriglyceridemia

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Abstract
Introduction: *Hyperlipidaemia is a major modifiable risk factor in primary and secondary prevention of coronary artery disease. Studies have shown that serum triglycerides were an independent risk factor for CAD events, irrespective of serum levels of high density lipoprotein cholesterol (HDL-C) or low density lipoprotein cholesterol (LDL-C). Many epidemiological and interventional studies suggest that omega 3 polyunsaturated fatty acids confer a protective role against atherosclerotic disease and having a greater impact in reducing serum triglyceride levels.*
Aims: *The aim of our study was to see the effect of omega 3 fatty acids on serum triglycerides in patients of hypertriglyceridemia. Effect on various variables of lipid profile was observed simultaneously.*
Material And Methods: *A total of 100 patients (46 males and 54 females) of hypertriglyceridemia (>150 mg/dl) were included. They received capsules of eicosapentaenoic acid with docosahexaenoic acid in a dosage of 3g/day for 8 weeks. To see the efficacy of the drug, lipid profile was measured at 0 week, after 4 weeks and 8 weeks of the treatment. The data from our present study was systematically collected, compiled and statistically analysed using software IBM SPSS 22.0 to draw relevant conclusions.*
Study Design: *The study done was a non-randomised, prospective therapeutic study. It consisted of a treatment period of 8 weeks for all the patients, after their written/informed consent and approval from the Institutional thesis ethical committee.*
Results: *Serum Triglycerides reduction (237.71±45.77 vs. 188.44±40.67mg/dl; p<0.001) and VLDL reduction (47.54±9.15 vs. 37.69±8.13 mg/dl; p<0.001), was highly significant after 8 weeks of treatment. HDL-cholesterol levels increased highly significantly (37.40±3.96 vs. 39.14±3.40 mg/dl; p<0.001).Total cholesterol also decreased highly significantly (221.71±25.22 vs. 213.97±22.31 mg/dl; p<0.001) but no significant change was found in serum LDL (p>0.05). The percentage reduction was highest in serum triglycerides and VLDL levels by 20.95% followed by a percentage rise of 4.90% in serum HDL levels.*
Conclusion: *Omega 3 fatty acids intervention have a positive role in improving lipid profile but with a greatest impact in reducing serum triglycerides which is an independent risk factor of CAD.*
Keywords: *Omega 3 fatty acids, Serum Triglycerides, Atherosclerosis, Serum VLDL, Serum HDL-C.*

INTRODUCTION

Atherosclerosis and its relevant vascular events including cardiovascular disease (CVD), stroke and peripheral arterial disease (PAD) have become a leading cause of disability and mortality in the modern society.[1] Amongst all, Hyperlipidaemia is one of the most well established modifiable risk factor for CVD and is a matter of concern.

Total cholesterol and LDL-C were particularly associated with the risk of CHD. Lately as predictors for risk of CVD today, levels of plasma triglycerides are independent of HDL and total cholesterol.[2] In Asian Pacific region, one meta analysis study was held which analysed the results from 25 cohort studies. The results supported serum triglycerides as a better predictor than total cholesterol, HDL-C, and LDL-C for CVD mortality.[3] In contrast to studies in western population, hypertriglyceridemia appeared to be more important than LDL-C for CVD in Asians.

Definite management of normalizing lipid profile for the prevention of CVD; therapeutic life style changes with dietary modifications, increased physical activity and weight control are considered the first line therapy. In those with greater risk, drug therapy needs to be started. Besides statins, fibric acid derivatives, cholestyr-amine resins, niacin, ezetimibe, bile acid sequesterants; omega 3 fatty acids were the newer established agents with a positive impact on hyperlipidaemia as shown by various clinical studies as well.

Lipid lowering effects of omega 3 fatty acids play a vital role in hypertriglyceridemia especially. They reduce hepatic synthesis of triglycerides and increase hepatic fatty acid beta-oxidation. Both eicosapentaenoic acid (EPA) and dexahexaenoic acid (DHA) are potent activators of peroxisome proliferator activator receptor (PPAR) alpha (found in the heart) and PPAR gamma.[4] EPA and DHA enhance the lipoprotein lipase activity that accelerates the metabolism of VLDL and chylomicrons.[5] EPA/ DHA effects do not appear to differ by sex or dietary fat intake. A clear linear trend towards greater TG reduction emerged with higher doses of EPA / DHA, regardless of source.[6]

Clinical trials of prescription of omega 3 fatty acids as monotherapy have supported its efficacy for improving the lipid profile (reducing triglycerides and triglyceride-rich lipoproteins and raising HDL-C) in individuals with hypertriglyceridemia or dyslipidaemia.[7]

The aim of our present study was to evaluate the effectiveness of omega 3 fatty acids as a lipid lowering novel agent, specially for serum triglycerides; by keeping in view of CVD risk reduction in future.

MATERIAL AND METHODS

Study Participants

A total of 100 patients (46 males, 54 females) were included in the study aged 40-70 years. Fasting serum triglycerides were taken >150mg/dl in all the patients in this study. The variables specifically recorded were: Serum triglycerides, total cholesterol, VLDL cholesterol, LDL cholesterol, HDL cholesterol, serum renal function test and liver function tests. Out of 100 patients included, 78 were found to have co morbidities (DM, HTN, IHD).

Drug given remained unchanged throughout the study. Patients excluded from the study were: with renal failure, with hepatic failure and pregnant/lactating women.

Study Design

The study done was a non-randomised, prospective therapeutic study. It consisted of a treatment period of 8 weeks for all the patients, after their written/informed consent and approval from the thesis ethical committee. All patients received capsules of omega 3 fatty acids (eicosapentaenoic acid + docosahexaenoic acid) in the dosage of 3g daily. To see the efficacy of the drug, lipid profile was measured at 0 week, after 4 weeks and 8 weeks of the treatment.

Laboratory Parameters

Besides the other routine investigations, 5 cc fasting venous blood samples were collected to obtain the lipid profile of the patients at various

visits and analysed in the department of Biochemistry.

Serum triglycerides were measured by enzymatic method by triglyceride kit (Lyphozyme). Total cholesterol estimation was done by Monozyme kit by an enzymatic method. Coloured complexes formed were measured by spectrophotometry. Phosphotungstate method was used to measure serum HDL cholesterol. VLDL, LDL and chylomicrons of serum are precipitated and HDL cholesterol is present in the supernatant measured.

Seum LDL cholesterol was calculated using Friedwald's formula (Total cholesterol-HDL-Triglyceridesx1/5).Whereas serum VLDL cholesterol was measured by the formula: Triglycerides/5.

Rest of the routine investigations were measured too.

STATISTICAL ANALYSIS

The data from our present study was systematically collected, compiled and statistically analysed using software IBM SPSS 22.0 to draw relevant conclusions. Data was expressed as means, standard deviation, number and percentages. The patient's characteristics were analysed using the x^2-test (Chi square test) and paired "t" test after 8 weeks. The p value of <0.05 was considered as significant, p>0.05 as non significant and p value of <0.001 as highly significant.

RESULTS

100 patients were enrolled with consent in the study. The mean age was 54.15±8.5 years, with maximum number in the age group of 40-50 years. Majority (54%) were females.

Omega 3 fatty acids were given to all patients included in the study and effects were observed on serum lipid profile after two months of the study. There was a reduction of 20.95% after 8 weeks of the treatment in serum triglycerides (237.71±45.77mg% at 0 week vs 188.44±40.67mg% at 8 weeks) with p<0.001. Same reduction (p<0.001) was seen in serum VLDL cholesterol (47.54±9.15 mg% at 0 week vs 37.69±8.13 mg% at 8 weeks). Highly significant reduction (p<0.001) was also found in serum total cholesterol (221.71±25.22mg% at 0 week vs 213.97±22.31mg% at 8 weeks) with 3.33% reduction.

Non significant change (p>0.05) was found in serum LDL cholesterol with the treatment. Whereas, there was a 4.90% rise in serum HDL cholesterol with p<0.001 and mean change of 37.40±3.96mg% at 0 week vs 39.14±3.40mg% at 8 weeks. No side effects were found during the treatment. No patient dropped out of the study.

Table 1. Baseline Characteristics of the study population

Mean Age	54.15±8.5 years
Sex(M/F)	46/54
With Diabetes Mellitus	20
With Hypertension	25
With Ischemic Heart Disease	7

Table 2. Change in all variables of lipid profile

SERUM VARIABLES (mg%)	BASELINE(0 WEEK)	AFTER 8 WEEKS
Triglycerides	237.71±45.77	188.44±40.67
Total Cholesterol	221.71±25.22	213.97±22.31
HDL Cholesterol	37.40±3.96	39.14±3.40
LDL Cholesterol	136.77±20.81	137.14±18.35
VLDL Cholesterol	47.54±9.15	37.69±8.13

Figure 1. Mean reduction in serum triglycerides after 8 weeks

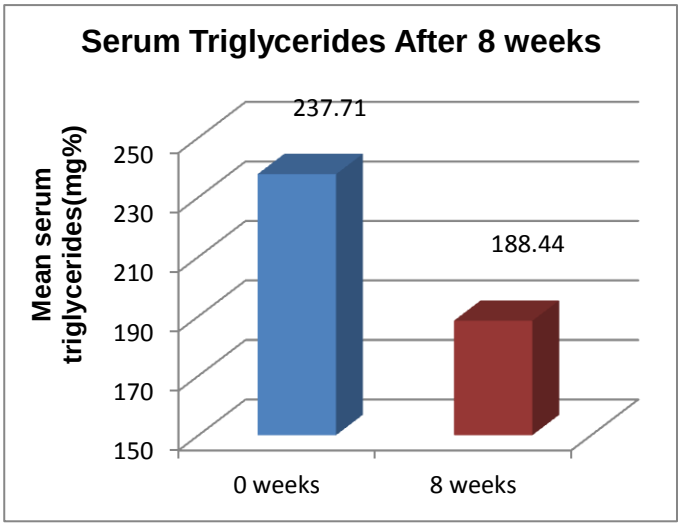
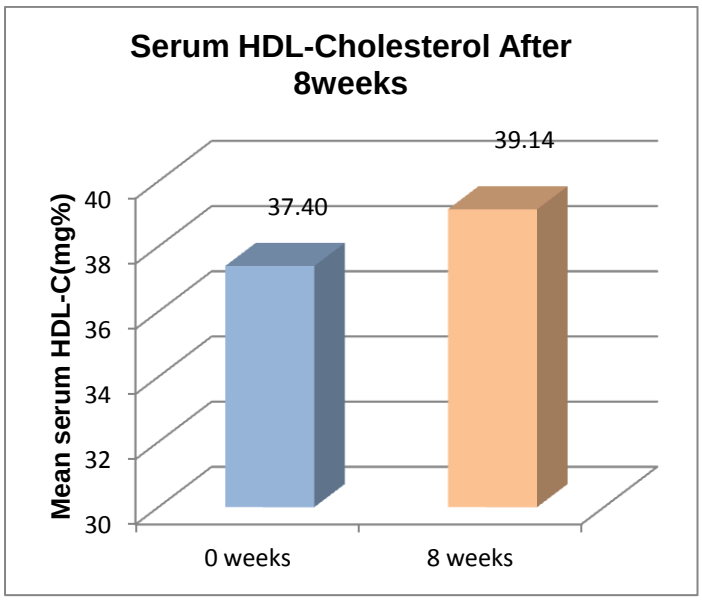


Figure 2. Mean reduction in serum HDL-C after 8 weeks



DISCUSSION AND CONCLUSIONS

Treating dyslipidaemia, and particularly reducing LDL-cholesterol and triglyceride levels, has been established as a highly efficacious means of reducing both morbidity and mortality of atherosclerotic vascular diseases.

A number of meta analysis are published showing an independent association between TG levels and CHD risk, independent of HDL-C levels.[8-10] A recent review has also listed 11 published reports of the independence of plasma triglycerides as a risk factor for CAD.[11]

Low levels of omega 3 fatty acids were independently correlated with the presence and degree of lumen occlusion of lipid-rich, atherosclerotic plaques.[12] Cardio protection associated with omega 3 PUFA is due to a complex web of anti-atherosclerotic, anti-inflammatory and anti-arrhythmic effects. Anti-atherosclerotic effects of omega 3 PUFA are not simply limited to reduction in triglyceride-rich particles, but may in part be due to the changes in particle sizes and a mild antithrombotic action as well. Omega 3 PUFA inhibit the induction of endothelial angiogenic markers, counter several proinflammatory actions of cyclooxygenase-2 leading to angiogenesis, and reduce tube formation and progression, all of which contribute to slower lesion progression and greater stability.[13]

The Copenhagen Male Study [14] included 2906 men who were free of cardiovascular disease at baseline, found that the risk for ischemic heart disease was 50% higher in those with TG levels in the middle tertile and 120% higher in the upper tertile as compared to those in the lowest TG tertile after adjustment for conventional risk factors.

Hypertriglyceridemia can be treated with fibrates, niacin, omega 3 acid ethyl esters, and statins but each with different efficacy. Our study showed that n-3 polyunsaturated fatty acids improved lipid profile with a greater impact on serum triglycerides, VLDL and HDL levels. N3 fatty acids were well tolerated during the study.

Grimsgaard[15] et al studied healthy non smoking men aged 36-56 years, who received omega 3 supplementation with 3.8 g EPA/d or 3.6 g DHA/d or 4.0 g corn oil/d (placebo) for 7 weeks. Serum triglycerides decreased by 26% ($p < 0.0001$) in the DHA group and 21% in the EPA group as compared with the corn oil group. Results of our study are consistent with this study. There was a significant 22% reduction in TG levels relative to the control following the DHA treatment in another study done by Buckley[16] et al.

In a study conducted by Calabresi[17] et al, the patients received four capsules daily of omega 3 fatty acids (providing 3.4 g EPA+DHA per day) or placebo for 8 weeks. They significantly lowered plasma triglycerides and VLDL-C levels, by 27 and 18%, respectively. Results on serum VLDL in our study are consistent with the previous studies.

Laidlaw[18] et al showed significantly higher HDL-C on day 28 than on day 0 in his study group by 7.0% after N-3 supplements. Another study done by Grimsgaard[15] et al for 7 weeks, also showed percentage rise in HDL-C by 4% in patients who received DHA. Our study shows consistent findings.

Effect on serum total cholesterol in our study is consistent with the study conducted by

Grimsgaard et al. Whereas serum LDL was statistically unaffected in the study conducted by Mackness[19] et al, and is consistent with our present study.

A limitation of our study is the lack of comparison with placebo and the short duration of 8 weeks. Longer trials may better characterize the long-term efficacy of omega 3 fatty acids though.

In conclusion, the percentage reduction of serum triglycerides and VLDL-C were found out to be the maximum (20.95%) after 8 weeks of taking omega 3 fatty acids, and was highly significant statistically. There was a highly significant reduction in serum total cholesterol as well, but was not comparable with serum triglycerides. No significant change was found in serum LDL-C levels with the drug.

The results of our study suggest that omega 3 fatty acids are very effective in treating hyperlipidae-mias but specially serum triglycerides with an additive advantage of raising serum HDL-C levels. And being an independent predictor for CVD, treating serum triglycerides have become important in the present day scenario.

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