Migration Letters

Volume: 21, No: S8 (2024), pp. 1387-1396

ISSN: 1741-8984 (Print) ISSN: 1741-8992 (Online)

www.migrationletters.com

Comparative Effect Of Fish Oil And Niacin Supplementation In Lowering Lipid Profile In Dyslipidemic Patients

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Received: January 15, 2024 Revised: February 25, 2024
Accepted: March 4, 2024

ABSTRACT

Fish oil and Niacin supplementation, both have shown to have potential in correcting lipid profile in dyslipidemic patients which is associated as an important [1]risk factor for developing cardiovascular disease. In this study we evaluated the effect of fish oil capsule and niacin supplementation in correcting lipid profile (reducing serum triglyceride, total cholesterol, LDL, and increasing HDL) separately and in comparison to each other in confirmed dyslipidemic patients. Total 90 dyslipidemic patients both male and female were included and were further divided into 3 groups of 30 participants in each group. Group A was taken as control group, group B was given fish oil supplementation 1g twice daily and group C was given extended release niacin 500mg/day for 2 months. Fasting serum lipid profile test was taken and recorded at initial (0 day), post 1 (30^{th} day) and post 2 (60^{th} day) to see any significant effect. Serum samples of each individuals was analyzed at different hospitals and clinics in two major cities of Pakistan namely of Lahore and Layyah and statistically evaluated as any significant difference among the groups. After analyzing the mean difference between three groups, it can be seen that group II (fish oil) had shown significant effect($p<0.05$) in reducing total cholesterol level, LDL level and triglyceride level, whereas group III (niacin) had shown significant effect ($p<0.05$) in increasing HDL level as compared to other groups from 0 day till 60^{th} day. We concluded that fish oil can be used if the goal is to reduce serum LDL level, triglyceride level and total cholesterol level whereas, if the goal is to increase HDL only then better choice could be Niacin as it has better effectin increasing HDL level more than fish oil capsule.

KEYWORDS: *Cardiovascular Disease, Dyslipidemia, Fish Oil, Lipid Profile, Niacin.*

Introduction

Dyslipidemia is defined as elevated low levels of high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol levels. It is an important risk factor for developing stroke and coronary heart disease (CHD) (Fodor et al., 2010; Achila et al., 2022). The

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prevalence of dyslipidemia in Pakistan was 97.18% in diabetic males and 87.15% in diabetic females (Sarfraz et al., 2016). Fish oil consist of omega 3 (n-3 LC-PUFA) including docosahexaenoic acid (DHA; 22:6 n-3) and eicosapentaenoic acid (EPA; 20:5 n-3) (Dyerber, 1978; Douglas 2019). Omega 3 fatty acids are long chains of polyunsaturated fatty acid having double bond three carbons away from the methyl end. Omega 3 such as Eicosapentaenoic acid (EPA) having 20 carbon chain and Docosahexaenoic acid (DHA) having 22 carbon chain are made up in the body in small amount (Whitney et al., 2015; Erdman 2011). Many studies among epidemiological and genetic studies show that increased levels of triglycerides (TG)-rich lipoprotein in circulation elevates the risk of developing cardiovascular diseases (Peter 2016; Robert 2021; Sapa 2022). By introducing omega3 fatty acids (docosahexaenoic acids and eicosapentaenoic acids) in patients of severe hypertriglyceridemia, shows a decrease levels of plasma triglyceride levels. Thus it has been approved for patients of hypertriglyceridemia to reduce serum triglyceride levels (oscarossan et al, 2017; Annette 2010). A study conducted on the effect of fish oil esters of plant sterols in improving the lipid profile of dyslipidemic patients as compared to sunflower oil esters or fish oil of plant sterols. It was a single blind, semi randomized study consisting of period crossover study consisting of experimental isoenergetic diets for the period of 4 week each and then next 4 week intervening as washout time period. These diets consisted of 30% of energy as fat, 70% of which was given from extra virgin olive oil and it differed only in the supplement oil. Fish oil esters of plant sterol and fish oil both provided total eicosapentaenoic acid and docosahexaenoic acid of 5.4 g /day. Whereas fish oil esters of plant sterol, olive oil and sunflower oil esters of plant sterols provided 1.7, 0.02, and 1.7 g free plant sterols per day. The results and conclusion shows that supplementation of fish oil esters of plant sterols and olive oil may reduce the risk of cardiovascular diseases than supplementation with sunflower oil esters of plant sterol and fish oil (Demonty et al,. 2006).The American Heart Association suggests a dose of omega 3 fatty acid upto 2-4g/day for those patients requiring to lower their triglyceride levels (Kris-Etherton, 2002).Niacin is a water-soluble vitamin also known as B3. It has two types of chemical structures; one is nicotinamide and the other is nicotinic acid. Niacin is a unique vitamin among B vitamins as our body can make it from tryptophan (amino acid). It only makes when its primary work is done which is in protein synthesis (Whitney et al., 2015).Niacin has been considered as the most powerful drug for increasing HDL-C. Niacin also is said to be an important drug for decreasing the concentrations of all apoB containing lipoproteins that is, LDL, VLDL, LP(a) , IDL. Recent studies show that decrease levels of thiamine, niacin and pyridoxine is associated with increased incidence of insulin resistance, cardiovascular diseases and diabetes (zeman et al,. 2015).According to Harvard health publishing, the typical doses for niacin range from 250mg twice daily to 500mg thrice daily (Simon et al.,2007).Studies have shown that Niacin Supplementation may decrease LDL cholesterol levels, triglyceride levels and raise HDL cholesterol levels (Whitney et al., 2015). A study conducted to investigate the effect of niacin on atherogenic mixed dyslipidemia. It was a randomized control tial. Total number of participants were 19 who were non-diabetic, obese and hypertriglyceridemic. They were given niacin extended release for 8 weeks. The results showed that extended release niacin supplements favored in normalizing plasma lipid profile and apolipoprotein profile, however insulin resistance was seen to be increased. (Adiels et al,. 2018).

The null hypothesis of the study was that both fish oil and niacin supplementation have same effect in correcting lipid profile of dyslipidemic patients. Whereas the alternative hypothesis was that both fish oil and niacin supplementation does not have the same effect in correcting lipid profile of dyslipidemic patients. The purpose of this study was to determine the effect of fish oil and niacin separately and in comparison to each other and with control group. There is not enough data on the comparison of fish oil capsules and niacin supplements in correcting

dyslipidemia so this research has provide practitioners a good choice in supplements to select in order to treat patients of dyslipidemia.

Materials and Methods

The study was approved from the institutional review board of Nur International University and was conducted in different private clinics of Lahore and Layyah. It was a randomized control trial. Total 90 dyslipidemic patients both male and female of age range between 20-60 years were included who were divided into 3 groups, group A (n=30) participants who were supplemented with fish oil capsules (1g, containing of DHA and EPA at least 300mg tablet twice daily), group B (n=30) participants who were supplemented with Niacin Extended release (500mg tablet once daily) and group C (n=30) participants who received no treatment and was the control group. The interventional study was completed in 2 months period, 3 samples were collected at 0 day, 30th day, and 60th day and the total time including analytical procedure was 4 months. Convenient sampling was used for this study. The results of both interventional group's tests (pre interventional and post interventional) were being compared with each other in reducing lipid profile (decreasing LDL cholesterol, triglyceride levels, cholesterol levels and increasing HDL cholesterol) and also with the control group. Written informed consent was obtained by the participants and any participant who were on statin drug therapy or who were suffering from diseases apart from hypertension, diabetes, dyslipidemia, hypothyroidisim and fatty liver were not included in the study.

Sample collection:

Fasting blood samples of 2.5cc were collected through 3cc syringe by the help of qualified phlebotomist from a credible laboratory and was then stored in yellow top serum vial. After clotting of the sample, it was centrifuged at 3000-4000rpm for about 1-3 minutes in order to get serum and was then stored at temperature of 2-8°C in a fridge until it was transported from collection center.

Bio chemical analysis:

Lipid profile were measured by using BT1500 Clinical chemistry. Analyzer (Biotecnia Instrument, Spain). We did cholesterol oxidation and esterification in the presence of cholesterol oxidase and cholesterol esterase and determine cholesterol. Under the catalysis of peroxidase, the hydrogen peroxidase formed reacts, and to form a red violet quinonemine dye ad indicator we used 4-aminophenazone and phenol.For low density lipoprotein, they were precipitated at their isoelectric point (pH 5.04) by heparin. After the centrifugation the very low density lipoprotein (VLDL) and the high density lipoprotein (HDL) remained in supernatant, and were determined by the enzymatic methods. In addition of phosphotungstic acid with magnesium ions the LDL fractions were precipitated quantitatively. After the centrifugation, the concentration of cholesterol in HDL fraction remained in supernatant were then determined by enzymatic method. We determined triglycerides after the enzymatic hydrolysis with lipases. From hydrogen peroxide, 4-chlorophenol and 4 aminophenazone the indicator which is quinonemine were formed under the catalytic influence of peroxidase (Jafri et al,.2015).

Preferred cut of values:

For serum lipids we used NCEP-ATP III Guidelines. According to these guidelines. According to these standard guidelines the normal range of LDL Cholesterol after 9-12 hour fasting is <100mg/dl, total cholesterol should be <200mg/dl, HDL should be >60mg/dl and triglyceride should be <150mg/dl.

Statistical analysis:

We used SPSS (version 12) to perform the statistical analysis. All the variables (continuous) were presented as mean value ± standard deviation. A sample of size 90 (30 in each group) has been selected using 5% level of significance, 95% confidence interval, 80% power of the test and 0.35 cohen suggested effect size. Sample size is calculated by using power analysis in R Statistical Computing programing language. ANOVA and Friedman test was used for the analysis of the variables.

Results

Table 1. EFFECT OF THREE GROUPS (CONTROL, FISH OIL AND NIACIN) IN REDUCING LDL LEVEL at 0, 30, 60 days.

	Groups	LDL	Total	P-Value
	Group I (control)	145.73±39.26		
Pre (0 day)	**Group II (**fish oil)	138.63±32.29	155.34±40.88	0.0001**
	Group III (niacin)	181.67±38.00		
	Group I (control)	141.10±36.63		
Post 1 (30th day)	**Group II (**fish oil)	130.40±27.78	148.76±37.79	0.0001**
	Group III (niacin)	174.77±34.06		
	Group I (control)	135.50±38.00		
Post 2 (60th day)	**Group II (**fish oil)	122.67±30.61	142.11±38.02	0.46
	Group III (niacin)	168.17±30.28		

All the variables are presented in form of Mean±SD

**(P<0.01)

A total of 90 dyslipidemic patients were tested for their lipid profile test and were divided into 3 groups (n=30). Among them 68 were male and 22 were female. The mean difference of LDL cholesterol between the groups is shown in table 1 as at 0 day it was 155.34mg/dl±40.88SD with p>0.05, at 30th day was 148.76mg/dl±37.79SD with p<0.05 and at 60th day was 142.11mg/dl±38.02SD with p>0.05. This shows that LDL was reduced significantly before and after 1 month of intervention between the 3 groups but it does not show any significant reduction after the 2nd month of intervention.

Table 2. EFFECT OF THREE GROUPS (CONTROL, FISH OIL AND NIACIN) IN DECREASING TOTAL CHOLESTEROL at 0, 30th and 60th day.

	Groups	Total Cholesterol	Total	P-Value
	Group I (control)	147.70±25.42		

Pre (0 day)	**Group II (**fish oil)	218.80±45.77	179.04±43.93	0.002*
	Group III (niacin)	170.63±21.39		
	Group I (control)	146.20±23.79		
Post 1 (30th day)	**Group II (**fish oil)	205.50±27.62	173.59±34.25	0.0001**
	Group III (niacin)	169.07±20.53		
	Group I (control)	143.83±22.40		
Post 2 (60th day)	**Group II (**fish oil)	182.33±25.56	164.46±27.66	0.0001**
	Group III (niacin)	167.20±20.38		

All the variables are presented in form of Mean±SD.

**(P<0.001)

The mean difference of total cholesterol level between the three groups is shown in Table 2 as at 0 day it was 179.04mg/dl±43.93SD with p<0.05, at 30th day it was 173.59mg/dl±34.25SD with p<0.05 and at 60th day it was 164.46mg/dl±27.66SD with p<0.05. Total cholesterol level has been seen between the groups to be significantly decreasing before and after the intervention.

Table 3. EFFECT OF THREE GROUPS (CONTROL, FISH OIL AND NIACIN) IN REDUCING TRIGLYCERIDE LEVEL:

	Groups	**Triglyceride**	**Total**	**P-Value**
	Group I (Control)	143.53±32.21		
Post (at 0 day)	**Group II (**Fish Oil)	267.27±80.82	211.59±80.05	0.000**
	Group III (Niacin)	223.97±62.78		
	Group I (Control)	142.83±31.61		
Post (at 30 day)	**Group II (**Fish Oil)	239.40±69.18	197.60±67.15	0.000**
	Group III (Niacin)	210.57±54.49		
	Group I (Control)	142.40±32.24		
Post (at 60 day)	**Group II (**Fish Oil)	213.80±61.74	184.48±57.62	0.000**
	Group III (Niacin)	197.23±49.48		

All the variables are presented in form of Mean±SD.

** (P<0.001)

Table 3 shows the mean difference of triglyceride between the three groups at 0 day as 211.59mg/dl±80.05SD, at 30th day was 197.60mg/dl±67.15SD at 60th day as 184.48mg/dl±57.62SD ($p<0.05$). Our results shows a significant decrease of serum triglyceride level among the participants before and after the intervention period.

TABLE 4. EFFECT OF THREE GROUPS (CONTROL, FISH OIL AND NIACIN) IN INCREASING HDL LEVEL at 0, 30th and 60th day.

	Groups	**HDL**	**Total**	**P-Value**
	Group I (Control)	38.37±9.20		
Post (at 0 day)	**Group II (**Fish Oil)	44.97±13.56	40.88±10.84	0.000**
	Group III (Niacin)	39.30±8.08		
	Group I (Control)	39.20±9.17		
Post (at 30 day)	**Group II (**Fish Oil)	48.10±12.81	43.27±10.74	0.001**
	Group III (Niacin)	42.50±8.02		
	Group I (Control)	40.13±9.08		
Post (at 60 day)	**Group II (**Fish Oil)	51.37±13.38	46.17±11.51	0.000**
	Group III (Niacin)	47.00±8.87		

All the variables are presented in form of Mean±SD.

**($P<0.01$)

Table 4 shows the mean difference of HDL level between the three groups at 0 day as 40.88mg/dl±10.84SD, at 30th day as 43.27mg/dl±10.74SD and at 60th day as 46.17mg/dl±11.51SD. It shows that there was significant increase in HDL before and after the intervention period of 2 months.

TABLE 5. EFFECT OF PLACEBO ON LIPID PROFILE OF GROUP I (CONTROL):

	Groups	**LDL**	**P-Value**
	Pre (0 day)	2.42	
Group 1 (control)	**Post 1 (30th day)**	2.03	0.002*
	Post 2 (60th day)	1.55	
	Groups	**HDL**	**P-Value**
	Pre (0 day)	1.38	
Group 1 (control)	**Post 1 (30th day)**	1.95	0.000**
	Post 2 (60th day)	2.67	
	Groups	**Cholesterol**	**P-Value**
	Pre (0 day)	2.27	
Group 1	**Post 1 (30th day)**	2.00	0.118

(control)			
	Post 2 (60th day)	1.73	
	Groups	**Triglyceride**	**P-Value**
	Pre (0 day)	2.07	
Group 1 (control)	**Post 1 (30th day)**	1.97	0.905
	Post 2 (60th day)	1.97	

All the variables are presented in form of Mean±SD

Friedman Test **(P<0.001)

Table 5 shows group 1(control) to be decreasing serum LDL level and increasing serum HDL level more after the 2nd month of intervention than at initial reading with p<0.05. Whereas insignificant decrease of serum total cholesterol level (p=0.118) and triglyceride level (p=0.905) after the intervention period was seen.

Table 6. EFFECT OF FISH OIL ON LIPID PROFILE IN GROUP II:

	Groups	**LDL**	**P-Value**
	Pre (0 day)	2.40	
Group 2 (Fish Oil)	**Post 1 (30th day)**	2.00	0.008*
	Post 2 (60th day)	1.60	
	Groups	**HDL**	**P-Value**
	Pre (0 day)	1.05	
Group 2 (Fish Oil)	**Post 1 (30th day**	1.95	0.000**
	Post 2 (60th day)	3.00	
	Groups	**Cholesterol**	**P-Value**
	Pre (0 day)	2.73	
Group 2 (Fish Oil)	**Post 1 (30th day)**	2.07	0.000**
	Post 2 (60th day)	1.20	
	Groups	**Triglyceride**	**P-Value**
	Pre (0 day)	2.97	
Group 2 (Fish Oil)	**Post 1 (30th day)**	1.93	0.000**
	Post 2 (60th day)	1.10	

All the variables are presented in form of Mean±SD

Friedman Test **(P<0.001)

Table 6 shows group 2 (Fish Oil) to be significantly decreasing serum LDL level, serum total cholesterol level and serum triglyceride level with p<0.05. Whereas it has been seen as significantly increasing serum HDL level with p<0.05 after the intervention period.

Table 7. EFFECT OF EXTENDED RELEASE NIACIN OF LIPID PROFILE OF GROUP III:

	Groups	**LDL**	**P-Value**
	Pre (0 day)	3.00	
Group 3 (Niacin)	**Post (30th day)**	2.00	0.000**

	Post (60th day)	1.00	
	Groups	**HDL**	**P-Value**
	Pre (0 day)	1.07	
Group 3 (Niacin)	**Post (30th day)**	1.93	0.000**
	Post (60th day)	3.00	
	Groups	**Cholesterol**	**P-Value**
	Pre (0 day)	2.47	
Group 3 (Niacin)	**Post 1 (30th day)**	2.07	0.000**
	Post 2 (60th day)	1.47	
	Groups	**Triglyceride**	**P-Value**
	Pre (0 day)	3.00	
Group 3 (Niacin)	**Post (30th day)**	2.00	0.000**
	Post (60th day)	1.00	

All the variables are presented in form of Mean±SD

Friedman Test **(P<0.001)

Table 7 shows group 3 (Niacin) to be significantly decreasing serum LDL level, serum total cholesterol level and serum triglyceride level with p<0.05. Similarly it has been shown to be significantly increasing HDL level with p<0.05 after the intervention period.

Discussion

Dyslipidemia is one of the major cause of cardio vascular diseases. There is said to be a relationship between ischemic heart disease and total plasma cholesterol concentration in the blood and the risk of morbidity and mortality. It is important to correct serum lipid without any harmful medication and can be done by introducing supplementation like fish oil and niacin which have been seen to be effective in correcting lipid profile. However only few researches have shown which treatment (fish oil or niacin) have shown the maximum effect in correcting dyslipidemia. This research provides a better choice in selecting supplement for correcting dyslipidemia. The study found that fish oil supplementation had shown the maximum difference in reducing LDL as compared to niacin and control as p<0.05 from 0 day till 60th day as it can be seen in table 1. Similarly fish oil had shown the maximum difference in reducing the total cholesterol level and triglyceride level as compared to niacin and control with p<0.05 from 0 day till 60th day (table 2 and 3). Our study also found that Niacin had shown the maximum difference in increasing as compared to fish oil and control with p<0.05 from 0 day till 60th day (table 4). A similar study conducted also showed similar results in decreasing LDL, total cholesterol and triglyceride levels by fish oil supplementation and in increasing HDL by niacin supplementation at the end of their intervention period (Savinova et al,. 2015).

Control group have shown to be effective in increasing HDL levels and decreasing LDL levels, however it had no effect on total cholesterol levels and triglyceride levels at the end of intervention period (table 5). Fish oil have shown a positive effect in reducing LDL, Total Cholesterol and triglyceride levels and in increasing HDL levels (table 6) whereas Niacin had shown a positive effect in reducing LDL, Total Cholesterol and triglyceride levels and in increasing HDL levels after the intervention period. A similar study was conducted showed their control group showed similarity to our study as they showed no effect on total cholesterol. Their fish oil group also had shown to be increasing HDL levels and decreasing triglyceride

levels .whereas it showed opposite results to our study as their fish oil group showed an increase in LDL levels and total cholesterol levels (Caslake et al,.2008).

Conclusion

It was revealed that both Fish oil and Niacin have played a role in correcting dyslipidemia. Significant association can be seen in fish oil in lowering lipid profile as the P<0.05 and had more strong effect on lowering LDL, Total Cholesterol and triglyceride levels. Niacin too have significant association in correcting dyslipidemia as P<0.05 and had more strong effect in increasing HDL levels. Fish oil can be used if the goal is to reduce serum LDL level, Triglyceride level and Total Cholesterol level as it showed no side effect. If the goal is to increase HDL only than better choice could be Niacin as it have an effective drug in increasing HDL level more than fish oil capsule. We faced some limitations that we could only include 90 patients of which males were more than females, this was due to covid-19 pandemic. Time duration should be extended for further studies in order to get more clear results.

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