Bioresearch Communications
Volume 06, Issue 01, January 2020
Journal Homepage: www.bioresearchcommunications.com

Original Article

Useful Effects of Omega-3 Fatty Acids on Serum Alkaline phosphatase And Gamma-glutamyl-transferase Levels in Middle Aged Patients with Diabetes mellitus

Tamnna Binte Habib[1*], Qazi Shamima Akhter[1], Hasan Imam[2], Nahid Yeasmin[3], Farhana Rahman[3], Sharmin Nahar[3], Shamima Akhter[3] and Tahmina Akhter[3]

[1]Department of Physiology, Dhaka Medical College, Dhaka. [2]Department of Anesthesia, Combined Military Hospital, Bogra. [3]Department of Physiology, Dhaka Medical College, Dhaka.

ABSTRACT:

***Background*:** Patients with type-2 Diabetes are augmented the risk of non alchoholic fatty liver disease that rises liver enzymes. Dietary supplementation of omega-3 fatty acid may reduce liver enzymes.

***Objective*:** To observe the favourable effects of fish oil capsule on ALP and GGT in patients with type 2 DM**.**

***Methods*:** This prospective interventional study was conducted during 2017 in Physiology department DMC on 52 diagnosed type 2 diabetic patients of both sexes were scrutinized with age ranging from 40 to 50 years. Among them, 27 type 2 diabetic patients those who taken oral fish oil gel (2g/day) for 12 weeks were preferred as study group. Another 25 type 2 diabetic patients without any supplementation were nominated as control group for juxtra-position. The study subjects were scrutinized from Outdoor of Endocrinology Department, DMC, Dhaka and personal contact from Dhaka city on the basis of inclusion and exclusion criteria. The research work was administrated with ethical clearance from concerned authority. The study parameters serum ALP and GGT were estimated by enzymatic colorimetric method in auto-analyzer in Department of Laboratory Medicine, DMC, Dhaka. Serum TG and FBG also measured .The parameters were studied 2 times in study and control groups i.e. at the beginning of study (base line) and after 12 weeks of study period. Data were collected in pre-designed structured questionnaire from the researcher by herself. For statistical analysis, Paired Student's 't' test and Unpaired Student's 't' test were performed as applicable using SPSS for windows version 16.0**.**

Results: In this study ALP (Alkaline- Phosphatase) and GGT(gamma-glutamyltransferase) were reduced in diabetic patients after supplementation with omega-3 fatty acid in comparison to that of their baseline value. Again, after 12 weeks, ALP(Alkaline Phosphatase) and GGT(gamma glutamyltransferase) were decreased in diabetic patients after supplementation with omega-3 fatty acid in comparison to control group.

***Conclusion*:** After analyzing the results of the study, it can be concluded that omega-3 fatty acid can reduce ALP and GGT levels in diabetic patients may be helpful to minimize the risk of fatty liver in type-2 diabetes mellitus

Keywords: Diabetes mellitus, fatty liver, ALP, GGT and Omega-3 fatty acid.

Article History
Received: 17 September 2019
Accepted: 19 December 2019

Scan the QR code to see the online version or,visit- www.bioresearchcommunications.com

Corresponding author
Tamnna Binte Habib
Department of Physiology, Dhaka Medical College, Dhaka.
Email: tamannapompy1234@gmail
Phone: +8801769101147

Citation: Habib, TB., Akhter, QS., Imam, H., Yeasmin, N., Rahman, F., Nahar, S., Akhter, S. and Akhter, T. Useful effects of omega-3 fatty acids on serum Alkaline phosphatase and Gamma-glutamyl-transferase levels in middle aged patients with diabetes mellitus . 2020 . ***Biores Comm*** . 6(1), 806-809.

INTRODUCTION

Diabetes mellitus (DM) is one of the multifactorial disorder characterized by hyperglycemia related with carbohydrate, protein and fat metabolism. The chronic hyperglycemia of diabetes is associated with long term damage of liver can causes non alchoholic fatty liver disease[1]. Diagnostic criteria of diabetes mellitus are fasting plasma glucose level ≥7.0mmol/l (126mg/dl) or

plasma glucose 2 hours after an oral glucose ≥ 11.1 mmol /L (200mg/dl) and HbA1c≥ 6.5%[2].Within 2030, the extensiveness of diabetes mellitus will be 11.1 million in Bangladesh[3]. The prevalence of NASH is steadily increasing and prevalent in patients of Diabetes mellitus[4]

The pancreatic hormone named insulin is needed for tissue development, growth and maintenance of whole body glucose homeostasis. Insulin maintains glucose homeostasis by improving the rate of glucose uptake into skeletal muscle and fat tissue. In the skeletal muscle, insulin fascilitates glucose uptake by stimulating translocation of GLUT-4 to plasma membrane[5] Insulin resistance occurs when the insulin sensitive tissue loses response to insulin. The basic effect of insulin resistance on glucose metabolism is to oppose the uptake and utilization of glucose by most cells of the body. As a result blood glucose concentration rises, cell utilization of glucose falls, utilization of fat increases and free fatty acid level increases in blood [6]

ω-3 Fatty acids are polyunsaturated fatty acids consists of alpha- linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA). They are found mainly in seafish including fatty fish (e.g. salmon, tuna and trout) and shellfish (e.g. crab, mussels and oysters).The omega 3 fatty acid; stimulates insulin sensitivity, reduces blood clotting, improves fat digestion, boost up fertility, lessen depression and causes brain development in babys[7].

Consumption of fish oil can decreases free fatty acid level, promotes insulin sensitivity as well as reduce the incidence of type 2 DM [8] Omega-3 capsule act directly on insulin sensitive tissues, rises number of insulin receptors thus inhibits insulin resistance[9]Intake of food rich in omega-3 fatty acid, facilitate the action of insulin through various metabolic pathways, which are reduction of hepatic lipogenesis, suppression of the release of triglycerols from liver, improvement in ketogenesis, and oxidation of fatty acids in hepatic cells [10]. Non alchoholic fatty liver diseases are very common in type 2 diabetic patients[11]Moreover, intake of polyunsaturated fatty acid decreases serum ALP and GGT level[12].

Omega- 3 fatty acid prevents this change by increasing peroxisome proliferator receptor gamma, increasing hepatic uptake and oxidation of free fatty acid in striated muscle [13].Therefore the present study is intended to assess the effect of supplementation of omega- 3 fatty acid in Bangladeshi diabetic patient that reduce liver enzymes.

MATERIAL AND METHODS

This prospective, interventional study was administrated from Department of Physiology, Dhaka Medical College, Dhaka from January 2017 to December 2017.The research work was carried-out by obtaining ethical clearance from related departments, Research Review Committee and Ethical Review Committee of Dhaka medical college, Dhaka. The patients were selected from outdoor of Endocrinology, Dhaka medical college and personal contact from Dhaka city. At the beginning of study 60 diagnosed type-2 diabetic patients were randomly nominated on the basis of exclusion and inclusion criteria. There were 30 patients of control group and 30 patients of study groups scrutinized for study purpose, After 6 weeks of study period, 3 patients were relinquished from study group and 5 patients were dropped out from control group. Finally, total 52 type diabetic patient of both sexes with the age ranging from 40-50 years with FBG 7.0 mmol/l or 126 mg/dl, HbA1c 6.5%, serum total cholesterol >200 mg/dl, serum triglyceride >150 mg/dl, LDL>130 mg/dl, BMI≤30 Kg/m^2 and patients with oral hypoglycemic drug were included in this study. Fatty liver was diagnosed by abdominal ultra-sonography Subjects having history of heart, endocrine disorder, insulin therapy, viral hepatitis, acute or chronic infections, pregnant and lactating women were excluded from this study. For this study 27 diagnosed type-2 diabetic patients with omega-3 fatty acid supplementation were selected as study group and 25 type-2 diabetic patients without any supplementation were selected as control group. Patients of both group were taken regularly oral antidiabetic drug. The study group again segmented into pre-supplementation group and after 12 weeks of supplementation as post supplementation group. The control group was sub-divided as pre and post follow-up group. After selection, the nature, purpose and benefits of the study were explained to each subject and informed written consent was taken from participants. Before taking blood detailed family and medical history were taken. Anthropometric measurement of the subjects was recorded and blood pressure was measured. All the information were recorded in a prefixed questionnaire. With aseptic precaution, 5 ml of venous blood was obtained from ante-cubital vein by a disposable plastic syringe from each subject after overnight fasting for biochemical tests. Serum ALP and GGT were estimated by enzymatic colorimetric method in auto-analyzer in department of Laboratory Medicine Dhaka Medical College Hospital, Dhaka. Fasting blood glucose and serum triglyceride levels were also estimated by autoanalyzer.Omega-3 fatty acid (2gm) was supplied to study group then they were asked to intake twice daily for 12 weeks with proper directions. Patients were instructed not to change their diet and physical activities during the course of the study. A regular telephonic communication was made to participants. For statistical analysis, Paired Student's 't' test and Unpaired Student's 't' test were performed as applicable using SPSS for windows version 16.0**.**Data were expressed as mean ± SE. The *p* value of < 0.05 was accepted as level of significance.

RESULTS

In this study no significant difference were observed in age, sex, systolic and diastolic blood pressure except BMI between study and control group (Table 1). In this study, the mean serum ALP and GGT levels were almost similar and there is no statistical difference were observed at the beginning of the study. Fasting blood glucose and serum triglyceride levels also similar at the beginning of the study.

In table (2) in study group, the mean serum ALP (p<.0.001), mean serum GGT (p<.01),mean fasting blood glucose (.001) and serum triglyceride level (p<.0.01), were found remarkable lower in post supplementation group, than pre-supplementation group. Again the mean serum ALP (p<.001) levels and mean serum GGT (p<.01) levels were found significantly lower and in study group compared to control group. Fasting blood glucose and serum triglyceride levels also found lower significantly in study group compared to control group. In control group, there was no statistical dissimilarity were perceived in mean serum ALP , GGT,FBG and triglyceride levels between pre-follow-up and post follow-up group.

Table 1. General characteristics of the patients in both groups (N=52)

Parameters	**Study group** (n=27)		**Control group** (n=25)	
Age (years)[a]	45.90 ± 3.80		44.92 ± 3.75	
Sex (%)[b]				
Male	18 (66.7%)		11 (44 %)	
Female	9 (33.3%)		14 (56%)	
BMI (kg/m^2)	At base line 25.03 ± 2.27	After 3 month with fatty acid supplementation 21.03 ±1.04	At base line 25.87 ± 1.75	After 3 months with fatty acid supplementation 24.67± 1.09
Systolic BP (mmHg)	119.07 ± 7.08		121.79 ± 4.47	
Diastolic BP [a] (mmHg)	79.63 ± 6.26		80.00 ± 0.00	
Duration of disease [a] (years)	5.43 ± 1.50		5.35 ± 1.57	

Results were expressed as mean ± SD. a=Unpaired Student's 't' test was performed to compare between the groups. b= Chi Square test was performed to compare male and female between the groups. The test of significance was calculated and p value < 0.05 was accepted as level of significance. N= total number of subjects, n = number of subjects in each group ns= non-significant */**/***= significant. T2DMS=Type 2 diabetes mellitus with supplementation T2DM=Type 2 diabetes mellitus without supplementation. BMI is measured with Paired students t test in between groups and unpaired student t test in two groups.

Table 2. Serum alkaline phosphatase and serum gamma-glutamyl transeferase, serum

Parameters	**Study group** (n=27)		**Control group** (n=25)	
	Pre-supplemenation group	***Post supplementation group***	***Pre-follow-up group***	***Post follow-up group***
ALP(IU/L)	74.6 ± 2.71	38.5 ± 1.67**	69.20 ± 4.20	61.96 ± 4.43##
GGT(IU/L)	48.3 ± 4.03	31.5± 1.02*	47.68 ± 2.68	46.8± 2.20##
TG(mg/dl)	170.04± 16.26	154.81± 27.08[8]	169.28± 24.92	166.80± 21.09[3]
FBG(mmol/l)	8.96± 1.18	6.83± 0.49[88]	8.86± 0.95	8.78± 0.78##

Results are expressed as mean ± SD. a= Paired student's t test was performed for comparison within groups and b=unpaired t test was performed to compare between groups. p value < 0.05 was accepted as level of significance. N= total number of subjects, n = number of subjects in each group, ALP=Alkaline Phosphatase , GGT=Gamma glutamyl transeferase TG = triglyceride, FBG= fasting blood glucose(*= study group baseline vs study group after 12 weeks of supplementation; # = study group after 12 weeks vs control group after 12 weeks); (* p<.01, **p<0.001;# p<.01,## p<0.001).

DISCUSSION

The present study observed the mean serum ALP and GGT levels were reduced in patients of T2DM after supplementation with omega-3 fatty acid in comparison to that of their baseline value. Here FBG and triglyceride levels also reduced in fish oil supplemented group compaired to baseline and control group. Insulin resistance leads impaired fatty acid oxidation in liver that causes accumulation of fat in liver.[14]When diabetic patient suffers from non alchoholic fatty liver diseases liver enzymes such as ALP and GGT rises .[15] Almost similar type of result were seen by different researchers

of different countries. [16,17] On the contrary, found no significant difference were observed on liver enzymes in patients after supplementation of omega-3 fatty acid in comparison to that of their baseline values and diabetic control group who were not supplemented with omega-3 fatty acid. There were a history of less physical activity in the study subjects that might be contributed the result of those study. Literature review suggested that, when fat stored in liver it leads to rise serum triglyceride level. When serum triglyceride level rises it rises serum ALP and GGT levels.[18]The binding of insulin with its receptor through releasing some inflammatory mediator from liver, that decreases insulin receptor signaling activity, this facts are influenced by rising serum TG level.Omega-3 fatty acid has a role on reducing serum triglyceride level. Peroxisome proliferator receptor–α exists in the liver which increase in number in presence of omega-3 fatty acid. An increase in PPAR–α leads to hepatic uptake of free fatty acid. It also uprise the free fatty acids oxidation in skeletal muscle. As a result, free fatty acid level is reduced in blood. The consequence of free fatty acid reduction helps to decrease triglyceride synthesis. Thus, fish oil capsules reduces serum triglyceride level that promotes the binding of insulin to its receptor and enhances insulin sensitivity. [19]Fish oil activate PPAR-@ (peroxisome proliferator activated receptor alpha) and down regulate sterol regulatory element binding protein-1c (SREBP-1)that enhance fatty acid oxidation and decreases liver enzymes.[11] Modulation of Alkaline Phosphatase enzyme can be done by dietary fish oil.[20]
In the present study serum ALP and GGT levels decreases in patients with T2DM after supplementation of omega-3 fatty acid in contrast to their baseline value and control group. Omega-3 fatty acid supplementation lessen ALP and GGT by increasing fatty acid oxidation. This premises the binding of insulin to its receptor and improves insulin sensitivity.

CONCLUSION

After analyzing the results of the study, it can be concluded that supplementation of omega-3 fatty acid can reduces serum ALP and GGT levels by reducing serum triglyceride level in patients with type-2 diabetes mellitus. Therefore, omega-3 fatty acid containing diet may be useful to keep down the complications in type-2 diabetes mellitus.

ACKNOWLEDGEMENT

The authors are thankful to the study subjects for their active, sincere and voluntary participation.

REFERENCES

1. Jun DW, Kim HZ, Bae JH, Lee OY.The clinical significance of HbA1c as a predictive factor for abnormal postprandial glucose metabolism in NAFLD patients with an elevated liver chemistry.Hepatogastroenterology.2011;58:1274-79.
2. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: Report of a WHO/IDF. Consultation. [Internet].Geneva: World Health Organization;2011. [Cited 2017 May 18].Available from ;https;//www.idf.org.
3. Baynest HW. Classification, pathophysiology, diagnosis and management of diabetes mellitus. J of Diabetes Metab 2015; 6:1-13. Doi:10.4172/2155-6156.1000541
4. Vernon G, Baranova A, Younossi ZM.Systemic review : the epidemiology and natural history of non-alchoholic fatty liver disease and nonalchoholic steatohepatititis in adults.Aliment Pharmacol Ther 2011;34:274-85.
5. Pessin JF and Saltiel S.Signaling pathways in insulin action: molecular targets of insulin.The J of Clin inv 2000;106(2) : 155-69.
6. Delarue J and Magnan C. Free acids and insulin resistance. Research Gate 2014 ;10(1): 142-48.
7. National Center for Complementary and Integrative Health n.d., Omega-3 supplements in depth. [Interenet] 2017[Cited on April 23]2017. Available from: http://nccih.nih.gov//omega-3 supplements in depth/html
8. Albert BB, Derraik JGB, Brenan CM, Smith GC, Glarg ML, Smith DC, Hofman PL and Cutfield WS, 'Higher omega-3 index is associated with increased insulin sensitivity and more favourable metabolic profile in middle-aged overweight men'.Sci Rep 2014;4:1-8.
9. Laila AZ and Lanza IR.Insulin –Sensitizing effects of omega-3 fatty acids: lost in translation. Nutr 2016;8 (6) :1-24.
10. Portillo-Sanchez P et al.High prevalence of Nonalchoholic Fatty Liver Disease in patients with type 2 Diabetes Mellitus and normal plasma Amnotranseferase level. J Clin Endocrinol Metab.2015;100(6):2231-38.
11.Parker HM, Johnson NA,Burdon CA,Cohn JS.Omega-3 PUFA supplementation and non alchoholic fatty liver disease.J Hepatol.2012;56:944-51.
12.Lopez AL, Ramos RV, Carrillo BE. Type 2 Diabetes, PUFAs and vitamin D: their relation to inflammation. J of Immun Res. 2014; 1:1-14.
13.Harikrashna B.Bhat,Robert J.Smith.Fatty liver diseases in Diabetes mellitus.Hepatobilliary Surg Nutr. 2015;4(2):101-08.
14.Mandal A, Bhattarai B, Kafle P, Khalid M. Elevated liver enzymes in patients with Type-2 Diabetes Mellitus and N on alchoholic fatty liver disease.Curious. 2018;10:1-9.
15. Shresta N, Bhatt NP, Neopane P, Dahal S. Hepatic involvement with elevated liver enzymes in Nepalese subjects with Type-2 diabetes mellitus.Int J of Biochem Res Rev. 2017;16:1-8.
16.Ni H, Soe HHK, Htet A:Determinants of abnormal liver function tests in diabetes patients in Myanmar.Int J Diabetes Res.2012;1:36-41.
17.Jameil NA, Khan FA,Arjumand S,Khan MF,Tabassum H.Associated liver enzymes with hyperlipidemic profile in type2 diabetes patients.Int J Clin Exp Pathol.2014;7(7)4345-49.
18. Shidfar F, Keshavaraz A, Hosseyni S, Ameri A et al. Effect of omega -3 fatty acid supplements on serum lipids, apo-lipopotein and malondehyde in type 2 diabetes patient. East Mediterranean Health J.2008;14(2):305-12.
19. Fernandez ML and West KL. Mechanism by which Dietary Fatty Acids Modulate Plasma Lipids. J Nutr 2005;135:2075-78.
20.W Rachel , C Uri and M Shoshana.Dietary fish oil modulates the Alkaline Phosphatase Activity and not the fluidity of Rat Intestinal Microvillous Membrane,The J of Nutr 1992;122(5):1077-84.doi.org/10.1093/jn/122.5.1077.