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Beneficial effects of omega-3 fatty acid on dyslipidemia in organs of alloxan-induced diabetic rats

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ABSTRACT

Diabetes Mellitus is one of the heterogeneous metabolic disorders associated with dyslipidemia, a major risk factor contributing to cardiovascular disease. This metabolic abnormality affects virtually all organs. Over the years, antidiabetic drugs which majorly aim at the hyperglycemic aspect of the disease have been used. Therefore, to address this dyslipidemia, omega-3 fatty acid (O3FA) supplement was employed. Its effects on lipid metabolism in the organs (heart, liver, kidney, pancreas, spleen and brain) of alloxan-induced (150mg/kg body weight, intraperitoneally) diabetic male rats were investigated. O3FA (0.4g/kg b.wt/day) was administered as pre- and post-treatment for 2 weeks. The lipid levels were significantly increased (p<0.05) in diabetic rats. O3FA administration significantly reduced (p<0.05) the levels of cholesterol, phospholipids, triacylglycerol by varying extents, in the examined organs without affecting hyperglycemia in the diabetic rats. The ratio of HMG CoA/mevalonate decreased in the liver of the diabetic rats by 28% indicating increased activity of HMG-CoA reductase. This diabetes-induced dyslipidemia was accompanied by a 28% increase in the activity of hepatic HMG-CoA reductase. Administration of O3FA to the diabetic rats however resulted in 10% and 17% decrease in the activity of this enzyme in the pre- and post-treated groups respectively. Also, lipid peroxidation was significantly reduced (p<0.05) by O3FA suggesting that it has protective effect against oxidative damage. This study reveals that O3FAsupplement has beneficial effects in attenuating dyslipidemia observed in diabetes mellitus and could be beneficial as an adjunct in the management of diabetes mellitus.

Keywords: Diabetes mellitus, omega-3 fatty acid, adjunct, dyslipidemia, ljpid peroxidation, organs

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INTRODUCTION

Diabetes mellitus is a disease of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism as a result of dysfunction and failure of various organs [1]. Amongst the various causes of diabetes are auto-immune reaction, insulin resistance, chronic pancreatitis, insulin gene mutation and glucagonoma [2, 3 and 4]. Complications associated with diabetes include keto-acidosis, hyper-osmolar non-

ketotic coma, atherosclerosis, retinopathy, neuropathy and intra-uterine death of foetuses in pregnant women [5 and 6]. A prominent biochemical mechanism of the pathogenesis of these complications is disorder of lipid metabolism. According to WHO 2002 report, it was estimated that 150 million people suffer from diabetes mellitus, and the number might double in 2025. Most of the cases of diabetes in developing countries occur due to population growth, unhealthy diets, ageing, obesity and sedentary lifestyle [7]. With an increase in the prevalence of diabetes, there is need to sort for alternative therapy for the management of diabetes.

Omega-3 fatty acids also known as polyunsaturated fatty acids are essential to the human body. They can be obtained from salmon, sardines, walnut, canola oil and flaxseed oil. Studies have revealed that omega-3 fatty acids reduce inflammation [8] and help in the prevention of risk factors associated with cancer, arthritis and dyslipidemia-associated disease like coronary heart diseases [9, 10, 11, 12 and 13]. This study therefore aimed at investigating the effects of omega-3 fatty acid as a treatment/adjunct on lipid metabolism in organs of alloxan-induced diabetic albino rats.

MATERIALS AND METHODS

Animals and chemicals

Thirty-five male Wistar rats, weighing 145-220g were used for this study. They were housed in a quiet room with 12:12-hr light-dark cycle room temperature, 25°C. All procedures used in this study followed the Principles of Laboratory Animal Care from NIH Publication No. 85-23 and were approved by the Ethics Committee of the College of Natural Sciences, Federal University of Agriculture, Abeokuta, Ogun State, Nigeria.

Omega-3 fatty acid (containing 1000mg Pure Salmon oil of 320mg EPA and 180mg DHA) was administered for 2 weeks to the rats orally at the dosage of 0.4g/kg body weight of rats/day. Omega-3 fatty acid capsules were obtained from NOW FOODS, Bloomingdale, IL, USA. Alloxan monohydrate and all other chemicals used were of analytical grade.

After acclimatizing the rats for two weeks, they were divided into seven groups of five animals each. The normal control rats were given distilled water and paraffin oil; diabetic control rats: alloxan and paraffin oil; omega-3 control rats: distilled water and omega-3 fatty acids; post-treatment (diabetic omega-3) rats: alloxan followed by omega-3 fatty acid; pre-treatment (omega-3 diabetic) rats: omega-3 fatty acid followed by alloxan; Control baseline and diabetic baseline rats were respectively given distilled water and alloxan only. Water and rat chow were provided ad libitum. The rats were checked daily and their body weights were recorded accordingly till the end of the experiment.

Induction of Diabetes

Diabetogenesis in the rats was induced by intraperitoneal injection of alloxan monohydrate following the methods of Al-Haj Baddar et al [14] and Rajasekaran et al [15] after 8hrs of fasting with modification. The rats were not allowed to eat but had free access to water over 2 days. They were then given 5% glucose solution over 24 hours after injection to overcome drug-induced hypoglycemia. The blood glucose level of the rats was determined before, during and after induction of diabetes at two days interval for seven days using an on-call glucometer and test strips manufactured by CAN laboratory, Inc., USA. Rats with fasting blood glucose greater than 200mg/dl were considered diabetic and used in the study.

Samples collection

After twenty-one days of treatment, the rats were weighed and sacrificed after overnight fast under light ether anaesthesia. The liver, heart, kidney, spleen, pancreas and the brain of each rat were excised, trimmed of connective tissues and rinsed in ice-cold normal saline solution. They were then blotted dry, weighed and stored at -20°C until analysis.

Biochemical analyses

Organ lipid profiles

Extraction of lipid from brain, liver, spleen, pancreas, heart and kidney was done as described by Folch et al [16]. 10% homogenate of the organs was prepared in chloroform: methanol (2:1) mixture. The mixture was then centrifuged at 4000rpm for 10 minutes and the supernatant containing the lipid was removed. After washing with

0.05M KCl, aliquots (0.1 ml each) of the chloroform-methanol extract was used for the determination of cholesterol, triacylglycerol and phospholipids after evaporating to dryness at 60°C.

For cholesterol determination, 0.1 ml of the extract was evaporated to dryness at 60°C and 20µl of Triton X-100/chloroform mixture (1:1, v/v) was added to the dried extract for resolution. This was evaporated again and then 1 ml of the cholesterol kit reagent was added, mixed and incubated for 30 minutes before reading the absorbance spectrophotometrically. The triacylglycerol concentration was determined by evaporating to dryness 0.1ml of the extract and adding 0.1 ml of 97% ethanol to re-suspend the dried lipid. To this, 1 ml of the triacylglycerol kit reagent was added, mixed and incubated for 30 minutes before the absorbance reading was taken. Determination of phospholipid concentration was assessed with ammonium ferrothiocyanate by the method of Stewart [17]. An aliquot of the extract, (0.1 ml) was evaporated to dryness at 60°C. After cooling, 2ml of chloroform was added to the dried extract, mixed and 2ml of Ammonium ferrothiocyanate was then added and then mixed for 1 minute. The mixture was left for 10minutes for separation to occur. The chloroform layer was then taken and the absorbance read at 488nm. Phospholipid concentrations were determined using a phospholipid standard as reference.

Estimation of lipid peroxidation

Lipid peroxidation was determined according to the procedure of Bouge and Aust [18] by measuring the thiobarbituric acid reactive substances (TBARS) in the organs spectrophotometrically. 10% homogenate of the organs was prepared in0.1M phosphate buffer (pH 7.2). The mixture was then centrifuged at 4000rpm for 10 minutes and the supernatant was removed.into clean Eppendorf tubes. An aliquot (0.1 ml) of the supernatant was treated with 2 ml of the TBA reagent (thiobarbituric acid, hydrochloric acid, Trichloroacetic acid in 1:1:1). It was incubated at 95°C for 15 minutes, placed on ice and then centrifuged. The clear supernatant was then read at 535nm.

Determination of hepatic HMG-CoA reductase activity

The activity of 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase was determined using the method described by Rao and Ramakrishnan [19] by measuring the hepatic concentrations of HMG-CoA and mevalonate. The ratio of HMG CoA: mevalonate is taken as an index of the activity of the enzyme. A decrease in this ratio indicates increased cholesterogenesis while an increase indicates an decreased choletesrogenesis.

Briefly 10% (w/v) homogenate of the liver was prepared in saline arsenate solution (1g/L). Equal volumes of fresh 10% (w/v) liver homogenate and dilute Perchloric acid (50ml/L) was mixed, allowed to stand for 5 minutes and centrifuged at 2,000rpm for 10 minutes. 1.0ml filtrate was treated with 0.5ml of freshly prepared hydroxylamine reagent (alkaline hydroxylamine in the case of HMG-CoA and neutral hydroxylamine in the case of mevalonate), mixed and after 5 minutes, 1.5ml of ferric chloride reagent was added and then shaken. The absorbance was read after 10 minutes at 540nm versus a similarly treated saline/ arsenate blank.

Statistical analyses

Results are expressed as mean ± standard deviation (S.D). The level of homogeneity among the results of groups was tested using analysis of variance (ANOVA) with $p < 0.05$ considered significant. Where heterogeneity occurred, the groups were separated using Duncan Multiple Range Test (DMRT). All analyses were done using Statistical Package for Social Sciences (SPSS) version 16.

RESULTS AND DISCUSSION

Table 1 depicts the mean body weight of the animals. The results showed a significant decrease ($p<0.05$) in the weight of the diabetic animals compared with the normal control. Though the cause was not investigated, but it might be classical symptoms of polyuria (frequent urination). It could also be attributed to the dysfunction of insulin in the diabetic rats and the toxicity of alloxan on the B-cell of the pancreas of the diabetic rats resulting in muscle wasting [9 and 20]. This decrease was attenuated by the administration of omega-3 fatty acid by 11% in the pre-treated group (indicating the use of omega-3 fatty acid as a preventive measure), and by 23% in the post-treated group (showing that supplementation of diet with this fatty acid could delay muscle wasting). Comparing the two treatments, it was observed that the effect of the diseased condition was better managed in the post-treated group than in the pre- treated group.

Table 1. Mean body weight of animals

Group	Body weight (g)	
	Initial	Final
Normal control	184.00±26.55[a]	213.00±18.57[d]
Control diabetic	182.50±13.54[a]	162.00±14.83[a]
Control omega-3	193.25±18.46[a]	240.00±26.46[e]
Diabetic omega-3	195.60±15.47[a]	200.00±11.00[c]
Omega-3 diabetic	186.50±12.12[a]	180.00±10.00[b]
Diabetic baseline	203.00±11.94[b]	157.50±15.00[a]

Values are mean ± S.D. (n=5). Values in the column with different superscripts are significantly different from one another (p<0.05)

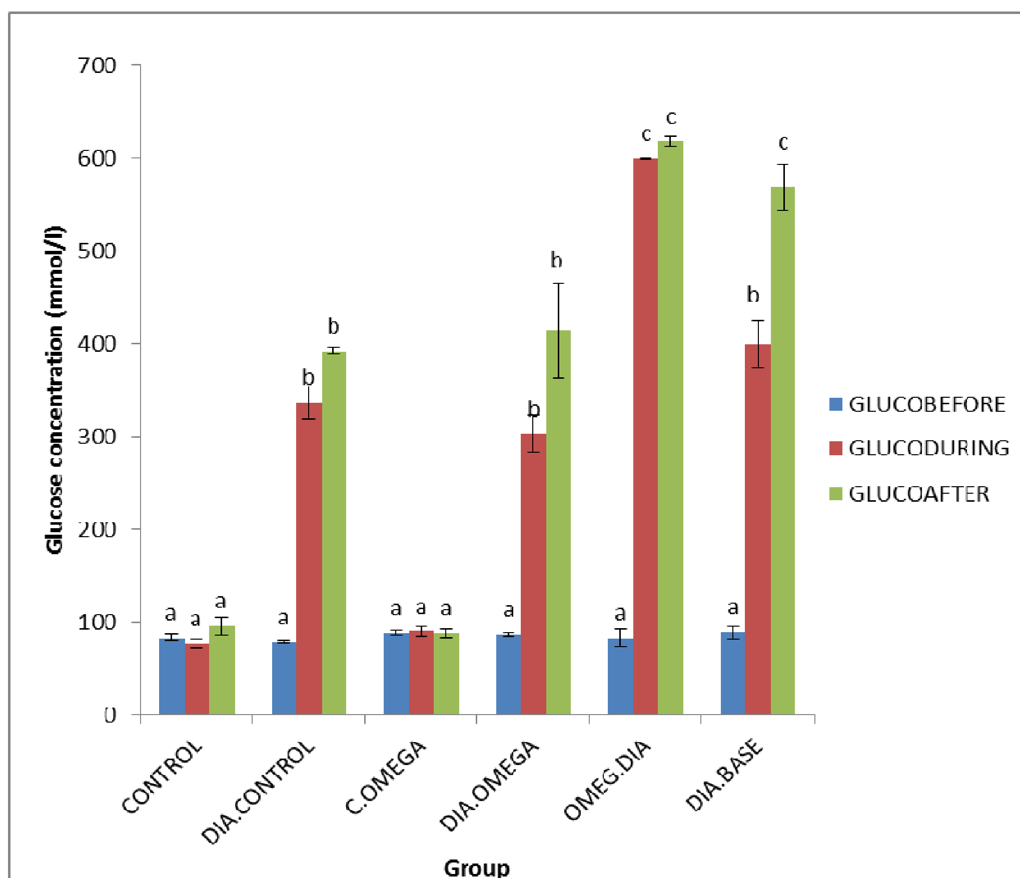

Figure1. Mean glucose concentrations of the groups before, during and after the experiment
Bars of the same colour with different letters of the alphabet are significantly different from one another (p<0.05)

Figure 1 depicts mean glucose concentrations of the groups before, during and after the experiment. The induced diabetes was sustained throughout the experiment. Omega-3 fatty acid supplementation did not have any effect on already present and or the onset of diabetic condition as shown by the pre- and post-treatment respectively (DIA.OMEGA and OMEG.DIA). This indicated that omega-3 fatty acid has no hypoglycaemic effect. This finding is in agreement with earlier studies, which reported that there is no significant difference in the fasting blood glucose of subjects after consumption of omega-3 fatty acid [21 and 22]. This might be because omega-3 fatty acid could not repair the damage done to the pancreatic cells hence inhibiting the activation of pancreatic secretion of insulin from the β-cells of islets. Again, due to its inability to decrease blood glucose it showed that omega-3 fatty acid could not stimulate the uptake of glucose by peripheral tissues [22].

Tables 2, 3 and 4 show the effect of omega-3 fatty acid on the cholesterol, phospholipid and triacylglycerol levels of the organs respectively.

Table 2. Effect of omega-3 fatty acid on organ cholesterol level (mg/g)

Group	Heart	Liver	Kidney	Pancreas	Spleen	Brain
Normal control	9.69±3.97[a]	30.86±1.05[b]	33.63±0.59[b]	14.06±0.72[a]	20.16±2.00[b]	16.12±5.08[a]
Diabetic control	21.49±3.26[c]	50.53±1.95[f]	42.17±1.11[f]	16.65±0.65[b]	24.58±0.75[c]	33.36±4.75[c]
Omega-3 control	9.92±0.61[a]	22.06±1.26[a]	25.48±1.64[a]	13.18±0.65[a]	16.02±0.75[a]	16.12±5.08[a]
Diabetic omega-3	13.98±2.57[b]	37.46±0.41[d]	37.41±0.49[d]	14.62±0.47[a]	19.86±1.25[b]	19.08±4.57[b]
Omega-3 diabetic	12.98±2.02[b]	32.84±1.23[c]	35.46±0.48[c]	16.42±1.01[b]	19.39±0.50[d]	21.87±2.09[b]
Control baseline	13.34±1.84[b]	31.35±1.75[b]	32.90±1.30[b]	16.22±1.08[b]	19.00±2.50[b]	15.39±1.18[a]
Diabetic baseline	29.14±1.55[c]	44.50±0.95[a]	40.61±0.51[a]	19.57±1.08[c]	25.59±0.50[d]	42.35±5.02[d]

Values are mean ± S.D. (n=5). Values in the column with different superscripts are significantly different from one another (p<0.05)

The diabetic groups, (normal diabetic and diabetic baseline) had significantly increased ($p<0.05$) levels of cholesterol compared with the normal control group (Table 2). The increase was markedly seen in the heart, liver, kidney, spleen and brain (122%, 64%, 25%, 22% and 107% respectively). In the pancreas, the increase, though significant ($p<0.05$), was low (18%) compared with the other organs. Omega-3 fatty acid supplement was observed to significantly reduce ($p<0.05$) the cholesterol levels back to near normal control levels in the pre- and post- treated groups at varying extents. In the pre-treated group, the decrease was observed to be highest in the heart (40%) and least in the pancreas (1%) while in the post-treated group; the decrease was highest in the brain (43%) and least in the kidney (11%). The decrease was however more prominent in the pre-treated group as regards the heart, liver, kidney and spleen while regarding the pancreas and brain, the decrease was more observed in the post-treated group. The same observations were made in the effect of omega-3 fatty acid in the phospholipid levels of the organs (Table 3). There was a significant increase ($p<0.05$) in the levels of phospholipid in the diabetic groups. Comparing the diabetic control with the normal control, the increase ranged from 33% in the pancreas to 76% in the heart. Omega-3 fatty acid significantly reduced ($p<0.05$) the levels in the organs, again at varying extents. In the pre-treated group, the decrease in phospholipid level was highest in the heart (24%) and least in the pancreas (6%) while in the post-treated group; the decrease was highest in the heart also (31%) and least in this case in the brain (13%). In all however, the degree of amelioration was more prominent in the pre-treated group compared with the post-treated group.

Table 3. Effect of omega-3 fatty acid on the organ phospholipid level (mg/g)

Group	Heart	Liver	Kidney	Pancreas	Spleen	Brain
Normal control	71.23±5.85[a]	27.82±0.51[a]	35.58±1.34[b]	41.34±4.29[a]	26.34±0.36[b]	220.97±38.32[b]
Diabetic control	125.15±2.26[c]	43.94±1.02[d]	53.87±0.80[f]	54.87±2.86[c]	36.44±0.28[c]	359.62±10.03[d]
Omega-3 control	70.17±11.68[a]	21.94±1.18[a]	31.05±1.04[a]	40.34±1.43[a]	19.20±0.43[a]	205.64±27.99[b]
Diabetic omega-3	101.23±21.37[b]	36.19±0.87[c]	43.35±2.56[d]	51.52±5.72[b]	29.75±0.21[b]	320.49±98.04[c]
Omega-3 diabetic	86.26±15.46[b]	32.75±0.60[b]	38.72±1.22[c]	45.44±2.86[b]	25.27±0.36[b]	312.55±20.78[c]
Control baseline	77.82±13.3[a]	28.21±1.30[a]	34.15±1.03[b]	43.86±1.86[b]	27.10±0.71[b]	116.95±6.46[a]
Diabetic baseline	161.23±39.27[d]	39.66±1.21[c]	46.76±1.09[e]	64.52±2.86[d]	45.00±0.43[d]	529.74±13.6[e]

Values are mean ± S.D. (n=5). Values in the column with different superscripts are significantly different from one another (p<0.05)

Table 4. Effect of omega–3 fatty acid on organ triacylglycerol level (mg/g)

Group	Heart	Liver	Kidney	Pancreas	Spleen	Brain
Normal control	37.44±3.33[b]	23.99±0.70[b]	23.94±1.03[b]	33.24±0.64[b]	27.54±0.91[b]	20.49±4.52[a]
Diabetic control	49.64±20.31[d]	40.12±1.23[e]	35.85±1.16[c]	52.39±4.46[e]	36.69±0.91[c]	32.67±0.04[c]
Omega-3 control	30.86±5.37[a]	16.91±1.14[a]	15.45±0.60[a]	28.61±0.91[a]	22.89±0.46[a]	20.68±2.60[a]
Diabetic omega-3	44.75±4.12[c]	33.90±1.14[d]	31.19±0.71[c]	34.69±1.09[b]	28.94±1.82[b]	26.13±2.32[b]
Omega-3 diabetic	37.39±6.49[b]	28.09±1.23[c]	25.94±0.40[b]	31.38±0.73[b]	25.93±0.91[a]	17.13±1.72[a]
Control baseline	40.42±8.89[b]	23.65±1.53[b]	23.67±1.12[b]	42.02±3.19[c]	31.10±1.82[b]	22.34±3.34[a]
Diabetic baseline	68.73±6.71[e]	44.92±2.30[e]	33.76±0.52[c]	45.07±6.19[d]	44.42±4.10[d]	33.73±11.21[c]

Values are mean ± S.D. (n=5). Values in the column with different superscripts are significantly different from one another (p<0.05)

The effect of omega-3 fatty acid on organ triacylglycerol level (Table 4) reveals that the diabetic groups had significantly higher ($p<0.05$) levels of triacylglycerol compared to the normal control group. The increase ranged from 33% in heart and spleen to 67% in the liver of the diabetic control group. Omega-3 fatty acid seemed to reduce

the dyslipidemia observed both in the pre- and post- treated groups, though the effect was more pronounced in the pre-treated group than in the post-treated group. In the pre-treated group, omega-3 fatty acid attenuated the level of triacylglycerol in the brain of the diabetic control from 32.67±0.04 to 17.13±1.72mg/g. In the post-treated group, this reduction was only to 26.13±1.72mg/g. In the pre-treatment, the decreasing effect omega-3 fatty acid had on the triacylglycerol level was most prominent in the brain (48%) and least in the heart (25%). However, in the post-treatment, the decreasing effect of omega-3 fatty acid was most prominent in the pancreas (34%) and least in the heart (10%).

Figure 2 shows the effect of omega-3 fatty acid on HMG-CoA/mevalonate ratio as an index of HMG-CoA reductase activity. A decrease in the ratio indicates an increase in the activity of the enzyme and vice-versa. The control diabetic group had a significantly ($p<0.05$) decreased ratio (25%) indicating a significantly increased activity of HMG-CoA reductase. Treatment with omega-3 fatty acid showed an increase in HMG-CoA/mevalonate ratio of 10% and 17% in the pre- and post- treated groups respectively from 25% in the control diabetic.

Comparing the two treatments, it was observed that the omega-3 fatty acid post-treated group showed a better response than the pre-treated group.

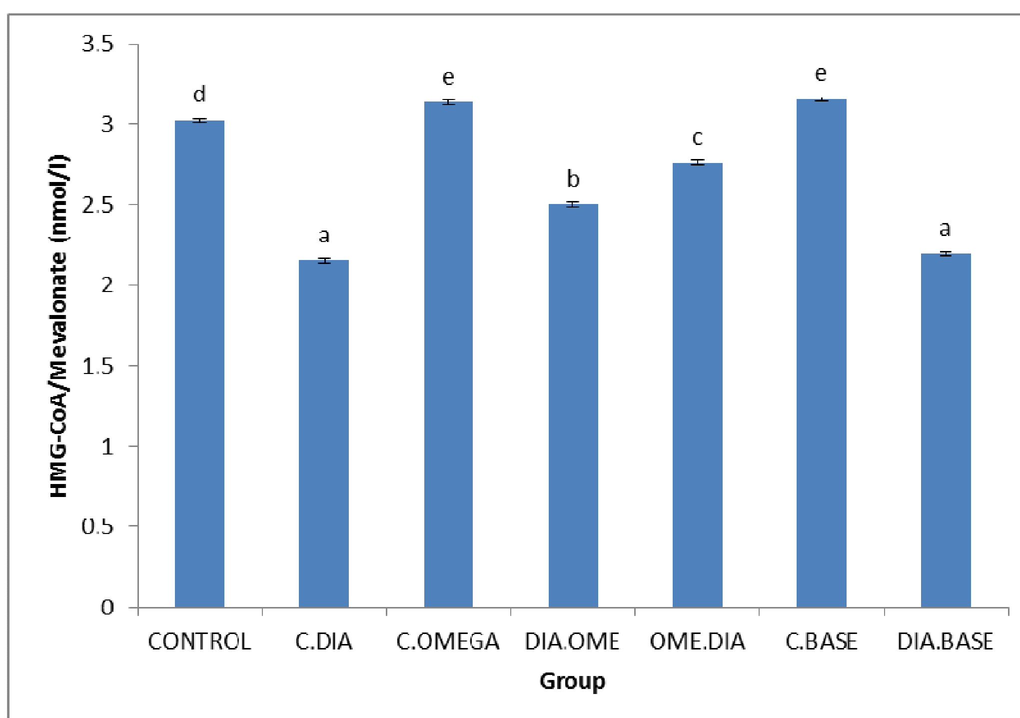

Figure 2. Effect of Omega-3 fatty acids on HMG-CoA/Mevalonate ratio as an index of HMG-CoA reductase activity
Bars with different letters of the alphabet are significantly different from one another ($p<0.05$)

Diabetes mellitus is a metabolic disorder that is associated with perturbations in lipid metabolism. These perturbations were observed in all the organs investigated. These observations were consistent with the results of earlier studies [23 and 24] which showed that lipogenesis is elevated in this condition. The organ that was most affected by this diseased condition was the heart as observed by the 122% and 78% increases in the cholesterol and phospholipid levels respectively. The next organ that was affected was the brain (cholesterol-107% and phospholipid-63%). These have buttressed that when this condition is not managed properly, it can lead to the onset of coronary heart disease, atherosclerosis and stroke among others [25]. This dyslipidemia in the diabetic animals could be as a result of alterations in the lipoproteins involved in the transportation of lipids from one organ or compartment to the other [26 and 27]. It has been reported that hepatic lipase; an enzyme that hydrolyses phospholipids and triacylglycerol on HDL and remnant lipoproteins is inhibited to an extent in insulin deficiency [26 and 27].

Triacylglycerol level was observed to be significantly high in all the organs of the diabetic animals compared with the normal control. This could be as a result of enhanced endogenous synthesis of triacylglycerol arising from an altered regulation of the metabolism of the lipid [26 and 27]. The level was observed to be up-regulated by 67% in the liver followed by 59% in the brain. This diseased condition can be said to greatly up-regulate the synthesis of the enzymes involved in the metabolism of lipids. This was supported by the decrease in the ratio of the hepatic HMG-CoA to mevalonate. The ratio is an index of the activity of the rate limiting enzyme, HMG-CoA reductase in the synthesis of cholesterol. A decrease in this ratio indicates enhanced cholesterogenesis [19]. It could also be that in this condition, there is an inability to excrete cholesterol in the form of neutral sterols or possibly that there is impairment in the transformation of cholesterol to bile acids which is the route of elimination of cholesterol from the body [28].

The effect of omega-3 fatty acid on the organs lipid peroxidation is shown table 5. The induction of diabetes mellitus in the rats caused significant increase ($p<0.05$) in lipid peroxidation of the rats' organs (heart-24%; liver-30%; kidney-17%; pancreas-29%; spleen-37% and brain–39%). Omega -3 fatty acid administrations reduced the level of lipid peroxidation in the diabetic to near normal levels both in the pre- and post-treated groups in comparison with the normal control. This reduction was however more observed in the pre-treated group than in the post-treated group, where the reduction was by 47% in the heart of the pre-treated group and it was by 17% in the post-treated group. The effect off omega-3 fatty acid was again observed to be high in the heart compared with the other organs.

Table 5. Effect of omega-3 fatty acid on the organs lipid peroxidation (nM)

Group	Heart	Liver	Kidney	Pancreas	Spleen	Brain
Normal control	3.33±0.65^a	3.12±0.03^b	2.94±0.02^c	6.15±0.51^b	3.64±0.44^a	3.78±1.04^b
Diabetic control	10.12±0.06^c	4.05±0.04^e	3.45±0.04^d	7.93±0.34^c	4.98±0.46^c	5.25±0.07^c
Omega-3 control	3.24±0.78^a	2.95±0.04^a	2.24±0.03^a	5.63±0.36^a	3.54±0.44^a	3.08±2.40^b
Diabetic omega -3	8.35±0.68^c	3.65±0.04^c	2.96±0.05^c	6.97±0.37^b	4.06±0.36^b	5.08±0.87^c
Omega-3 diabetic	5.39±1.82^b	3.50±0.03^c	2.55±0.04^b	6.86±0.31^b	3.75±0.50^b	4.57±0.11^b
Control baseline	6.29±1.90^b	3.09±0.05^b	2.45±0.02^b	5.49±0.85^a	3.75±0.64^b	1.45±0.52^a
Diabetic baseline	16.15±1.45^d	3.88±0.02^e	3.26±0.03^d	8.64±0.19^d	6.38±0.57^d	8.19±1.27^d

Values are mean ± S.D. (n=5). Values in the column with different superscripts are significantly different from one another ($p<0.05$)

Oxidative stress and lipid peroxidation are risks observed in diabetic mellitus and act as major sources of free radicals which can cause damage to the tissues [29]. The increased level of lipid peroxidation in the organs of diabetic animals was in agreement with the study of Kesavulu et al [30] and Garman et al [8]. The observed decrease in lipid peroxidation by omega-3 fatty acid is in concordance with reports by Sarsilmaz et al [31] and Iraz et al [32]. This may be due to the ability of omega-3 fatty acid to up-regulate expression of the antioxidant enzymes and molecules, and also down-regulate the genes associated with or suppression of the production of reactive oxygen species [33] thereby resulting to an increased resistance to lipid peroxidation. This study is in support of the idea by Iraz et al [32] that omega-3 fatty acid may have a free radical scavenging activity suggesting that it is a possible beneficial adjunct in the treatment of diseases associated with oxidative stress like diabetes.

The administration of omega-3 fatty acid alleviated the dyslipidemia observed in the alloxan-induced diabetic rats. This is in accordance with suggestions that omega-3 fatty acid modify the fatty acid composition of phospholipids of cell membranes [34 and 35] and has antiatherogenic effects [12]. The mechanism by which omega-3 fatty acid lowers cholesterol levels is similar to that of statins, a hypocholesterolemic drug which inhibits the activity of HMG-CoA reductase or probably down-regulating by way of modulation of the gene expression for the enzyme [36] leading to an increase in the number of hepatic apoprotein B receptors [37]. This is shown by the increase in the ratio of hepatic HMG-CoA to mevalonate indicating an inhibition of cholesterogenesis.

CONCLUSION

This study therefore, demonstrates that omega-3 fatty acid significantly ameliorated lipid metabolism as shown in the organs' lipid profile, lipid peroxidation and HMG-CoA reductase activity. The effect of the omega-3 fatty acid supplementation is however more beneficial in the pre-treatment than in the post-treatment. It is therefore worthy to suggest that omega-3 fatty acid should be included in the diet to prevent/suppress the development of disorders relating to diabetes mellitus, cardiovascular diseases among many others.

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