Original Article

Miraculous Therapy for Diabetes: Use of Omega-3-Fatty Acids

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ABSTRACT

Objective: To evaluate the anti-diabetic effects of Omega-3-Fatty Acids on insulin resistance.
Study Design: Case control Study
Place and Duration of Study: This study was conducted at the jointly conducted at Isra University, Hyderabad and SAU, Tandojam from December 2016- December 2018.
Materials and Methods: 75 male albino Wistar rats were grouped (n =15 /group) as negative control group A and experimental groups as B, C, D and E. Group A & Group B (Diabetic control) received lab chow, while experimental streptozocin induced diabetic groups C,D and E received food supplemented with Omega-3-fatty acids with the different doses respectively for 90 days**.** All animals were euthanized by cervical dislocation. Blood samples were analyzed for blood glucose and serum insulin level to assess insulin resistance via HOMA-IR. Their pancreas was removed and weighed. The specimens were processed under light microscope using H & E stains.
Results: The administration of Omega-3-fatty acids, Blood glucose, serum insulin and HOMA-IR were observed to be normalized to almost normal and the pancreatic morphology of tissues showed significant improvement in the histological features at 03 different doses in the experiment groups. It is concluded that Omega-3-fatty acids ameliorated insulin resistance.
Conclusion: The present study found significantly favorable impact of O3FAs on insulin resistance with improved glycemic status, HOMA-IR and histologic features of pancreatic tissue at different doses and concludes that the use of Omega-3-Fatty Acids could be prescribed as supportive remedial treatment along with anti-diabetic medications.
Key Words: Diabetes mellitus, HOMA-IR, Insulin Resistance, O3FAs, Pancreas

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INTRODUCTION

Diabetes is huge rising burden globally, with unsustainable health issue facing by the society. According to the prevalence rate of 2017, 425 million of population affected by this penetrating disease globally.[1] Major factors that trigger the disease ratio including the obesity with sedentary life style and poor dietary habits that should be controlled by an individual.[2]

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WHO reported in 2016, diabetes a serious illness that gradually involved the person and risk factors strongly targeted the individuals. It's an acute treat to the metabolic environment and silently alters the glycemic control along with other disbalanced.[3] Potentially a behavior, chemical, biological and environmental cause behind the type II diabetes, while the genetic involvement might be a cause behind the type I diabetes.[4-5] Inside the pancreas there are islands or more commonly termed as islets of Langerhans which play a major role in the formation of both insulin and glucagon[6]. Studies indicate that the islets numbers inside the pancreas can range from 3.2 million to 14.8 million, with the Human islets of Langerhans consisting of 30% of Alpha cells which secrete glucagon, 60% beta cells which produce insulin, while the remaining 10% is a mixture of different types of cells[7-10]. Insulin is a pivotal protein that helps in the maintenance of blood glucose concentration and thanks to advancement in technology and medicine as well, it is now commercially available for people with poor sugar control[11]. Insulin resistance, which is a defect in the ability of the insulin to control the metabolism of the glucose in the body.[12,13]. Type II diabetes mellitus occurs due to the aforementioned insulin resistance developing in the body[14]. Omega-3-fatty acids are

dietary lipids are essential fatty acids as they cannot be synthesized by the organisms, hence they need to be taken up by external sources. O3FAs are found in fish, nuts, and seed oils[15]. Literature suggests that O3Fas reduce the potential for cardiovascular diseases as well as having protective actions on cancer related complications[16-17]. To further study the potential of O3FA on insulin resistance, an experimental study was conducted to see if O3FA has a protective action on insulin resistance in rats induced with diabetes.

MATERIALS AND METHODS

This experimental study was conducted after ethical approval from concerned authority, conducted at the Parasitology department of Isra University, Hyderabad and Sindh agricultural university, Tandojam. Total 75 male albino rats were selected randomly. After selection, rats were first acclimatized to the environment of the laboratory for one week. They were kept in a separate cage. Food and water were given to the rats ad libitum. All rats have a weigh between 200-250gms. 60 rats were selected which were to be induced with diabetes, for which all of the rats were injected intraperitoneally with 65mg/kg body weight of streptozotocin (STZ), Before the administration of STZ, 110mg/kg body weight of Nicotinamide which was dissolved in 0.9% normal saline solution. The remaining groups were described below. All the rats in the experimental groups were first fasted on Day 1 of the experimental for 6-8 hours prior to be treated with STZ and Nicotinamide. Fasting glucose was determine using a glucometer on the first and third day of the experiment to confirm that indeed the rats have diabetes. All the rats that have a blood glucose of greater than 250mg/dl or greater were then included in the study.

Group A: Negative control group, given a normal diet
Group B: Diabetic control group of animals
Group C: Diabetic induced rats group given 0.3g/kg body weight of O3FAs
Group D: Diabetic induced rats group given 0.4g/kg body weight of O3FAs
Group E: Diabetic induced rats group given 0.5g/kg body weight of O3FAs
All treatments were given for 90 days

Blood samples were at the end of the experiment. All the animals were given ketamine and a retro-orbital puncture was done to obtain the blood samples. Blood was placed in EDTA tube and plain red tops tube. The pancreas was removed and weighted. The specimen of pancreas was processed and 0.5 um sections were collected and stained using H & E stains. The slides were studied under the light microscope. Blood glucose, hexokinase procedure was done on an automatic analyzed to measure serum insulin. The homeostasis model assessment (HOMA) was used for insulin resistance. The insulin resistance estimated using HOMA was then calculated using fasting plasma insulin being multiplied by fasting plasma glucose and then divided by 405. The variables were represented in mean and standard deviation form. One-way ANOVA was done for analysis of mean values among different groups of rats. Post-hoc test was done to compare multiple parameters. The value of significance was set at $P \leq 0.05$.

RESULTS

Once the administration of Omega-3-fatty acids took place, there was a reduction in the homeostasis model assessment insulin resistance (HOMA-IR), this can be seen in table 3. Significant difference can be appreciated in the serum insulin levels by the action of O3FAs in group C, D, and E in contrast to the positive control group. The positive control group B, didn't experienced a significant decrease in the serum insulin level.

The level of serum insulin levels is appropriately shown in Table 1. The level of blood glucose showed significant improvement once O3FAs were used in group C, D, and E, however, the same could not be said for the control group B. The blood glucose levels are illustrated in Table 2.

Table No.I: Level of serum insulin (uIU/ml)

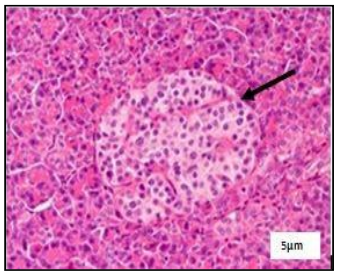
Groups	Mean	Standard deviation	p-value
Group A	4.2	0.62	
Group B	1.9	0.20	
Group C	2.1	0.30	
Group D	3.1	0.31	0.001
Group E	3.4	0.35	

Table No.2: Glucose levels (mg/dl)

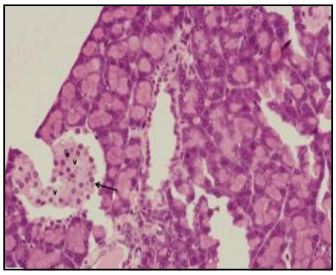
Groups	Mean	Standard deviation	p-value
Group A	77	13.23	
Group B	452	39.8	
Group C	353	33.4	
Group D	243	30.5	0.001
Group E	149	28.9	

Table No.3: HOMA-IR (%)

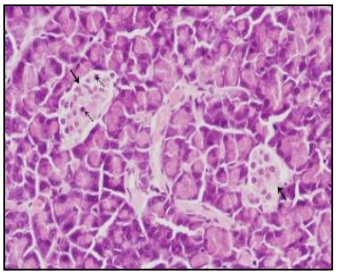
Groups	Mean	Standard deviation	F ratio	p value
Group A	0.9	0.26		
Group B	2.3	0.31		
Group C	1.8	0.34		
Group D	1.7	0.21		
Group E	1.1	0.47	37.8	0.001



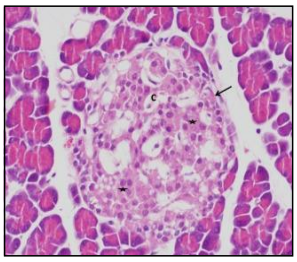
group A showed large and defined Islets of Langerhans. Normal histology along with endocrine cells in cord (Fig I).



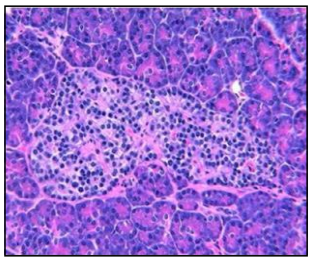
Group B (diabetic control) showed shrunken distorted structure cells in the islets, with loss of normal cellular structure with Pyknotic nuclei (Fig II).



Group C comparison to Group B shows mild cord like arrangement of cells in the of islets of Langerhans (arrows). Appearance of pyknotic nuclei (Fig III).



Group D animals as compared Group B showed appearance of fewer areas of defined islets of Langerhans (arrows). pale and acidophilic cytoplasm (stars). Fig IV



Group E compared to Group B showed numerous a high number of islets of Langerhans with defined cord of cells of the endocrine region, along with a vesicular rounded nuclei and a acidophilic pale cytoplasm. Fig V

DISCUSSION

In 2017, the international diabetes federation (IDF) has gone onto rank Pakistan at number 10 out of the 221 countries in the world having the highest number of diabetes patients [18-20]. According to the literature, it has been found that the O3FAs did indeed possess a positive effect on insulin sensitivity improvement, which is also in line with the current study[21-22]. The combined therapeutic effect of EPA and DHA with pioglitazone was also reported in another study, which demonstrated a improvement in the glycemic status and a halting in the insulin resistance which was being developed, all the while demonstrating very little side effects[23,24]. Furthermore, there was also dilation of intralobular blood vessels within the section. Cytoplasmic vacuoles were evident. Pyknotic changes and degeneration of the nuclei was clearly visible as well. Many of the islets of Langerhans experienced loss of continuity number of cells[25]. In present study, pancreatic tissue of experimental groups showed significant improvement in the histological features. Previous study have reported that increased intake of O3FAs was associated with maintenance of integrity of pancreatic ß-cells[26]. The antidiabetic effect of O3FAs is confirmed by the disappearance of severe degenerative and necrotic changes of endocrine cells of the pancreatic islets in O3FAs treated experimental groups as compared to diabetic control group B. this is supported by EI, Desouky et al, 2019[27] However, there was a moderate amount of sensitivity improvement in hepatic-insulin in relation to EPA and DHA, but it didn't possess any clinically relevant outcomes at all[28].

CONCLUSION

The study concludes on the grounds that the use of O3FAs serves to deliver a positive impact on the insulin resistance and subsequently improves the glycemic status, histological features of the pancreatic tissues, and HOMA-IR at different doses. Hence, O3FAs should be prescribed by clinicians as an adjunct along with anti-diabetic medications to improve the glycemic control of diabetic patients.

Author's Contribution:

Concept & Design of Study: Abroo Fatima Qazi

Drafting:	Syna Pervaiz Singha, Maria Kazi
Data Analysis:	Kamran Afzal, Sayyada Humaira Masood, Alina Atif
Revisiting Critically:	Abroo Fatima Qazi, Syna Pervaiz Singha
Final Approval of version:	Abroo Fatima Qazi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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