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EFFECT OF FISH LIVER OIL AND PUMPKIN SEED OIL AGAINST TYPE II DIABETES. A RANDOMIZED CONTROL TRIAL

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Abstract:
Diabetes type II is a metabolic disorder that usually occurs with increasing age, and is associated with insulin resistance and insulin deficiency. It typically does not require insulin treatment for survival. Omege-3 is effective for diabetes and its linked problems in which cholesterol and other lipid levels increase. Pumpkin seed oil and fish liver oil both show effects for diabetes. This study aims to evaluate the combined impact of fish liver oil and pumpkin seed oil on type II diabetes. Currently, there isn't any research that examines the combined effect of these two oils. The research was conducted on diabetes type II males and females aged 40 or above at Mayo Hospital Lahore. The study design of this research was a randomized controlled trial (RCT). The sample size was calculated and all the participants were divided into two equal groups. The duration of this study was 3 months. Group -1 was the control group, given a Placebo treatment, and Group 2 was the intervention group which was given fish liver oil and pumpkin seed oil. Pre and post-testings' were done and the data was analyzed. Results show that fish liver oil and pumpkin seed oil have significant effects ($p<0.05$) on HbA1c and lipid profile (HDL, LDL, TG) and show no significant results for total cholesterol.

Keywords: fish liver oil, pumpkin seed oil, type II diabetes, insulin resistance, insulin deficiency, metabolic disorder, Omega-3, cholesterol, HbA1c, HDL, LDL, serum triglyceride, total cholesterol

INTRODUCTION:

Diabetes Mellitus type II is a long-lasting condition caused when there is a problem in the way our body utilizes sugar as a fuel, leading to hyperglycemia and metabolic disorders. (Mukhtar et al., 2020). It increases the risk of other diseases such as heart disease, and obesity (Rochlani et al., 2017). According to the American Diabetes Association, this condition is classified into various types such as type 1, type 2, gestational, and other inherited forms as monogenic diabetes of the youth (MODY) (American Diabetes Association, 2020). Type II diabetes is the most common type of diabetes and generally develops in people over 40 years of age (Mordarska et al., 2017). This happens when the pancreatic gland that produces insulin hormone is working but the cell is not responding against that insulin otherwise called insulin resistance (Smushkin et al., 2010). Insulin resistance and reduced pancreatic beta-cell synthesis and secretion of insulin are the main reasons for type 2 diabetes (T2D).

(Reed et al., 2021). Almost 90% of the individuals suffering from diabetes have type 2 (mainly older people as compared to young or adolescents) and the remaining 10% have type 1 diabetes (Saeedi et al., 2019). Type II diabetes symptoms include increased thirst, blurry vision, fatigue, slow wound healing, and numbness of hands or feet. Causes include genetics, obesity, high blood pressure, cholesterol, triglycerides, and excess belly fat. A cross-sectional study was conducted in Lahore Private sector employees about the investigation of lifestyle and its relationship with type II diabetes. The study involved 174 diabetic patients, of whom 42 were pre-diabetic (Hussain et al., 2023). Obesity is the major cause of type II diabetes and mostly affects the quality of life. Increasing weight in adults may increase the risk factor of high blood sugar levels (Shah et al., 2022). Lifestyle factors like smoking, inactivity, stress, and poor sleep also increases risk (Drivsholm et al., 2005).

Fish liver oil is a good source of omega 3, vitamin A, vitamin B3 (nicotinamide), B6 (pyridoxine), B12 (cobalamine), E (d-tocopherol), and D (Sidhu et al., 2003). The fatty acids found are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). This helps in reducing inflammation in the body also supports a healthy brain, supports skin health and fetal development, reduces joint pain and waist circumference, helps improve cognitive impairment, reduces pain, prevents heart problems such as hypertension and cardiovascular disease, and liver health (Conus et al., 2019). Increasing omega-3 consumption has a minute or no effect on the risk of Type II diabetes. Other measures of diabetes risk – including blood glucose and insulin– were unaffected by fish oil consumption. The scholars maintain that people should not be encouraged to take omega-3 oil supplements to treat type -II diabetes (Shaban et al., 2017).

Pumpkin seeds may include health-promoting beneficial compounds such as tocopherol, phenolics, carotenoids, and sterols. Its oil, derived from the seeds, consists of various fatty acids such as palmitic, palmitoleic, stearic, oleic, linoleic, and linolenic acids. It has been utilized as conventional medicine in general treatments in several countries and it has gained importance due to its health-protective properties (Irnawati et al., 2022). It is the most common oil used in cooking or supplementation. One tablespoon of this oil provides 14 grams of fat most of which are polyunsaturated and mono-unsaturated fatty acids. It is mainly a rich source of omega-6 fatty acid and linoleic acid which helps to improve heart and blood sugar management. Pumpkin seeds are rich in antioxidant compounds that may protect against inflammation (Šamec et al., 2022). They are packed with essential minerals such as potassium, magnesium, calcium, iron, and zinc. Research indicates that consuming unsaturated fats can reduce the risk of heart disease and type II diabetes by improving blood cholesterol levels.

Pumpkin seed oil is a type of oil that should be used in moderate amounts (Dotto & Chacha, 2020). The materials inside pumpkins such as the fruit flesh, oil from un-germinated seeds, and protein from germinated seeds have glucose-lowering properties. Initial study showed that pumpkin seeds and the macromolecules, such as Trigonelline (TRG), Nicotinic acid (NA), and D-chiro-inositol (DCI) own glucose-lowering properties and could support sustaining glycemic control (Adams et al., 2014). A study conducted on type II diabetes patients shows that vitamin C and chromic have positive effects on hypertension and hyperlipidemia (Faizan et al., 2024). Diabetes type II is a metabolic condition that can increase the risk for other chronic diseases which are inter-linked. The study's aim is to evaluate the effect of fish liver oil and pumpkin seed oil to lower blood glucose.

Method and Methodology

Subject and Design

The study was a randomized controlled trial conducted in Mayo Hospital from October 23 to December 23. It includes a total of 46 participants, both male and female. All of the participants included in the research were informed about every detail regarding the research.

Sample Size:
The sample size was calculated from the online calculator Raosoft (Sample Size Calculator by Raosoft, Inc., n.d.)

Inclusion and Exclusion Criteria:
The **inclusion criteria** for the selection of the research were:

- Individuals with type 2 diabetes, at least 1 year old diagnosis
- blood sugar levels should be 126 mg/dL or higher, HbA1c (hemoglobin A1c) levels 6.5% or higher
- Aged 40 or higher, both male and female
- Subjects able to understand simple instructions independently or with the help of family.

The **exclusion criteria** were the following:

- Patients with any other type of diabetes except type II
- Age group below 40
- History of psychological disorders, Smokers, and Urinary tract infections.

Tools: The tools used for pre and post-assessment of type II diabetes are listed below:

Anthropometric measurement:
During the first visit, demographic data was gathered including age, weight, gender, height, and BMI (Body Mass Index). Where BMI is calculated by the formula kg/m^2 (Misra et al., 2019)

Biochemical measurement:
Throughout the research study, pretesting and post-testing were conducted on all participants to ensure accurate and reliable results. At the beginning of the study, before any interventions or treatments, a pretest was carried out on each patient. This pretest included a series of biochemical tests that were performed to assess various health parameters. These tests included the measurement of HbA1c, and lipid profile tests (total cholesterol, triglycerides, HDL, and LDL). The HbA1c sample was analyzed using fully automated HbA1c analyzers based on HbA1c technology. For lipid profile testing, a chemistry analyzer was used. All of the tests were performed following a fasting period of 10 to 12 hours. By conducting these tests, it became easier to establish a baseline for each patient's health and monitor any changes that occurred due to the study.

Intervention:
A total of 46 participants with type II diabetes were randomly divided into 2 groups of 23 people each, both male and female. One group was called the placebo group in which a 1000 mg starch capsule twice a day was used with 500 mg of metformin. In the other group, 1000 mg of pumpkin seed oil and 1000 mg of fish liver oil capsule were consumed at alternate times. Pumpkin seed oil was consumed at day, and fish liver oil was consumed at night with 500 mg metformin for 3 months (90 days). Pumpkin seed oil was typically consumed on an empty stomach, or added to breakfast. The recommended amount is around 1/4 teaspoon.

Fish liver oil was typically taken in capsule form. It is best to take fish liver oil after dinner, before bed. The placebo capsules were taken once in the morning and once at night. A statistical analysis was conducted to compare the effects of both groups. Data was evaluated by descriptive statistics. For Qualitative variables frequency of gender and age was calculated. For the quantitative variable Mean and the standard deviation (S.D) were calculated, where ($p<0.05$) was considered as a level of significance. T-test was also applied. For data analysis SPSS software was used.

Results:
Of the 46 total participants all were included in the study. The gender distribution is shown in figure 1. Among the participants in the control group 26.1% were male and 73.9% were females. In the

intervention group 17.4% were male and 82.6 % were females. The mean age of the total patients was 52.06 ± 7.9 years. The baseline data for the control group was BMI 27.0 ± 4.23, HbA1c 7.74 ± 1.35, TC 181.0 ± 51.27, HDL 37.69 ± 11.34, LDL 119.6 ± 42.14, TG 207.65 ± 91.162 whereas in intervention group BMI 29.21 ± 4.06, HbA1c 9.23 ± 1.95, TC 196.3 ± 68.4, HDL 39.65 ± 8.44, LDL 109.6 ± 35.59, TG 204.78 ± 92.9 (table 1).

After consumption of fish liver oil and pumpkin seed oil for 3 months, the results show a significant reduce ($p<0.05$) in HbA1c, LDL and TG, on the other hand HDL values significantly improved ($p<0.05$) but no such drastic difference was shown in the effect on total cholesterol (TC).

Endpoint analysis represents that consuming pumpkin seed oil and fish liver oil regulated the blood sugar levels in intervention group. HbA1c levels improved 8.23 ± 1.57 from 9.23 ± 1.95, this shows significant results in lowering blood sugar levels.

Table 1: Baseline characteristics of patients (n=46) before intervention (mean and standard deviation)

Parameters	Control group	Intervention group
	Mean ± S. D	**Mean ± S. D**
Age	52.34 ± 9.75	51.78 ± 5.76
Weight (kg)	69.86 ±12.81	74.74 ± 10.96
BMI (kg/m^2)	27.0 ± 4.23	29.21 ± 4.06
HbA1c (%)	7.74 ±1.35	9.23 ± 1.95
TC (mg/dl)	181.0 ±51.27	196.3 ± 68.4
HDL (mg/dl)	37.69 ± 11.34	39.65 ± 8.44
LDL (mg/dl)	119.6 ± 42.14	109.6 ± 35.59
TG (mg/dl)	207.65 ± 91.162	204.78 ± 92.9

Table 2. Comparison between control and intervention groups before and after consumption of fish liver oil and pumpkin seed oil

Parameter	Groups	Before Intervention	After Intervention
		Mean ± S. D	Mean ± S. D
Weight (kg)	Control Group	69.86 ± 12.81	69.13 ± 12.2
	Intervention Group	74.73 ± 10.96	73.02 ± 10.53
BMI (kg/m^2)	Control Group	27.04 ± 4.23	26.43 ± 3.97
	Intervention Group	29.21 ± 4.06	26.86 ± 3.59
HbA1c (%)	Control Group	7.74 ± 1.35	8.51 ± 1.89
	Intervention Group	9.23 ± 1.95	8.23 ± 1.57
TC (mg/dl)	Control Group	181.04 ± 51.27	187.0 ± 49.70
	Intervention Group	196.30 ± 68.43	199.56 ± 63.03
HDL (mg/dl)	Control Group	37.69 ± 11.34	39.60 ± 10.77
	Intervention Group	39.65 ± 8.44	54.26 ± 6.77
LDL (mg/dl)	Control Group	119.60 ± 42.14	125.60 ± 41.48
	Intervention Group	109.60 ± 35.59	100.30 ± 23.95
TG (mg/dl)	Control Group	207.65 ± 91.16	221.52 ± 83.61
	Intervention Group	204.7 ± 92.93	185.7 ± 83.88

The table shows no significant difference in total cholesterol, but on the contrary, significant differences in weight, BMI, HbA1c, HDL, LDL, and TG were observed in the intervention group.

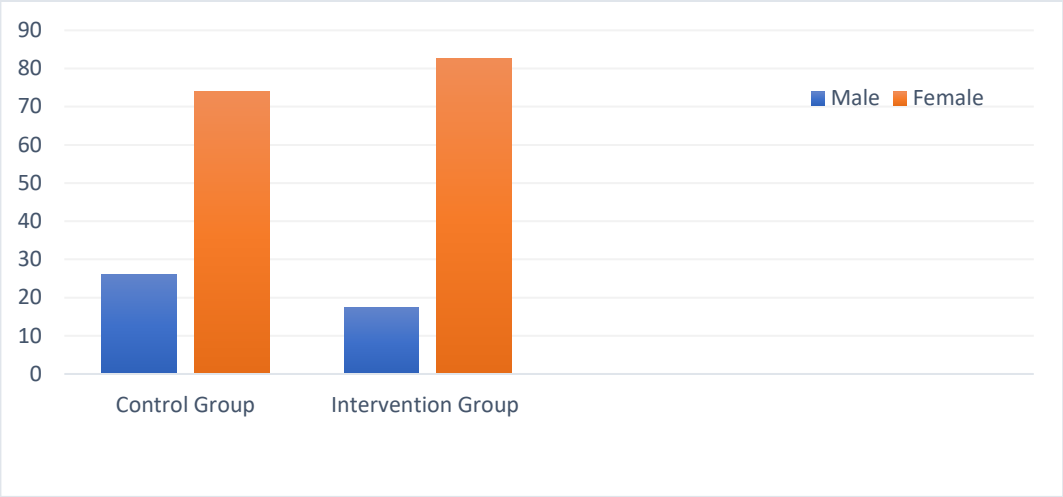

Figure 1: Gender distribution between control and intervention group

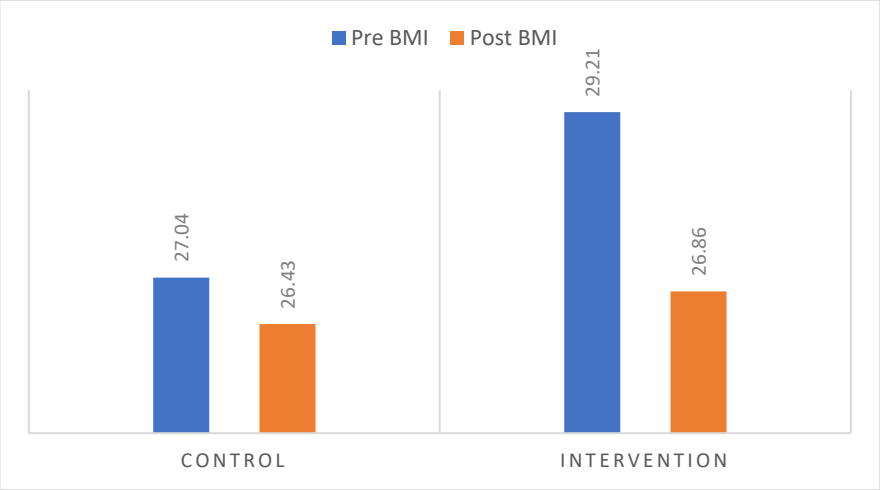

Figure 2: Pre and Post BMI of participants (average)

Discussion:

The current study showed a positive effect of fish liver oil and pumpkin seed oil on lowering the blood sugar level of type II diabetes patients without any harmful effects. For this purpose, the intervention group was given 1000mg of fish liver oil and 1000mg of pumpkin seed oil for 3 months. Results indicated a significant decrease in weight from 74kg to 73kg and also showed a significant decrease in blood sugar levels (HbA1c) from 9.23 to 8.23. It was found that taking these oils for 90 days had a beneficial effect on serum triglyceride, HDL cholesterol, LDL cholesterol, and hemoglobin A1c. However, there was no beneficial effect on total cholesterol. Similarly, a study conducted in 2020 showed that fish liver oil has a beneficial effect on reducing total lipids including triglyceride, LDL cholesterol, and significantly increases HDL cholesterol levels but has no significant effect on blood glucose (Gao et al., 2020) while the current study also shows a significant decrease in mean Triglycerides levels from 204.1mg/dl to 185.7mg/dl, mean LDL levels from 109.6mg/dl to 100.3mg/dl and a significant improvement in HDL levels from 39.65mg/dl to 54.2mg/dl.

A study conducted in 2016 on rats showed the effect of fish oil supplementation on plasma lipid levels in rats with a duration of treatment of 14 days. The lipid and sugar profiles of rats were taken on day 8^{th} and at the end of the intervention. After fish oil consumption there was an increase in the liver DHA and EPA. This showed an increase in total cholesterol, triglyceride, and non-high-density lipoproteins (Barbosa et al., 2016). The present study showed a significant decrease in triglyceride levels from 204.7mg/dl to 185.7mg/dl, and LDL levels from 109.6 to 100.3mg/dl on contrary the total cholesterol levels increased from 196.3mg/dl to 199.5mg/dl.

A study indicated that pumpkin seed oil (PSO) has multiple nutritional properties that can reduce blood glucose levels. The primary efficacy of pumpkin seeds has been tested on experimental animals and has been shown to contain many nutrients that affect hypoglycemic activity (Tasya et al., 2022) similarly, the current study also showed decreased glycated hemoglobin levels from 9.23 to 8.23 and improved HDL levels from 39.6 to 54.2mg/dl.

The present study proved to be significant in decreasing mean HbA1c levels from 9.23 to 8.23, mean TG levels were 204mg/dl to 185.7mg/dl, mean LDL levels from 109.6mg/dl to 100.3mg/dl, HDL levels increase significantly 39.6mg/dl to 54.26mg/dl on contrary the total cholesterol level increased from 196.3 to 199.5mg/dl. Similarly, a previous study in 2019 aimed to evaluate the effect of pumpkin seed oil on glucose and lipid profile in diabetes-induced rats for 4 weeks, total of 60 rats involved in this study were divided into 6 groups, all rats were injected with alaxon for induction of diabetes. The levels of blood sugar, HDL, LDL, TG, and cholesterol were evaluated before and after the study. Results showed that the use of pumpkin seed powder and oil in diabetic rats resulted in a significant decrease in glucose, glycated hemoglobin, TG, LDL, cholesterol, VLDL, and improved HDL levels (Abd-Elnoor et al., 2019).

Conclusion:

Based on the findings of the study it was demonstrated that fish liver oil and pumpkin seed oil can positively impact blood sugar levels and improve lipid profile in patients with type II diabetes. There was no significant difference shown for total cholesterol. Further studies with longer duration of intervention and a bigger sample size are needed to confirm the validity of our findings.

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