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Original Article

EFFECTS OF EXTRA VIRGIN OLIVE OIL VERSUS RICE BRAN OIL ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE-2 DIABETES MELLITUS

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ABSTRACT

Objective*:* The purpose of this study was to determine the effect of extra virgin olive oil (EVOO) and rice bran oil (RBO) on glycemic control and lipid profiles in patients with type-2 diabetes mellitus (T2DM).

Methods*:* Ten patients with T2DM received 15 ml/day of EVOO or RBO. Levels of fasting blood glucose (FBG), postprandial blood glucose (PBG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), and triglycerides (TGs) were measured. RBO or EVOO was administered for 4 consecutive weeks. During a 2-week interval, the treatment was not administered. After this washout period, a crossover design was implemented by exchanging EVOO supplementation with RBO supplementation and *vice versa* for 4 consecutive weeks.

Results*:* Changes in levels of FBG, PBG, TC, LDL-C, and TGs were not significantly different in the two groups. However, significantly decreased the levels of HDL-C were observed in both groups.

Conclusion*:* RBO and EVOO had no significant influence on levels of FBG or PBG.

Keywords: Type 2 diabetes mellitus, Olive oil, Rice bran oil, Glucose level, Lipid level

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INTRODUCTION

Diabetes mellitus (DM) is a major public-health problem worldwide. In 2015, the American Diabetes Association stated that DM is a "collection of symptoms caused by an increase in blood glucose levels due to impaired secretion and insulin resistance or the effects of both" [1]. The International Diabetes Federation estimated that, in 2016,>415 million people worldwide experienced DM. It is estimated that by 2040, population of approximately 642 million will have DM symptoms [2].

The pathophysiology of type-2 diabetes mellitus (T2DM) is insulin resistance. The latter occurs due to the inability of insulin to stimulate glucose absorption in its target cells (muscle, fat) despite hyperinsulinemia [3, 4].

The main goal of ongoing nutritional therapy for DM is to maintain glucose levels in the blood close to normal to stop hyperglycemia and hyperlipidemia and lower the risk of complications. This goal can be achieved by eating a balanced diet (carbohydrates, 45%–65%; fat, 20%–25%; protein 10%–15%) in accordance with the calorie and nutritional needs of each individual. Patients are expected to maintain regularity in terms of meal schedule as well as the type and amount of food [5, 6].

Olive oil is extracted from *Olea europaea*. This small tree is found in the Mediterranean, Asia, and Africa [7]. Olive oil consists of a glycerol fraction (90%–99% of olives) and a non-glycerol fraction (0.4%–5% of olives). The glycerol fraction of olive oil comprises 78% monosaturated fatty acids (MUFAs), 8% polyunsaturated fatty acids (PUFAs) and 12% saturated fatty acids (SFAs). The other 2% comprises>230 chemical compounds, including tocopherols, squalene, fatty alcohols, triterpene alcohol, phytosterols, polar pigments and hydrophilic compounds, especially polyphenols such as oleuropein and their metabolites hydroxytyrosol and tyrosol, which make up about 80% of the phenolic content of olive oil. These phenolic compounds are found in virgin oil and extra-virgin olive oil (EVOO). The olives are crushed mechanically, and the polyphenols within them disappear during distillation [8-10]. The phenolic compounds in olive oil are mainly hydroxytyrosol, tyrosol, and ligtroside [11, 12].

Rice bran oil (RBO) is extracted from the outer layer of rice grains. RBO contains saponifiable fractions and unsaponifiable fractions. The ionized fraction is in the form of triglycerides (TGs) and small amounts of diglycerides, monoglycerides, free fatty acids, waxes, glycolipids, and phospholipids. RBO contains 37% PUFAs, 38% MUFAs and 25% SFAs. A component of RBO is oryzanol, which is a mixture of steryl and other triterpenyl esters of ferulic acids. Oryzanol is absorbed by the intestine and reaches a maximum concentration in<1 h. It is metabolized in the liver to become a ferulate, which is then carried to the blood circulation. Other ingredients in RBO are phytosterols in the form of cholesterol, β-sitosterol, and stigmasterol. The structure of phytosterol is similar to that of cholesterol but it contains ethyl groups in the branch chain. RBO is also rich in vitamin-E derivatives such as tocotrienols and tocopherols [13].

Studies conducted by the research teams of Rivellese [14], Carnevale [15], Lai [16], Devarajan [17], and Violi [18] have shown that RBO and EVOO can reduce blood sugar levels and control levels of cholesterol and TGs in T2DM patients. However, it is not known if RBO or EVOO is more effective in daily use, a question that we attempted to answer in the present study.

MATERIALS AND METHODS

Ethical approval of the study protocol

The study protocol was approved by Medical Ethics Committee of the University of Indonesia (0407/UN2. F1/ETIK/2018). The present study has been registered at clinical. trial. gov (NCT03544411).

Inclusion criteria

The inclusion criteria were individuals suffering from T2DM: aged 30–60 y; with a body mass index (BMI) of 20–30 kg/m^2; diagnosed<3 y; and taking anti-DM drugs.

Exclusion criteria

The exclusion criteria were individuals suffering from T2DM: with acute complications (hypoglycemia, diabetic ketoacidosis or hyperosmolar hyperglycemic non-ketotic syndrome); with chronic complications (coronary heart disease, gangrene, neuropathy, retinopathy); who were pregnant; taking cholesterol-lowering drugs, corticosteroids or other

drugs that affect fat metabolism; smoking>10 cigarettes/day; with glycated hemoglobin (HbA1C)>10%; taking a nutritional supplement containing phytosterol or other antioxidants; suffering from gastrointestinal, thyroid, cardiac, hepatic, or kidney disorders; suffering from cancer; who had suffered a stroke.

Reasons for dropping out of the study

Participants dropped out of the study because they: refused to continue the study; had a severe illness that necessitated hospital treatment during the study; consumed alcohol occasionally; had a level of compliance<80%; did not consume RBO or EVOO per protocol on three consecutive occasions.

Study participants

The study was carried out at FKUI Kayu Putih Family Clinic in Jakarta, Indonesia. The study was carried out from July to September 2018.

Treatment

We undertook a randomized, single-blind, crossover clinical trial to compare changes in levels of glucose, total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C) and TGs for study participants treated with 15 ml/day of EVOO or RBO.

RBO or EVOO was administered for 4 consecutive weeks. During a 2-week interval, treatment was not administered. After this washout period, a crossover design was implemented by exchanging EVOO supplementation with RBO supplementation and *vice versa* for 4 consecutive weeks.

Biochemical analyses

Peripheral blood was taken from study participants and centrifuged at 1000 g for 10 min at room temperature to obtain serum. Serum samples were placed in Labgeo™ (Samsung, Seoul, South Korea) to obtain values for blood glucose, TC, LDL-C, HDL-C, and TGs within minutes.

Statistical analyses

Data were analyzed using SPSS v20 (IBM, Armonk, NY, USA) and the Data Analysis Tools within Office™ 2013 (Microsoft, Redmond, WA, USA). The Shapiro–Wilk test was undertaken to test for a normal distribution of values. Differences among groups were assessed by the paired *t*-test and Wilcoxon test. Values are the mean±SD. $p<0.05$ was considered significant.

RESULTS

The study comprised 10 patients (9 females, 1 male) of mean age 48.9 y. The mean BMI was 25.6 kg/m^2. Dietary analyses are shown in table 1 and show no significant difference in the intake of calories, carbohydrates, lipids or fiber before and after treatment. With regard to protein intake, there were significant differences before and after treatment with RBO ($p = 0.005$) and EVOO ($p = 0.031$).

Table 1: Mean daily intake of energy, carbohydrates, proteins, lipids, and fiber of the RBO group and EVOO group at baseline and post-intervention

	RBO	p	EVOO	p
Energy intake, Kcal/day				
Baseline	1732.2±116.7	0.108^t	1732.2±116.7	0.295^t
Post-intervention	1624.1±136.9		1686.3±82.9	
Carbohydrate intake, g				
Baseline	247.9±27.8	0.158^t	247.9±27.8	0.134^t
Post-intervention	227.6±27.1		228.6±23.3	
Protein intake, g				
Baseline	67.4±11.7	0.005^t	67.4±11.7	0.031^t
Post-intervention	53.9±7.6		59.0±7.0	
Fat intake, g				
Baseline	57.4±11.6	0.432^t	57.4±11.6	0.218^t
Post-intervention	60.0±8.0		64.5±11.2	
Fiber intake, g				
Baseline	17.0±6.1	0.191^t	17.0±6.1	0.235^t
Post-intervention	14.4±2.2		15.0±3.6	

Values are the mean±standard deviation or median, t: paired t-test, w: Wilcoxon test, $p<0.05$, significant. RBO, rice bran oil; EVOO, extra virgin olive oil.

Fasting blood glucose (FBG) levels

FBG levels were not significantly different before and after treatment with RBO and EVOO as shown in table 2. There was a tendency of decreasing FBG levels. FBG levels before treatment was 198.9±54.7 mg/dl and after treatment was 192.5±57.3 mg/dl with RBO. After giving EVOO, the FBG level was 191.5±50.7 mg/dl.

Table 2: Levels of fasting blood glucose and postprandial blood glucose in the RBO group and EVOO group at baseline and post-intervention

	RBO	p	EVOO	P
Fasting blood glucose				
Baseline	198.9±54.7	0.731^t	198.9±54.7	0.674^t
Post-intervention	192.5±57.3		191.5±50.7	
Postprandial blood glucose				
Baseline	276.2±93.9	0.688^t	276.2±93.9	0.669^t
Post-intervention	264.4±80.0		262.4±95.3	

Values are the mean±standard deviation or median, t: paired t-test, w: Wilcoxon test, $p<0.05$, significant. RBO, rice bran oil; EVOO, extra virgin olive oil.

Postprandial blood glucose (PBG) levels

PBG levels were not significantly different before and after treatment as shown in table 2. The PBG level before treatment was 276.2±93.9 mg/dl. Upon treatment with RBO, this changed to 264.4±80.0 mg/dl; upon treatment with EVOO, it changed to 262.4±95.3 mg/dl. After treatment with RBO or EVOO, the mean level of FBG and PBG was high. These results suggested that, although there was a downward trend in levels of FBG and PBG, there was no improvement in clinical status.

Lipid profiles

With regard to TC levels, administration of RBO and EVOO did not result in a significant difference as shown in table 3. The baseline value was 177.0±54.7 mg/dl. Upon treatment with RBO, it changed to 187.1±27.8 mg/dl; upon treatment with EVOO, it changed to 194.8 mg/dl. Although there was a tendency to increase, TC levels remained within the normal threshold.

Table 3: Lipid profiles of the RBO group and EVOO group at baseline and post-intervention

	RBO	p	EVOO	P
TC, mg/dl				
Baseline	177.0±26.7	0.288[t]	177.0±26.7	0.169[w]
Post-intervention	187.1±27.8		194.8(163.264)	
LDL-C, mg/dl				
Baseline	97.1±21.5	0.178[t]	97.1±21.5	0.103[w]
Post-intervention	109.7±25.8		116.7(84.177)	
HDL-C, mg/dl				
Baseline	58.9±11.5	0.012[w]	58.9±11.5	0.025[t]
Post-intervention	52.8 (46.63)		54.7±10.9	
Triglycerides, mg/dl				
Baseline	106.3±31.5	0.078[t]	106.3±31.5	0.209[t]
Post-intervention	122.1±37.9		117.1±35.2	

Values are the mean±standard deviation or median, t: paired t-test, w: Wilcoxon test, p<0.05, significant. RBO, rice bran oil; EVOO, extra virgin olive oil.

In regard to LDL-C levels, administration of RBO and EVOO did not result in a significant difference. The baseline value was 97.1±21.5 mg/dl. Upon treatment with RBO, it changed to 109.7±25.8 mg/dl; upon treatment with EVOO, it changed to 116.7 mg/dl.

There were significant differences in HDL-C levels in both groups before and after treatment. The baseline value was 58.9±11.5 mg/dl. Upon treatment with RBO, it changed to 52.8 mg/dl; after treatment with EVOO, it changed to 54.7±10.9 mg/dl. Nevertheless, these decreases in HDL-C levels were in the normal range.

For TGs, there were no significant differences before and after treatment. The baseline value was 106.3±31.5 mg/dl. Upon treatment with RBO, it changed to 122.1±37.9 mg/dl; after treatment with EVOO, it changed to 117.1±35.2 mg/dl.

DISCUSSION

Changes in blood glucose levels upon RBO administration in the present study were not significantly different from those recorded in other studies. In research conducted by Devarajan and colleagues using a mixture of RBO with sesame seeds in a large study for 8 w, changes in blood glucose levels showed a significant change (p<0.001) [17].

Decreases in blood glucose levels after EVOO administration in the present study are in accordance with those documented by Carnevale and co-workers, as well as with large studies in which olive oil was added to a Mediterranean diet [15, 19, 20].

MUFA content in RBO and EVOO can change the composition of fatty acids in target cell membranes so that the function of insulin receptors is affected. MUFA causes changes in the composition of cell membranes so that they are richer in *cis*-type fatty acids. This alteration of composition results in the formation of more spaces between membrane head groups so that they are more broadly hydrophilic. This change increases the fluidity of cell membranes and activates key receptor proteins (G proteins, protein kinase Cα subunits), which can reach the membrane surface readily and increase signal sensitivity. MUFAs also improve the entero-insular axis by increasing the secretion and activity of glucagon-like peptide (GLP)-1 and gastric inhibitory polypeptide. This increase can increase the secretion and biosynthesis of insulin. In addition, GLP-1 can reduce glucagon levels, which makes GLP-1 effective as nutritional therapy in DM. MUFAs also reduce damage and trigger neogenesis of pancreatic beta cells. The main mechanism that causes damage to pancreatic beta cells is toxicity to glucose and lipids [21].

The results of the present study are contrary to those of Lai and colleagues showing a decrease in TC levels upon RBO administration [16]. However, our data for EVOO administration are in accordance with those of Carnevale and colleagues [15]. The study by Lai and colleagues employed a different method by giving "modified" RBO in the form of milk with a larger dose (18 g of RBO) and longer time (5 w) compared with our study. The decrease in TC levels due to RBO administration occurs due to the γ-oryzanol content in RBO, which can inhibit levels of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase and increases expression of cytochrome P450 (CYP)7A1. Phytosterols found in RBO and EVOO can reduce TC levels.

Our results for RBO are different from those of Lai *et al.*, who showed a significant decrease in LDL-C levels after RBO treatment. The decrease in LDL-C levels is influenced by the γ-oryzanol and phytosterol in RBO, which increase expression of hepatic LDL-C receptors so as to increase cholesterol catabolism. γ-oryzanol can also inhibit levels of HMG-CoA reductase and reduce cholesterol levels in the liver by increasing expression of LDL-C receptors in the liver and blood [16].

Devarajan and co-workers found a significant increase in HDL-C levels at 8 w in 300 newly diagnosed DM patients given a mixture of EVOO and sesame seeds [17]. Previous studies on EVOO showed no significant changes in olive oil [15]. Increased HDL-C levels in RBO and EVOO could be due to the activity of the antioxidant phytosterol and vitamin E. In RBO, γ-oryzanol acts as an antioxidant [13, 23, 24].

Our results do not correspond with studies showing significantly decreased levels of TGs [14, 15, 17, 25]. Kuriyan and colleagues used RBO for daily cooking so that it did not change the proportion of daily fat intake. That method was different to our method, whereby RBO was consumed directly. Hence, fat consumption from oil was greater and the proportion of fat intake was greater, as can be seen from analyses of food intake after treatment [25].

An additional benefit of lowering levels of FBG and PBG can be achieved using RBO and EVOO. Thus, we recommend using RBO and EVOO for cooking, dressing salads or frying food.

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AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

All authors have none to declare

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