Extra Virgin Olive Oil and Postprandial Blood Glucose in Type 2 Diabetes Mellitus Patients: A Randomized Controlled Cross-over Trial

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Abstract

Introduction: Dietary intervention remains an important factor in the management of diabetes mellitus, and many patients have employed herbs and oils to help manage their chronic diseases. Extra virgin olive oil (EVOO) is widely known for its cardio-vascular benefits. However, its effect on the blood glucose of type 2 diabetes mellitus patients has not been extensively studied. In this study, we aimed to determine if the addition of EVOO to meals results in a lower postprandial blood glucose among type 2 diabetes mellitus patients.

Methods: Thirteen patients were included in this randomized controlled cross-over trial. They were randomized to receive a meal with or without EVOO followed by a one week washout period, where they were given the other intervention. The primary outcome is the trans-meal blood glucose, which was calculated as the percent change in two-hour postprandial blood glucose.

Results: In group A, there was a noted 88.55% increase in two-hour postprandial blood glucose in taking meals with EVOO, versus 72.11% change in meals without EVOO. The same was observed in Group B, with a 71.08% and 49.22% increase in two-hour postprandial blood glucose in meals with EVOO and without EVOO, respectively. The difference was significant with a *p*-value of 0.044. Free fatty acids inhibit glucose transport and insulin secretion, this effect may be more predominant in asian type 2 diabetes mellitus patients.

Conclusion: This study found that adding extra virgin olive oil on top of meals provided no additional benefit in terms of post-prandial glucose excursion.

Keywords: diabetes mellitus, diet, diettherapy, fatmetabolism, oliveoiltherapeuticuse

Introduction

Diabetes mellitus is a devastating global pandemic that poses an enormous public health challenge. Despite the efforts of the public and the drugs currently available in the market, the burden of diabetes mellitus continues to grow. Many individuals with chronic medical conditions are now resorting to complementary and alternative medicines to serve as adjuncts in the treatment of their diseases.[1] Therefore, efforts should be made to find the most effective and safe options.

Olive oil believed to be the most powerful factor in the Mediterranean diet, has long been known for its health benefits.[2] However, the fascination with olive oil started only in the last decade, when the PREDIMED trial, a Spanish primary intervention trial on the Mediterranean diet suggested its protective role against several chronic diseases.[3] The article was eventually retracted due to detected bias, but its influence prospered and even paved way for further investigation on the health benefits of olive oil.

Previous studies on healthy individuals have shown that olive oil consumption was associated with a decreased risk of developing type 2 diabetes mellitus, along with an improved lipid profile decreased blood pressure and a reduced the risk for major cardiovascular events.[2-4]

The literature on olive oil and type 2 diabetes mellitus is less consistent. A small study in Italy showed that intake of EVOO was associated with a lower postprandial glucose compared to control.[5] This was supported by a systemic review which observed a reduction in glycosylated hemoglobin (HbA1c) and fasting blood sugar on olive oil supplementation.[4] However other studies on type 2 diabetes patients have contrasting results. Olive oil intake did not elicit an improvement in postprandial glucose compared to control in a small clinical trial in Denmark.[6] Another study comparing the glycemic effect of olive oil and canola oil also did not result in a significant difference.[7]

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As far as we know, no previous research has investigated the effects of extra virgin olive oil on the glucose control of type 2 diabetes mellitus especially among Filipinos. It is known that Asians, due to genetics and visceral obesity, are more at risk for dysglycemia than Caucasians whom most studies were done.

In order to address this question, the general objective of this study is to evaluate the effect of EVOO on the postprandial blood glucose of patients with type 2 diabetes mellitus, more specifically:

1. To identify whether a significant difference exists in the trans-meal blood glucose 2 h after a meal with EVOO compared to meals taken without EVOO
2. To determine whether EVOO is an effective adjunct to anti-diabetes medications in lowering the postprandial blood glucose of type 2 diabetes mellitus patients

We hypothesized that among Filipino type 2 diabetes mellitus patients, there is a statistically significant difference in the trans-meal blood glucose 2 h after a test meal with EVOO versus meals taken without EVOO. Hence, it may be a useful dietary intervention to achieve glycemic goals, in conjunction with adherence to anti-diabetes drugs.

Methods

This study was a randomized controlled crossover trial conducted from September to November 2018. The participants were selected from a pool of patients with type 2 diabetes in the outpatient Diabetes Clinic of Makati Medical Center, a tertiary hospital in the Philippines. The technical aspect of this study was reviewed and approved by the Institutional Review Board (IRB).

Patient selection

All adult patients aged 30–65 years old, diagnosed with type 2 diabetes mellitus and with body mass index under the overweight or obese class I category (by Asia Pacific guidelines), were recruited to participate in this study.
The following exclusion criteria were used: 1) pregnancy, 2) history of frequent hypoglycemic episodes, 3) high risk of developing ketoacidosis and hyperglycemic hyperosmolar syndrome, 4) identified acute stress during the study (illness, fever or trauma leading to hospitalization), 5) current intake of steroids, 6) olive oil allergy or intolerance, and 7) digestive disorders.

Conduct of the study

During their first visit, the participants were orientated to the conduct of the study, after which their informed consent was explicitly sought. Since this study used a crossover design, all subjects served as their own control. To avoid the confounding effects of diabetes medications on blood glucose, the participants were instructed to continue their prescription medications and no adjustments were made throughout the duration of the trial.

On their second visit, they came to the Makati Medical Center laboratory waiting area in the morning after a 6-8h overnight fast. Their serum samples were taken for blood glucose analysis using the hexokinase method. This was then recorded as fasting blood sugar. After this, the participants were led to a designated table in the hospital cafeteria, where they were randomly allocated (period 1) to receive a standard breakfast without EVOO or a meal admixed with one tablespoon of EVOO. The standard meals were prepared by a registered dietician and labeled with serial numbers. They were randomized by the dietician through a coin toss, and both the participants and the investigator were blinded to the intervention.

Immediately prior to eating, the patients were asked to take their usual anti-diabetes medications due before breakfast and these were recorded. The standard meals were consumed steadily in 15 to 20 min, after which the food containers were collected to ensure its full consumption. The participants were asked to sit in the waiting area of the laboratory until the 2h postprandial blood sugar samples were drawn.

After a one-week washout period, the participants revisited for a crossover to the other treatment arm (period 2). The participants were provided exactly the same standard breakfast, and were advised to take the same medications they did during period 1, to eliminate the confounding effects of food and anti-diabetic medications, respectively, on the postprandial blood glucose.

The main outcome measured in the study was the trans-meal blood glucose, which is expressed as percent change in 2h postprandial blood glucose. This was calculated as the fasting blood sugar subtracted from the 2h postprandial glucose divided by the fasting blood sugar multiplied by 100.

Extra virgin olive oil

This study used an FDA-approved EVOO readily available in local supermarkets. Its free acidity expressed as oleic acid was determined to be 0.26%, comparable with the international food standards set by the International Olive Oil Council.[8]

Standard breakfast

Calories were calculated based on the ideal body weight of each participant multiplied by a factor of 25, for obese or overweight individuals, divided by 3. The meal was composed of 50% carbohydrates (rice), 20% protein (beef), and 30% fat (beef). Water (250 ml) was served with each meal. The short-grain white rice used in the study has an estimated glycemic index of 76 per 150g. Cooking oil was not used in the food preparation. Breakfast was chosen in order to avoid a second meal bias.

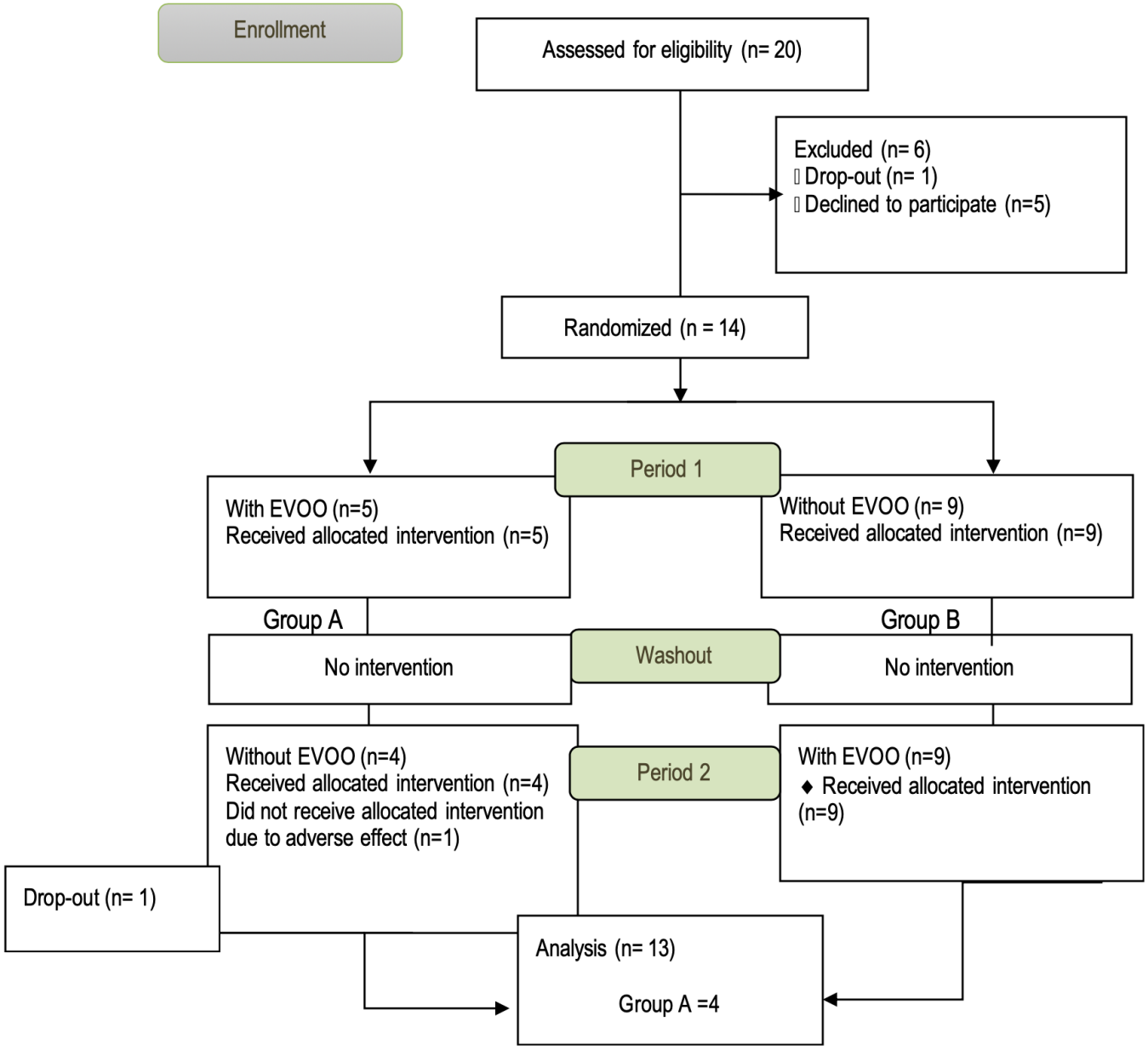

Figure 1. Flow diagram of the conduct of the study (Group A: With EVOO to Without EVOO = 4/Group B: Without EVOO to With EVOO = 9)

Sample size calculation

A minimum total of 12 patients were needed for this study with a crossover design, setting a two-sided significance level of 0.05, power of 90% to detect a significant difference between the two interventions, and population variance taken from the study of Violi et al.[9]

Formula:[1]

$$n = \frac{(z_\alpha + z_\beta)^2 \sigma^2}{2(\mu - \mu_0 - \delta)^2}$$

Legend:
n=sample size per arm
zα = critical value for 2-sided alpha of 0.05
zβ = critical value for power of 90%
μ-μ0 = true difference between the two mean values at which the power is calculated
δ = superiority margin or non-inferiority margin
σ = population variance

Calculation:

$$n = \frac{(1.96 + 1.282)^2 23.33^2}{2(0 - 5)^2}$$

$$n = 5$$

The minimum number of participants needed per arm is 5, or a study population of 10. To compensate for a possible dropout rate of 20%, the sample size is recalculated.

Adj. N = 10 (120%) = 12

Data analysis

Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for nominal data, median and range were used for nonparametric data, and mean and standard deviation were used for parametric data. ANOVA for crossover studies was used to determine the relative effect of EVOO or no intervention, magnitude of treatment effect, period effect, and treatment or period interaction. A treatment effect *p*-value of less than or equal to 0.05 means that there is sufficient evidence that the independent variables (EVOO or no EVOO) hava a significant contribution in explaining the dependent variable (change in blood glucose).

Results

A total of 14 patients were randomly assigned to the first allocation in the study, however, one patient withdrew from the study owing to watery diarrhea experienced 1h after eating the meal with EVOO. Of the 13 patients included in the final analysis, four were assigned to Group A (with EVOO to without EVOO) and nine were assigned to Group B (without EVOO to with EVOO). The mean age of these patients were 57.92 (±5.01) years; seven (53.85%) were female; all were either overweight (53.85%) or obese (46.15%); and nine (69.23%) had hypertension, whereas four (30.77%) had coronary artery disease 'Table I.'

Table I. Baseline characteristics of participants (N = 13)

	Mean ± SD; Frequency (%)
Age (years)	57.92 ± 5.01
Sex	
Male	6 (46.15)
Female	7 (53.85)
Weight (kg)	61.75 ± 5.04
Height (cm)	155.72 ± 8.79
BMI (kg/m^2)	24.56 (23.51 – 31.07)
Normal	0
Overweight	7 (53.85)
Obese	6 (46.15)
Comorbidities	
Hypertension	9 (69.23)
Coronary artery disease	4 (30.77)
Liverdisease	0
Renal disease	0
Chronic obstructive pulmonary disease.	0
Others	0
Smoking history (pack-years)	2
Never smoker	10
Current smoker	0
Quit smoking	1 (7.69)
Alcohol drinking	0

The average vital sign values were within normal range 'Table II.' The most common medications used were metformin (84.62%), DPP4 inhibitor (61.54%), insulin (38.46%), and sulfonylurea (38.46%). The median HbA1c (%) was 7.7 (range 6.77–11.12). A significant difference was found between groups, with treatment effect at p=0.044. For both groups and both periods, whenever EVOO was used, the percent increase was significantly higher with the use of EVOO 'Table III.'

The sequence in which EVOO was administered had no statistical effect on the blood glucose levels (p=0.280) and no interaction with treatment effect (p=0.754). The period effect or the carryover effect, likewise, had no statistical effect on the blood glucose levels (period effect, p=0.754) and no interaction with treatment effect (p=0.161). We verified normality of the data for both EVOO-first (p=0.986) and EVOO-second groups (p=0.552) 'Table III.'

Discussion

The present study demonstrated that adding a tablespoon of EVOO significantly increased the postprandial glucose levels of type 2 diabetes mellitus patients in comparison with having the same meal without EVOO (p=0.044). This finding is contrary to those reported in previous studies, which showed EVOO to have positive effects on the glucose metabolism of healthy subjects and subjects with type 1 diabetes mellitus.[9,10] Proposed mechanisms include prolongation of the effect of incretins by the high content of monosaturated fats (MUFAs) in EVOO, ultimately causing

Table II. Clinical and laboratory profile of participants (n = 13)

	Mean ±SD; Median (Range); Frequency (%)
Vital signs	
Heart rate (/min)	76.77 ± 7.00
Respiratory rate (/min)	20 (16 – 20)
Systolic blood pressure (mmHg)	115.38 ± 11.98
Diastolic blood pressure (mmHg)	74.62 ± 7.76
Medications used	
Metformin	11 (84.62)
DPP4 inhibitor[a]	8 (61.54)
Insulin	5 (38.46)
SUR[b]	5 (38.46)
Pioglitazone	1 (7.69)
SGLT2 inhibitors[c]	1 (7.69)
Lipid profile (mg/dL)	
Total cholesterol	183.35 ± 37.40
LDL-C [d]	97.77 ± 33.37
HDL-C[e]	56.07 15.63
Triglyceride	102 (54.91 – 708.85)
Blood glucose control	
HbA1c (%)[f]	7.7 (6.77 – 11.12)
Serum creatinine (mg/dl)	0.89 ± 0.25
Liver profile (U/L)	
Alanine transaminase	26 (13 – 117)
Aspartate transaminase	30 (17 – 88)

[a]Dipeptidylpeptidase; [b]SUR- Sulfonylurea; [c]Sodium Glucose Transporter [d]HDL-C, high density lipoprotein cholesterol; [e]LDL-C, low density lipoprotein cholesterol; [f]Glycosylated hemoglobin

Table III. Serum glucose before and after interventions (n = 13)

	Period 1			Period 2		
	Fasting	2 hours post-prandial	% Change	Fasting	2 hours post-prandial	% Change
	Mean ± SD					
With-Without EVOO	144.57 ± 17.48	275.80 ± 71.22	88.55 ± 26.92	138.87 ± 27.35	241.28 ± 68.15	72.11 ± 20.34
Without-With EVOO	148 ± 71.17	208.79 ± 65.02	49.22 ± 36.08	125.87 ± 13.80	214.38 ± 43.50	71.08 ± 34.88
p-value	0.928	0.123	0.079	0.267	0.403	0.958
Sequence effect (p-value):				0.280		
Period effect (p-value):				0.754		
Treatment effect (p-value):				0.044		
Interaction of sequence and treatment (p-value):				0.754		
Interaction of period and treatment (p-value):				0.161		
Normality:	With-Without: 0.986			Without-With: 0.552		

inhibition of hepatic glucose production, suppression of glucagon release, and prolongation of gastric emptying.[11] The difference in our findings led us to explore factors in carbohydrate and fat metabolism that may cause a good fat to be metabolically adverse. Elevated free fatty acids can impair glucose metabolism by competing with glucose for substrate oxidation, causing a 50% reduction in glucose oxidation. Apart from this, fatty acids can also reduce insulin-mediated glucose uptake by affecting insulin signaling at the level of protein kinase C.[12]

Interestingly, a study on glucose metabolism among Southeast Asians demonstrated that the type of fat (either monounsaturated or saturated fatty acids) did not exert a differential effect on glucose homeostasis, insulin sensitivity, insulin secretion, and gastrointestinal peptide release under fasting and postprandial conditions.[13] The subjects in our study were Filipinos. Asian patients with type 2 diabetes mellitus are known to have more visceral adiposity than Caucasian patients, which contributes to lipotoxicity and insulin resistance.[12] Hence, it is plausible that the difference in ethnicity may account for the nuances of insulin and fat metabolism in these populations.

The present study has many limitations. One is that the number of participants was relatively small. However, owing to the crossover design of our study, our data were sufficient for reaching statistical significance. Another limitation is that the effect of EVOO added to meals was only measured at one point. Although other studies[6] have estimated their outcomes with just one dose of EVOO, it is recommended that long-term EVOO consumption be employed in future studies, as it remains to be established whether changes in the glucose profile will be observed if EVOO is consumed over longer periods. A study design with a longer-term EVOO use will also enable the measurement of HbA1c, which is an important indicator of glucose control among diabetes mellitus patients.

Despite its limitations, however, this study was able to demonstrate a disadvantageous increase in postprandial blood sugar when EVOO was added to a standard meal, in contrast to the improved glucose control reported in published literature exploiting the benefits of EVOO monosaturated fatty acids.[9,10] This discrepancy highlights the need for further evaluation of the effects of different dietary fats and our carbohydrate metabolism.

Conclusion

In conclusion, this study showed that adding a tablespoon of EVOO significantly increased the postprandial glucose levels of type 2 diabetes mellitus patients. Therefore, at this point, EVOO cannot be recommended as an effective dietary intervention in the management of type 2 diabetes mellitus.

Disclosure

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About the paper

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