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Effect of a high monounsaturated fat diet supplemented with antioxidants on dyslipidemia in type 2 diabetes in Saudi Arabia

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Abstract

Dyslipidemia is a common disorder associated with type 2 diabetes and is the major cause of vascular disease. Antioxidants have been shown to improve dyslipidemia. Also, a diet rich in monounsaturated fatty acids (MUFA) has been recommended for diabetic patients. The effect of a high-MUFA diet alone or with antioxidants in diabetic dyslipidemia has not been previously investigated. The aim of this study was to investigate the effect of consuming a high-MUFA diet alone or with a combination of vitamin E and C, or lycopene on dyslipidemia in diabetic patients from Saudi Arabia. Forty eight type 2 diabetic patients participated in an intervention study lasting 20 weeks divided into three 4 week intervals separated by a washout interval. Subjects consumed 35 g/day olive oil throughout the study. After the first 4 weeks, participants took vitamin E (400 mg/day) and vitamin C (1000 mg/day) supplements. After 4 weeks washout, participants consumed 45g tomato paste (12 mg lycopene/day). Fasting blood samples were analyzed for glucose, lipid profile and total antioxidant status at baseline and at the end of each interval. The high-MUFA intake alone resulted in a significant increase only in HDL-cholesterol ($p<0.001$). Supplementation with vitamin E and C resulted in a decrease in total, and LDL-cholesterol ($p<0.001$), but not in HDL-cholesterol, or triacylglycerol (TG). Lycopene consumption significantly increased HDL-cholesterol ($p<0.001$), with the lowest TC/HDL ($p=0.002$) ratio among intervals. No change in glucose, TG or TG/HDL ratio was observed at any interval. The total antioxidant status was significantly increased following a high-MUFA diet and with vitamin and lycopene supplementations. Supplementation of a high MUFA diet with vitamin E and C, or lycopene indicated a beneficial effect on dyslipidemia in type 2 diabetes.

Keywords: *diabetes, lycopene, monounsaturated fatty acids, vitamin C, vitamin E, lipidemia*

Introduction

Diabetes mellitus type 2 is associated with dyslipidemia, characterized by the accumulation of triacylglycerol-rich lipoproteins, small dense LDL particles, reduced HDL-cholesterol and increased postprandial free fatty acid flux.[1] These dyslipidemic features contribute to the increased risk of developing vascular diseases, such as atherosclerosis, the leading cause of mortality in diabetes. The increased small dense LDL are more liable to oxidation, and readily adhere to and subsequently invade arterial wall leading to atherosclerosis.[2] Furthermore, the small LDL particles present in diabetes are more susceptible to glycation which aggravates the oxidative stress associated with diabetes.[3] Reduced antioxidant capacity may underlie the development of diabetic complications. Indeed, patients with poorly controlled type 2 diabetes suffering from complications have higher serum lipoperoxidation than patients with complication-free diabetes.[4,5] Vitamin C, vitamin E, and lycopene are major antioxidants that may protect against the development of diabetic complications via reduction of oxidative stress.[6] However, the administration of antioxidants to attenuate oxidative stress is still considered a controversial issue in diabetes management. Routine supplementation with antioxidants, such as vitamins E and C and carotene, is not advised because of lack of evidence of efficacy and concern related to long-term safety.[7]

In addition, type 2 diabetic patients are advised to reduce saturated and *trans* fat intakes to avoid vascular complications and the dyslipidemia associated with diabetes.[7] Clinical trials indicate that high MUFA diets are associated with lower glucose concentrations compared to carbohydrate-rich diets but without major differences in lipid concentrations.[8] A one-year comparison of a high-monounsaturated fat diet with a high-carbohydrate diet in type 2 diabetes indicated that high-MUFA diets are an alternative to conventional lower-fat, high-carbohydrate diets with comparable beneficial effects on body weight, body composition, cardiovascular risk factors, and glycemic control.[9]

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Table 1: Demographic data of participants in the intervention study (n=48).

Sex	Age (years)	Duration of diabetes (months)	Body mass index (kg/m^2)
Male (n=18)	57.00 ± 8.55	11.73 ± 9.14	28.21 ± 3.84
Female (n=30)	51.60 ±10.73	7.75 ± 5.72	33.03 ± 5.97
Total (n=48)	53.62 ± 10.22	9.24 ± 7.36	31.22 ± 5.73

Table 2: Concentrations of fasting plasma glucose, lipids and total antioxidant status in diabetic subjects at baseline, following a high MUFA diet, a high MUFA diet with combined vitamin E and C supplementation and a high MUFA diet supplemented with lycopene. Results are presented as mean ± SD (n=48).

Interval	Baseline	MUFA	MUFA + Vitamins E and C	MUFA + Lycopene
Fasting plasma glucose (mmol/L)	9.47 ± 3.20	9.88 ± 3.24	9.03 ± 2.73	9.33 ± 2.80
Total cholesterol (mmol/L)	4.79 ± 1.19	5.03 ± 1.26	4.31 ± 1.20 ($p<0.001$ vs baseline and MUFA)	5.57 ± 0.99 ($p<0.001$ vs MUFA and MUFA + vitamins E and C)
LDL-cholesterol (mmol/L)	2.66 ± 0.96	2.81 ± 1.01	2.27± 0.83 ($p<0.01$ vs MUFA)	3.23 ± 0.93 ($p<0.001$ vs MUFA + vitamins and MUFA)
HDL-cholesterol (mmol/L)	0. 90 ± 0.34	1.03 ± 0.42 ($p<0.001$ vs baseline)	0.96 ± 0.53	1.29 ± 0.44 ($p<0.001$ vs MUFA + vitamins and MUFA)
Triacylglycerols (mmol/L)	2.04 ± 1.49	2.39 ± 2.35	2.22 ± 3.16	2.54 ± 2.46
Total cholesterol/HDL ratio	5.76	5.41	5.13	4.60 ($p=0.002$ vs MUFA)
Total triacylglycerol/HDL ratio	2.69	3.07	3.77	2.10
Total antioxidant status (mmol/L)	1.26 ± 0.16	1.43 ± 0.30	1.59 ± 0.16	1.66 ± 0.40

The role of administering high MUFA diets in combination with antioxidants and their effects on lipid profiles of diabetic patients has not been fully investigated. Therefore, the aim of this study is to clarify the effects of a high MUFA diet, alone, or combined with the antioxidants vitamin E and vitamin C or lycopene on the lipid profile of type 2 diabetic patients.

Materials and Methods

Subjects

Forty eight type 2 diabetic subjects (18 males, 30 females), age range 32-75 years, were recruited from King Abdul Aziz University Hospital, Jeddah, Saudi Arabia. The study was approved by the Hospital's Ethics Committee. All subjects gave informed consent prior to participation in the study. Forty six patients were on oral hypoglycemic drugs, while two were on insulin. No one reported intake of vitamin E or C supplements.

Dietary Intervention

The study period consisted of four consecutive intervals, each of four weeks duration. At the start of each interval, subjects were asked to consume a high-monounsaturated fat (high MUFA) diet (35 g/day) of extra virgin olive oil (Pons; Euroaliment S.L.Pol, Lleida, Spain) with the reduction in saturated fats and refined carbohydrate-rich foods. During the first interval, subjects followed a high MUFA diet by consuming the daily assigned 35 g olive oil. In the second interval, subjects followed the same high MUFA intake diet with a daily combination of vitamin E (400 mg) and vitamin C (1000 mg) supplements. During the third interval, which was a washout period, the same high-MUFA diet was followed without any supplements. During the last interval, the high MUFA diet was consumed along with a daily intake of 40 g of tomato paste (Saudi tomato products company, Kingdom of Saudi Arabia) as a source of lycopene (12 mg). Constant follow-up by telephone was made to encourage participants to comply with their dietary intervention.

Blood Collection

Fasting blood samples were taken at baseline and at each visit thereafter. Overnight (12 hours) fasting blood samples (2 ml) were collected in ethylenediaminetetraacetic acid (EDTA) plasma tubes. The plasma was separated by centrifugation at 2500 x *g* for 10 minutes at 25° C.

Biochemical Analysis

Plasma glucose was determined using a kit based on an enzymatic method[10] on an automated analyzer (Hitachi 917). Plasma was analyzed for total cholesterol concentrations using an enzymatic method,[11] LDL-cholesterol concentrations were determined in serum[12] and HDL-cholesterol concentrations according to an established method.[13] Triacylglycerol concentrations were determined using an automated analyzer (Hitachi 917, Japan) according

to a published method.[14] Total antioxidant status was determined using a kit method (Randox Laboratories Ltd. Antrim, UK) and based on an established procedure.[15]

Statistical Analysis

Data was analyzed using the statistical package SPSS version 13.0. The mean ± standard deviation (SD) was estimated for age, time of onset of diabetes, BMI, and the concentrations of fasting plasma glucose, plasma total cholesterol, LDL-cholesterol, HDL-cholesterol and TG for each interval of the study. Analysis of variance (ANOVA) was performed to test for change in concentrations between different intervention intervals. Thereafter, where ANOVA results indicated a significant difference, a paired comparison t-test was undertaken for every two intervals to test for further significance.

Results

Subject Characteristics

Basic demographic data of the participants in this study is presented in Table 1. The duration of diabetes was in the range 0.20- 32 years with a mean duration 9.24 ± 7.36 years (mean ± SD). The body mass index (BMI) for all 48 subjects was in the range of 21.1-52.8. Females had a higher BMI (33.03 ± 5.97) than males (28.21 ± 3.84). There was no significant change in BMI for different intervals of the intervention study.

Fasting Plasma Glucose

The fasting plasma glucose concentration was 9.47 ± 3.20 mmol/L as baseline and this did not change significantly throughout the intervention study (Table 2).

Plasma Total Cholesterol

The fasting plasma cholesterol concentrations were as follows: 4.79 ± 1.19, 5.03 ± 1.26, 4.31 ± 1.20 and 5.57 ± 0.99 mmol/L (mean ± SD) at baseline, after MUFA intake alone, MUFA with vitamins, and after MUFA with lycopene intake respectively (Table 2). A repeated measure ANOVA test indicated significant differences between the intervals ($p< 0.001$). There was a significant decrease after the MUFA with vitamin interval compared to baseline and to MUFA alone ($p<0.001$). However, total cholesterol concentration increased significantly following MUFA with lycopene intake ($p< 0.001$) when compared to MUFA alone and MUFA with vitamin intervals (Table 2).

Since total cholesterol concentration increases with age, the ANOVA test revealed a significant variance of interaction ($p= 0.009$) between total cholesterol and age. That significance was more pronounced between MUFA alone and MUFA with vitamin ($p= 0.004$) intervals. Moreover, there was a significant variance as a result of interaction for total cholesterol with the duration of diabetes ($p= 0.009$).

Plasma LDL Cholesterol

The mean LDL-cholesterol concentration was 2.66 ± 0.96, 2.81 ± 1.01, 2.27 ± 0.83 and 3.23 ± 0.93 mmol/L (mean ± SD) at baseline and after MUFA alone, MUFA with vitamins, and MUFA with lycopene intervals respectively (Table 2). The ANOVA test indicated that there were significant differences between intervals ($p = 0.001$). The paired comparison test between intervals showed a significant decrease ($p< 0.001$) in LDL cholesterol occurred after administration of MUFA with vitamin supplement compared to the preceding interval where they were placed on MUFA alone. There was a significant increase in LDL-cholesterol after MUFA with lycopene consumption compared to the MUFA with vitamins and to the MUFA only interval ($p< 0.001$).

Plasma HDL-Cholesterol

HDL-cholesterol concentrations were 0.90 ± 0.34, 1.03 ± 0.42, 0.96 ± 0.53 and 1.29 ± 0.44 mmol/L (mean ± SD) at baseline, after MUFA intake, after MUFA with vitamin intake, and after MUFA with lycopene intake respectively (Table 2). The mean fasting HDL-cholesterol concentration was lowest at baseline. There was a significant increase ($p< 0.001$) in HDL-cholesterol after MUFA intake alone compared to baseline, followed by a slight but insignificant decrease after the MUFA with vitamin interval. However, a significant increase in HDL concentration ($p<0.001$) occurred after the MUFA with lycopene interval compared to the MUFA alone and MUFA with vitamin intervals respectively.

Plasma Triacylglycerols

The concentrations of plasma TG were 2.04 ± 1.49, 2.39 ± 2.35, 2.22 ± 3.16 and 2.54 ±2.46 mmol/L (mean ± SD) at baseline, after MUFA intake alone, after MUFA with vitamin intake, and after MUFA with lycopene intake, respectively (Table 2). The repeated measure ANOVA test indicated no significant difference in TG concentration between intervals.

Ratio of Total cholesterol to HDL-cholesterol and of Triacylglycerols to HDL

The means for the ratios of total cholesterol to HDL-cholesterol (TC/HDL) were 5.76 at baseline, 5.41 after MUFA alone, 5.13 after MUFA with vitamin intake and 4.60 after MUFA with lycopene intake (Table 2). The means for the ratios of TG to HDL (TG/HDL) were 2.69 at baseline, 3.07 after MUFA alone, 3.37 after the MUFA with vitamin interval, and 2.10 after the MUFA with lycopene interval (Table 2). The repeated measure ANOVA test indicated a significant difference in the TC/ HDL ratio only ($p=0.005$), whereas no difference was found in the TG/ HDL ratio. A paired comparison between intervals indicated a significant difference in TC/HDL between the MUFA and MUFA with lycopene interval ($p=0.002$) as shown in Table 2.

Plasma total antioxidant status

Pairwise comparison between intervals indicated that the total antioxidant status was significantly higher after the interval of MUFA intake compared to baseline ($p= 0.012$), and continued to rise significantly after supplementation with vitamins ($p = 0.022$) compared to MUFA alone (Table 2). A significant increase was also observed following the lycopene interval compared to the concentration after the MUFA interval ($p= 0.009$), but not different from the concentration after the MUFA with vitamin supplementation.

Discussion

This study found no significant change in glycaemia following a high MUFA diet and is consistent with some[16,17] but not all previous human studies.[18] Furthermore, supplementation with combined vitamin C and E had no effect on glycaemia as reported previously.[17] The lack of effect of lycopene on glycaemia in this study contrasts with the finding that dietary lycopene reduction is associated with a low fasting plasma glucose.[19] This discrepancy is unclear as there is limited information on biological mechanisms linking carotenoids and glucose metabolism
.

Type 2 diabetes is associated with high plasma total cholesterol concentration. The high dietary intake of total fat, especially saturated fat, is linked to elevated total cholesterol concentrations. Other factors, such as age and duration of diabetes also contribute to the high levels of cholesterol among type 2 diabetic subjects. According to the recommendations of the European Atherosclerosis Society, total cholesterol levels within the range 5.2-7.8 mmol/L are considered high if HDL-cholesterol is below 0.9 mmol/L whereas cholesterol concentration above 7.8 mmol/L reflects dyslipidemia.[20] The baseline total cholesterol and LDL-cholesterol concentrations in this study were lower than that reported by other studies in type 2 Saudi diabetics.[21, 22, 23] This could be due to differences in age, duration of diabetes, type of diet, activity level, and the intake of lipid-lowering drugs in this study and those in other studies.

Dietary intervention with the high-MUFA diet did not result in any significant change in total cholesterol or LDL-cholesterol concentrations. Controversial results have been reported from studies comparing high-MUFA diets to high polyunsaturated fatty acid (PUFA) diets,[24,25, 26, 27, 28] or to high-carbohydrate diets[29, 30, 26, 16, 31] or to low-fat diets.[17] A study in 1999 found both high-MUFA and high-carbohydrate diets in type 2 diabetic relatives to induce similar lowering effects on total and LDL-cholesterol concentrations.[32] Similarly, another study indicated a reduction in plasma total and LDL-cholesterol concentrations with a high-MUFA diet and isocaloric low-fat diet.[17] The similarity in settings between our study and another study[16] where patients consumed home-prepared meals rich in olive oil, indicates that high-MUFA diets are neutral in their effect on total and LDL-cholesterol. Contrary to previous studies, a study in 2001 reported that PUFA-rich diet resulted in a reduction of total cholesterol concentration compared to a high-MUFA diet.[27] However when three types of low-calorie diets were compared: a high-MUFA diet (32% fat, 7% saturated), high-carbohydrate diet (10% fat, 4% saturated) and a high-saturated fatty acid (SFA) diet (32% fat, 17% saturated) in free-living, obese, type 2 diabetics, there was a 10% and 17% reduction in LDL-cholesterol with the high-carbohydrate and high-MUFA diets, respectively, but no change with the high-SFA diet.[30] Moreover, it has been reported that a change from linolenic to oleic acid diet improved LDL-cholesterol in diabetic subjects, an outcome that was not observed in this study.[33] It is thus clear, from this study and the previously mentioned studies, that a high-MUFA diet has no adverse effects on total and LDL-cholesterol concentrations.

The intake of the high-MUFA diet with vitamin E and C supplements resulted in a significant reduction in both total and LDL-cholesterol concentrations compared to MUFA alone. This could suggest that vitamin supplementation promotes a better effect on total and LDL-cholesterol concentrations compared to the high-MUFA intake alone. In addition to their antioxidant effects, these vitamins have been shown, in some studies, to improve lipid metabolism in type 2 diabetic subjects.[34] Although the supplementation dose used in this study (400 mg/day) is considered lower than that of other studies, this indicates that vitamin E supplementation need not be administered in high doses to be effective in reducing cholesterol levels. On the other hand, the dose should not be lower than 400 mg/day such as one study where a dose of 200 IU/day did not show significant changes in the blood lipid levels of diabetic patients.[35] The administration of both vitamins E and C with MUFA intake could possibly be another factor in lowering cholesterol and LDL levels. Daily supplementation with 1000 mg vitamin C for 2-months significantly reduced LDL-cholesterol and TG in type 2 diabetic subjects,[36] whereas a daily supplementation with 500 mg of vitamin C alone showed no significant change on serum cholesterol concentration.[37] This suggests that vitamin C supplementation has to be as high as 1000 mg/day to have a lipid-lowering effect. Moreover, a study found no significant changes in the serum levels of LDL-cholesterol after 3-months supplementation with combined vitamins (200 mg vitamin C, 150 mg vitamin E and the minerals: 200 mg magnesium and 30 mg zinc) to type 2 diabetics.[38] This might suggest that the doses of the vitamins used in our study for 4-weeks were beneficial in reducing the cholesterol and LDL- cholesterol concentrations.

Despite the fact that the intervention with MUFA and lycopene resulted in a significant increase in total and LDL-cholesterol concentrations compared to other intervals, this effect was counterbalanced with a significant rise in HDL-cholesterol. Studies on the use of lycopene-rich sources, without additional MUFA, on lipid particles have been controversial. It has been shown that a four-day food record of raw and processed tomato products revealed a positive association between plasma lycopene and total cholesterol.[39] However, another study reported that consumption of lycopene-rich foods did not affect plasma lipid concentration.[40] In addition, some studies indicated no changes in serum total cholesterol concentration[41] or total cholesterol and LDL-cholesterol concentrations[41] after consumption of lycopene-rich foods. Except for one study,[42] others did not investigate the effect of a MUFA diet combined with lycopene. The results of this study were different from earlier ones possibly because the subjects were consuming *ad-libitum* diets and that the intervention with lycopene came after a period of 15-weeks after the start of the study. This might indicate that the subjects have been consuming a diet high in cholesterol during that

interval which could be related to the elevation in the cholesterol and LDL-cholesterol. Also, there could have been a bias in the subjects reporting of their MUFA intake during that period. A study on overweight diabetic patients, reported of such a bias where there was an overestimation in the diet history specifically with MUFA intake.[43]

A low HDL-cholesterol concentration is a characteristic of dyslipidemia in type 2 diabetes.[44] HDL-cholesterol of ≥ 1.1 mmol/L has been recommended by the American Diabetes Association to avoid the development of coronary heart disease in diabetes. At baseline, the mean HDL-cholesterol concentration was lower than the recommended level. Another study on Saudi diabetics reported a mean HDL-cholesterol concentration of 1.0 mmol/L[22], which is slightly higher than the value reported in this study. This low HDL-cholesterol indicates the need for a dietary intervention to attenuate dyslipidemia in diabetes.

The introduction of the high-MUFA diet in this study which resulted in a significant increase in HDL-cholesterol concentration is a good indicator that diet enrichment with olive oil improves HDL-cholesterol. This is consistent with studies comparing high-MUFA diets to low-fat diets where the former caused a significant increase in HDL-cholesterol[8], and a beneficial effect on both TG and HDL-cholesterol concentrations.[45] This effect, however, was not achieved with healthy adults consuming either a MUFA-rich or a PUFA-rich diet for a short period.[27] However, studies comparing high-MUFA diets to high- carbohydrate diets reported controversial results as to their effect on HDL-cholesterol concentrations. Our findings are consistent with other studies[32,26] which indicated slightly higher levels of HDL-cholesterol with a high-MUFA diet compared to high-carbohydrate diets. One study reported that HDL-cholesterol significantly decreased in diabetic patients on a high-MUFA diet and implies inconsistent results[33].

While the consumption of a high-MUFA diet for the first 4-weeks of the study improved HDL-cholesterol concentration, supplementation with vitamin E and C for the following 4-weeks, resulted in a non significant reduction of HDL-cholesterol concentration. Previous studies indicated different effects of vitamin E or both vitamin E and C supplementations on HDL-cholesterol concentrations. In healthy volunteers, the administration of either 200 mg/day, or 400 mg/day of vitamin E for 50 days, did not significantly change HDL-cholesterol concentration.[46] On the contrary, other workers found a significant increase in HDL-cholesterol after 3-months supplementation of combined vitamins and minerals.[38] In our study, although the concentration of HDL-cholesterol decreased after vitamin supplementation compared to the MUFA interval, that decrease was not significant. Also, in contrast to their results, our supplementation induced a significant decrease in total cholesterol which might also explain the accompanying reduction in HDL-cholesterol concentration.

Supplementation of the high-MUFA diet with lycopene resulted in a significant rise in HDL-cholesterol concentration compared to baseline, MUFA, or MUFA with vitamin levels. This indicates a beneficial effect for the combination of lycopene with high-MUFA intake. A few studies have investigated the effects of a high-MUFA diet rich in lycopene on lipid profile. However, one group compared a high-olive oil high-lycopene diet to low-oil high-carbohydrate diet in healthy adults for a short period (10-days) and indicated a significant increase in HDL-cholesterol and a lower ratio of TC:HDL.[47, 42] A four-day food record of raw and processed tomato products revealed a positive association between plasma lycopene with HDL-cholesterol.[39] Another study showed that a one week dietary supplementation of lycopene in healthy subjects does not change HDL-cholesterol concentrations.[41] Thus, the effect of a high-MUFA diet on HDL-cholesterol concentration in type 2 diabetes remains unclear.

Hypertriacylglyceridemia is a common abnormality in type 2 diabetes and considered an independent risk factor for cardiovascular disease.[48] High TG concentrations are associated with reduced HDL-cholesterol, indicating insulin resistance and small dense LDL, were shown to be associated with coronary disease.[49] Although clinical trials, have suggested that high-MUFA diets are associated with lower TG levels,[50, 45] other studies[30] showed no change in TG with a high-MUFA, a high-carbohydrate or a high-SFA diet in type 2 diabetics. Furthermore, other workers showed no change in TG concentration in type 2 diabetic subjects after the consumption of a high MUFA diet compared to an iso-caloric low-fat diet.[17] Our results, thus, are consistent with those of two other groups.[30, 17]

It has been reported that a high-MUFA diet produced 2.2 to 2.3 times greater reductions in plasma TG, very low-density lipoprotein cholesterol, and total cholesterol/HDL-cholesterol ratio in type 2 patients compared to an iso-energic high-carbohydrate diet.[31] Similarly, compared to a high-carbohydrate diet given to type 2 diabetic relatives, a high-MUFA diet showed similar lowering effects on TG concentration[32]. However, a PUFA-rich diet reduced total TG concentrations and very low density lipoprotein (VLDL)-TG levels to a significantly greater extent than the MUFA-rich diet after 2-weeks administration in diabetics.[27]

The high-MUFA diet alone or combined with vitamin C and E did not affect TG concentrations. Indeed one study reported no significant change in the serum TG concentrations after 3-months in type 2 diabetic subjects on a combined vitamin and mineral supplementation.[38] Other workers also observed no significant differences in fasting TG concentrations when supplementing 500 mg of vitamin C daily or a placebo in type 2 diabetic patients[37]. Inconsistent with our results was a study which indicated a significant reduction in TG concentrations in type 1 diabetic patients after supplementation with vitamin E capsules (100 IU/day) for 3-months.[51] This could be related to a longer duration of vitamin E administration than in our study.
Similarly, the supplementation of a high-MUFA diet with lycopene did not result in a significant change in TG compared to the MUFA interval or to the MUFA with vitamin interval. This was not in agreement with previous

studies[47, 42]who found a reduction in TG after giving healthy adults a high-olive oil high-lycopene diet compared to a low-oil high-carbohydrate diet for 10-days. However, the reduction of TG level in a short period (10-days) might have not sustained for a longer period, which could explain why the TG concentration did not change in this study.

Although absolute values of total cholesterol, LDL cholesterol, and HDL cholesterol have been recommended as determinants of cholesterol risk, other estimates have been developed and have been accepted as biomarkers for predicting risk of heart disease. Based on large scale epidemiological evidence on the correlation of TC/HDL and LDL/HDL ratios as strong predictors of coronary artery disease, more studies have been adopting these ratios in the interpretation of their results.[52] Moreover, since HDL and LDL particle size precisely corresponds to the functional biomarker of lipoprotein quality, the fractional esterification rate of cholesterol (FERHDL), and the atherogenic index of plasma (AIP) (a logarithmically transformed ratio of molar concentrations of TGs to HDL-cholesterol), have been shown to be the strongest predictor tests of positive findings on coronary angiography and have a potential to predict the cardiovascular risk.[53] In this study, there was a gradual decline in the TC/HDL-cholesterol ratio along the duration of the study. The lowest ratio was encountered after the intervention with MUFA and lycopene. That ratio, which was significantly lower than the intake of MUFA alone, implies that lycopene ingestion with MUFA conveys beneficial attributes in type 2 diabetics. In the study of Helibronn *et al.* (1999),[30] where one of three types of low-calorie diets (1,600 kcal/day): a high-MUFA diet (32% fat, 7% saturated), high-carbohydrate diet (10% fat, 4% saturated) and a high-SFA diet (32% fat, 17% saturated), were given to obese patients with type 2 diabetes, showed that TC/HDL ratio was significantly reduced on the high-MUFA diet. Another study also showed that a high-MUFA diet produced reductions in total cholesterol/HDL-cholesterol ratio in type 2 diabetic patients[31]. Additionally, two studies[47, 42] indicated a lower TC/HDL ratio with a high-olive oil high-lycopene diet compared to a low-oil high-carbohydrate diet in healthy adults. Moreover, despite no significant changes were observed in TG/HDL-cholesterol ratio among intervals, the ingestion of lycopene with MUFA, showed the lowest ratio compared to previous intervals. This further indicates that the administration of lycopene together with MUFA in the diabetic diet provides a protective effect against CHD risk which is common in diabetes.

The minor antioxidant phenolic components of virgin olive oil provided by the diet in this study resulted in a significant rise in total antioxidant status compared to the baseline. Supplementation with vitamins E and C caused an increase in total antioxidant status compared to the olive oil diet alone. Consistent with our findings, it has been shown that α-tocopherol administered to diabetics for six weeks resulted in an increase in serum total antioxidant status.[54] Consuming a high-MUFA diet with vitamin E and C suggests that the combined antioxidant effects of the vitamins and olive oil further enhance antioxidant potential in diabetes. In addition, the intake of lycopene resulted in a significant rise in total antioxidant status. However, our results were not consistent with others where supplementation of different forms of lycopene rich products in healthy subjects did not change their plasma antioxidant status[40]. This could be because the diabetic subjects in this study exhibited lower antioxidant status associated with hyperglycaemia compared to healthy subjects. Consistent with this study, is the finding that consumption of tomato products with olive oil caused a significant rise in the plasma antioxidant capacity compared to that observed with sunflower oil.[55]

In summary, the significant increase observed in HDL-cholesterol level with MUFA alone, and also after the intake of lycopene with MUFA, along with the significant decrease in total cholesterol and LDL-cholesterol after the MUFA with vitamins intake, suggest positive effects of such treatments. The lowest ratios of TC/HDL-cholesterol and TG/HDL-cholesterol resulting from the ingestion of lycopene with MUFA imply an additional benefit of this antioxidant for type 2 diabetic patients. Moreover, since dyslipidemia is common in type 2 diabetes, constant dietary counseling and medical intervention should be implemented to reduce further complications of diabetes.

Future studies need to be undertaken to understand the interrelation between dietary intake and antioxidants on oxidative stress in type 2 diabetes. More clinical trials are needed to elucidate if any synergistic effects exists between vitamin E, vitamin C and lycopene combinations in type 2 diabetes. In Saudi Arabia, more attention should be focused on educating diabetic patients about the potential benefit of life style modification through implementing the recommended dietary measurements with physical exercise and constant follow up.

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