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Effects of avocado oil supplementation on lipid profile and atherogenic indices in a double-blind and randomised intervention in patients with metabolic syndrome

Efeitos da suplementação de óleo de abacate sobre o perfil lipídico e índices aterogênicos em intervenção duplo-cego e randomizada em pacientes com síndrome metabólica

Abstract

Introduction: Metabolic syndrome is defined as a set of clinical conditions that affect approximately 25% of the world's population and 29.6% of Brazilians. This syndrome is related to increased cardiovascular outcomes, which may be predicted by the lipid profile. Bioactive compounds, such as monounsaturated fatty acids (MUFAs), are strong allies in preventing these outcomes. Avocado is an important food because it contains abundant bioactive compounds and MUFAs. However, few studies evaluated the effects of pure/virgin avocado oil on the lipid profile in humans with metabolic syndrome, and its effects on atherogenic indices are not known. **Objective:** This study evaluated avocado oil supplementation on lipid levels and atherogenic indices in patients with metabolic syndrome. **Method:** Thirty-one obese adults were randomised into a control group (soybean oil) and an intervention group (avocado oil). These groups were evaluated in the pre- and post-intervention periods (12 weeks) via clinical anamnesis and nutritional assessment. **Results:** The control group and the intervention group had higher intakes of lipids and saturated fat than recommended. For the lipid profile and atherogenic indices, no significant difference was observed between the pre- and postintervention periods. **Conclusion:** These results may have been due to the absence of dietary control, medication overload, intervention duration, mode of administration and dose of the supplement. Therefore, future studies on the effects of avocado oil are needed in this population to better control these variables.

Keywords: Metabolic Syndrome. Persea. Cholesterol. HDL-Cholesterol. LDL-cholesterol. Triglycerides.

Resumo

Introdução: A síndrome metabólica é definida como um conjunto de condições clínicas que acometem cerca de 25% da população mundial e 29,6% dos brasileiros. Essa síndrome está relacionada ao aumento dos desfechos cardiovasculares, que podem ser preditos através do perfil lipídico. Compostos bioativos, tais como os ácidos graxos monoinsaturados (MUFA), são fortes aliados na prevenção desses desfechos. Um alimento importante por conter compostos bioativos e MUFA em abundância é o abacate. Há, porém, poucos estudos avaliando o efeito do óleo puro/virgem de abacate sobre o perfil lipídico em humanos com síndrome metabólica, e seus efeitos sobre os índices aterogênicos inexistem. **Objetivo:** O estudo buscou avaliar a suplementação de óleo de abacate sobre os níveis lipídicos e índices aterogênicos em pacientes portadores de síndrome metabólica. **Método:** 31 indivíduos adultos e obesos foram randomizados em grupo controle (óleo de soja) e grupo intervenção (óleo de abacate). Estes foram avaliados

nos períodos pré e pós-intervenção (12 semanas) através de anamnese clínica e avaliação nutricional. **Resultados:** Observou-se que tanto o grupo controle quanto o grupo intervenção tinham a ingestão de lipídeos e gordura saturada maior que o recomendável. Quanto ao perfil lipídico e índices aterogênicos, não foi observada diferença significativa entre os períodos pré e pós. **Conclusão:** Os resultados podem ter se dado pela ausência do controle alimentar, sobrecarga de medicamentos, duração da intervenção, modo de administração e dose do suplemento. Logo, são necessários estudos futuros sobre os efeitos do óleo de abacate nessa população, que controlem melhor essas variáveis.

Palavras-chave: Síndrome Metabólica. Persea. Colesterol. HDL-Colesterol. LDL-Colesterol. Triglicerídeos.

INTRODUCTION

Metabolic syndrome (MetS) is defined as an association of conditions, such as excess weight (represented by high waist circumference), insulin resistance (altered fasting glucose), arterial hypertension and dyslipidaemia (an elevation in triglyceride levels or low concentrations of high-density lipoprotein (HDL)). Among the diagnostic criteria for MetS, the International Diabetes Federation (IDF) proposes the mandatory presence of central obesity associated with two more of the factors described.¹ The most recent classification for MetS establishes the presence of at least three of these risk factors.²

It is estimated that 25% of the world's population exhibits the characteristics for the diagnosis of MetS,³ but the prevalence in Brazil is 29.6% in the adult population.⁴ MetS triples the risk of occurrence of cardiovascular outcomes.⁵ Approximately 17.9 million people died due to cardiovascular diseases in 2019, which represents 32% of the total deaths worldwide.⁶ In Brazil, The forecast in Brazil is approximately 400,000 deaths from cardiovascular diseases by the end of 2021.⁷

Some of the main mortality risks associated with MetS are related to dyslipidaemia. Cardiovascular risk may be predicted from the analysis of lipid parameters, such as an increase in total cholesterol (TC), low-density lipoprotein (LDL-c) and triglyceride (TG), and a decrease in HDL-c.⁸ However, atherogenic indices are more sensitive in predicting this risk of cardiovascular death.^{8,9} The Castelli I and II indices are calculated from the TC/HDL-c and LDL-c/HDL-c ratios, and the plasma atherogenic index (PAI) is calculated using the ratio $[\log(\text{TG}/\text{HDL-c})]$.^{8,10}

The dietary pattern interferes with the occurrence of MetS and cardiovascular risk. Many studies related a diet rich in saturated fats, low-quality carbohydrates, sugary drinks and ultra-processed foods to the onset of MetS, and a diet rich in fibre, mono- and polyunsaturated fats and low in low-quality carbohydrates and saturated fats was protective against the development of MetS.¹¹

Several interventions combine food in the prevention and treatment of MetS and cardiovascular outcomes, including functional foods, such as flaxseed, ginger, and cocoa.¹² The avocado (*Persea americana*) has been highlighted in the literature. This fruit is a cardiovascular risk reducer due to the effect of its bioactive compounds and the presence of good levels of monounsaturated fatty acids (MUFAs), which provide high nutritional value and beneficial health effects, such as hypoglycaemic, antioxidant, hypolipidemic, antihypertensive and anti-obesity effects.⁵

Positive changes in the lipid profile from the peel, seed, pulp and leaves of avocado have been reported.⁵ However, few studies evaluated the effects of pure/virgin oil on the lipid profile in humans with MetS, and studies of the effects on atherogenic indices do not exist. Therefore, the present study evaluated avocado oil supplementation on lipid levels and atherogenic indices in patients with MetS.

MATERIALS AND METHODS

The present study was a 12-week randomised, experimental, double-blind, placebo-controlled clinical trial. Participants were randomly assigned to avocado oil or placebo (soybean oil) supplementation. The levels of MUFAs and polyunsaturated fatty acids (PUFAs) in the avocado oil were determined on a gas chromatograph. The percentages of MUFAs and PUFAs were 48.7% and 40.9%, respectively. Commercial soybean oil (Liza®, Cargill, Mairinque, SP) was used as a control, and its lipid composition was obtained from the product label. The control was composed of 27% MUFAs and 56% PUFAs. No significant concentrations of carbohydrates or fibre were observed in either oil.

Participants were recruited at the outpatient clinics of the University Hospital of the Federal University of Juiz de Fora. Patients of both sexes, aged between 30 and 60 years, with a body mass index (BMI) $> 30 \text{ kg/m}^2$, without evidence of coronary artery disease, who met the criteria for the diagnosis of MetS according to the IDF were included.¹ Participants with fasting blood glucose $> 300 \text{ mg/dL}$, limiting genetic and hormonal disease, alcohol and drug abuse, smoking, pregnancy and lactation, life expectancy < 6 months, renal failure with indication for dialysis, congestive heart failure, previous organ transplantation, use of vitamin/food supplements, exacerbated weight loss in the last 3 months (voluntary or involuntary), use of non-steroidal anti-inflammatory drugs, corticosteroids or immunosuppressants were excluded from the study.

The participants were instructed about the research and underwent clinical anamnesis and nutritional assessment, which consisted of anthropometric, biochemical and dietary assessments. After the interviews and initial assessments, the volunteers blindly ingested a vial of avocado or soy oil (containing 10 mL each) daily and retain their dietary and lifestyle habits. No dietary changes were requested. At the end of the 12-week study period, the subjects underwent clinical anamnesis and anthropometric and biochemical evaluations. Flaconettes of avocado or soy oil were provided each month, and contact was offered to resolve doubts.

For the anthropometric evaluation, measurements of weight (kg), height (m) and waist circumference (cm) were taken, with the participants standing, wearing light clothes without shoes or carrying heavy objects. Weight was measured on a digital scale, with the participant positioned in the centre of the scale, lower limbs parallel, upper limbs at the side of the body and looking at the horizon. Height was measured using a portable stadiometer with a stabiliser, with the participant positioned with feet and heels parallel and shoulders and buttocks touching the equipment. BMI was obtained as the ratio of weight (kg) to height squared (m^2) and classified according to the criteria defined in the current literature.¹³ Waist circumference was measured using an inelastic anthropometric tape at the midpoint between the lower costal bone and anteroposterior iliac crest. The classification was in accordance with the World Health Organization.^{13,14}

For the biochemical evaluation, peripheral blood samples were collected after a 12-hour fast at the Clinical Analysis Laboratory of the University Hospital by a duly trained professional. The laboratory parameters evaluated were TC, HDL-c, LDL-c and TG. Based on these parameters, the Castelli I and II indices were calculated from the CT/HDL-c and LDL-c/HDL-c formulas, respectively. The cut-off values for Castelli I were ≤ 5.1 for men and ≤ 4.4 for women, and the cut-offs for Castelli II were ≤ 3.3 for men and ≤ 2.9 for women.¹⁵ The PAI was calculated by the formula $[\log(\text{TG}/\text{HDL-c})]$, with levels of TG and HDL-c expressed in mg/dL . The classification was -0.3 to 0.1 low cardiovascular risk, 0.1 to 0.24 intermediate risk and > 0.24 high risk.¹⁰

The dietary assessment was performed using the Quantitative Food Frequency Questionnaire (QFFQ) with 67 food items.¹⁶ The QFFQ was applied remotely via Google Meet or telephone call, subject to the limitations of the COVID-19 pandemic. The questionnaire evaluated food consumption based on total calories, percentage of calories from macronutrients according to AMDR (acceptable macronutrient distribution range) and amount of saturated fatty acids, MUFAs and PUFAs in grams, according to the I Brazilian Guideline of MetS.^{17,18}

Statistical analyses were performed using SPSS 21 software, and $p < 0.05$ was considered significant. Descriptive statistics are presented using means, standard deviation, medians, minimum and maximum values, and the difference between the pre- and postintervention periods was evaluated using the Wilcoxon test. ANOVA was performed to verify the possible relationships between the variables.

This study was supported by the Empresa Brasileira de Serviços Hospitalares (EBSERH). The Research Ethics Committee of the Federal University of Juiz de Fora (UFJF) approved the study protocol (opinion number 3.685.349). All participants read and signed the informed consent form.

RESULTS

Thirty-one adults with MetS participated in this study, including 27 females and four males, who were divided into a control group (n=17) and an intervention group (n=14). The control group consisted of 15 female and two male participants, six of whom were obese with grade I classification, two were obese with grade II classification, and nine obese were classified as grade III. The intervention group consisted of 12 female and two male participants, five of whom were classified as grade I obese, six obese were classified as grade II, and three were obese with grade III classification.

Usual food consumption is shown in Table 1. According to AMDR, the control and intervention groups had percentages of lipids that were higher than acceptable and totalled 36.98% for the intervention group and 39.56% for the control group. According to the Brazilian guideline on metabolic syndrome,¹⁸ the control group and intervention group had higher than recommended percentages of saturated fat, which totalled 10.37% for the control group and 12.64% for the intervention group. to the values of other macronutrients and MUFAs and PUFAs were consistent with the recommendations.

For cardiovascular risk classification, the Castelli I, Castelli II and PAI indices were calculated. During the pre-treatment period, 82.35% of the individuals in the control group did not present cardiovascular risk according to Castelli I and II, 5.88% were at risk based on these indices, and 11.76% showed risk via Castelli I but not Castelli II. For PAI, 11.76% were at intermediate risk for cardiovascular events, 5.88% had low risk, and 82.35% had high cardiovascular risk. During the post-treatment period, 82.35% of the individuals in the control group did not present cardiovascular risk according to Castelli I and II, and 17.65% were at risk based on these indices. For post-treatment PAI, 5.88% were at intermediate risk for cardiovascular events, 5.88% had low risk, and 88.23% had high cardiovascular risk.

For the intervention group in the pre-treatment period, 57.14% of the individuals did not present cardiovascular risk according to Castelli I and II, 35.71% were at risk based on these indices, and 7.14% were at risk via Castelli I but not Castelli II. For the PAI, 7.14% had an intermediate risk for cardiovascular events, and 92.86% had a high cardiovascular risk. During the post-treatment period, 42.86% of the individuals did not present cardiovascular risk according to Castelli I and II, 50% were at risk based on these indices, and 7.14% showed risk based on Castelli I but not Castelli II. For the PAI, 100% of the individuals had high cardiovascular risk.

Table 1. Characteristics of food consumption of participants in the control and treatment groups, in mean and standard deviation. Juiz de Fora-MG, 2021

Variables	Soybean oil (n=17)		Avocado oil (n=14)	
	Mean	SD	Mean	SD
Total Kcal	2,053.85	1,327.32	2,016.93	571,15
Protein Kcal	260.12	80.43	338.17	130.38
Carbohydrate Kcal	959.91	368.11	913.64	297.37
Fat Kcal	812.65	1116.29	745.95	230.85
SATURATED	23.67	21.36	28.34	13.21
MUFA	41.50	91.48	25.199	8.24
PUFA	16.52	13.98	17.02	5.77

In addition to atherogenic indices, BMI values, waist circumference and lipid profile parameters were evaluated in both groups (control and intervention) in the pre- and post-treatment periods. These values are shown in Table 2 as means, standard deviation, medians, minimum and maximum values and mean differences between the pre- and post-intervention periods in the control and intervention groups. There was no correlation or significant difference between the pre- and post-intervention periods in any of the variables evaluated in this clinical trial.

Table 2. Mean, standard deviation, median, minimum and maximum values and mean difference between the pre- and post-intervention periods in the control and treatment groups. Juiz de Fora-MG, 2021

Variables	Pre-intervention					Post-intervention					
	Soybean oil (n=17)										
	Mean	SD	Median	Mínimum	Maximun	Mean	SD	Median	Mínimum	Maximun	Mean difference
Weight	100.54	17.06	99.40	72.40	132.70	101.16	17.00	100.90	72.90	130.30	0.62
Height	1.59	0.05	1.60	1.51	1.73	1.59	0.05	1.60	1.51	1.73	0.00
BMI	39.57	6.89	40.53	30.10	51.20	39.83	6.98	41.22	29.30	50.30	0.26
Circumference Abdominal	119.94	14.48	116.00	95.00	144.00	120.50	14.37	119.00	99.00	143.00	0.56
Triglycerides	156.00	81.84	144.00	68.00	336.00	142.17	52.55	138.00	42.00	251.00	-13.83
LDL-cholesterol	109.23	43.04	111.00	48.00	236.00	107.23	39.89	111.00	46.00	197.00	-2.00
HDL-cholesterol	46.70	10.34	48.00	29.00	69.00	46.64	10.12	49.00	29.00	68.00	-0.06
Total cholesterol	187.17	51.79	188.00	101.00	327.00	182.35	48.79	184.00	110.00	296.00	-4.82
Castelli I	4.08	1.05	3.90	2.50	6.30	3.97	0.94	4.10	2.20	5.80	-0.11
Castelli II	2.34	0.77	2.28	1.10	4.50	2.32	0.77	2.31	1.10	3.70	-0.02
PAI	0.48	0.27	0.53	0.00	1.00	0.46	0.24	0.50	-0.20	0.80	-0.02
	Avocado oil (n=14)										
	Mean	SD	Median	Mínimum	Maximun	Mean	SD	Median	Mínimum	Maximun	Mean difference
Weight	102.63	17.03	99.35	81.00	142.00	103.23	17.88	99.40	81.80	146.70	0.60
Height	1.65	0.08	1.63	1.55	1.83	1.65	0.08	1.63	1.55	1.83	0.00
BMI	37.70	5.70	36.72	30.90	52.80	37.93	6.16	36.87	31.20	54.50	0.23
Circumference Abdominal	117.28	12.29	115.00	101.00	146.00	118.78	13.33	115.00	102.00	146.00	1.50
Triglycerides	177.78	102.83	138.50	70.00	379.00	182.21	80.17	152.00	86.00	330.00	4.43
LDL-cholesterol	116.85	31.04	115.50	52.00	154.00	115.85	33.03	109.00	53.00	180.00	-1.00
HDL- cholesterol	44.28	7.55	43.50	31.00	61.00	45.21	7.74	46.00	30.00	55.00	0.93
Total cholesterol	196.64	36.08	195.50	120.00	268.00	197.50	34.24	203.00	127.00	259.00	0.86
Castelli I	4.53	0.99	4.54	2.60	6.1	4.48	1.00	4.65	2.40	5.90	-0.05
Castelli II	2.66	0.68	2.73	1.10	3.80	2.62	0.76	2.92	1.00	3.50	-0.04
PAI	0.55	0.27	0.46	0.20	1.00	0.57	0.22	0.50	0.30	1.00	0.02

BMI: Body Mass Index; PAI: Plasma Atherogenic Index (PAI).

DISCUSSION

The present study evaluated whether avocado oil supplementation improved lipid levels and atherogenic indices in individuals with MetS. The results showed that avocado oil did not improve the lipid profile or atherogenic indices in these patients. Chikwendu et al.¹⁹ fed mice cakes supplemented with 0%, 10%, 30% and 50% avocado for 14 days and showed a decrease in LDL-c and an increase in HDL-c. The cake supplemented with 50% avocado pulp showed the greatest improvement in these parameters. The mice in this study had controlled intake (something more possible in an experimental model), which was not possible with our participants. However, the study does not provide sufficient information to make a comparison of the equivalent of the avocado oil.

The consumption of avocado in natura (1 unit and a half/day) for three weeks by women without an explicit diagnosis decreased TC and LDL-c and preserved HDL-c.²⁰ This effect was also observed in a study with avocado supplementation for two weeks by healthy patients with a calculated diet, in which there was a reduction in TC, LDL-c, and TG and an increase in HDL-c.²¹ For a sample of patients whose disease had been present for some time and who had a large medication overload, perhaps avocado is not sufficient to improve the lipid profile.

The intervention time should also be addressed because the treatment used in this research was prolonged, and most of the studies in the literature used an average time of four weeks with avocado supplementation. Ledesma et al.²² evaluated healthy patients who received avocado for one week. Colquhoun et al.²⁰ evaluated undiagnosed patients who received avocado pulp for three weeks. Alvizouri-Muñoz et al.²¹ evaluated healthy patients with two weeks of avocado supplementation. All studies found satisfactory results for lipid parameters. Pieterse et al.²³ evaluated individuals in free-living conditions who consumed 200 g/day of avocado for six weeks and did not observe improvement in the levels of lipid parameters. Grant²⁴ evaluated patients who consumed up to 1.5 avocados per day for eight weeks and only observed improvement in TC.

The food consumption of the individuals involved is an important variable when developing a clinical trial of a possible nutraceutical. When a specific dietary model is not established or there is no diet control, it becomes difficult to assess the effect of an intervention because there may be interference from the routine diet of each individual. Most studies involving intervention with avocado as a potential lipid-lowering agent established a diet protocol or controlled for this variable. Carranza et al.²⁵ and Alvizouri-Muñoz et al.²¹ used a diet rich in monounsaturated fatty acids, with avocado as the main source of these fats. López Ledesma et al.²² established a diet that calculated the exact amounts of total fat, monounsaturated fat and saturated/unsaturated ratio, and Pieterse et al.²³ used a calorie-restricted diet as a strategy.

The dose and mode of administration of avocado supplementation are not standardised across studies. Grant²⁴ used 0.5-1.5 avocados administered in natura in 16 men for eight weeks and confirmed a reduction of total cholesterol and serum phospholipids. Pieterse et al.²³ used 200 g/day of fresh avocado in a randomised trial of 61 individuals for six weeks on a hypocaloric diet and found no significant changes in the lipid profile. Pahuja-Ramos et al.²⁶ used 2 g/kg/day of avocado paste for seven weeks in rats with a diet rich in fructose, and reported a reduction in TC, LDL-c and TG. Werman et al.²⁷ used avocado seed oil (10% w/w) in rats for four weeks and showed a decrease in TG and hepatic lipogenesis. This variation makes it difficult to establish a therapeutic dose and the best administration route for the supplement and complicates comparisons of the results obtained in this clinical trial with other studies in the literature.

CONCLUSION

Consumption of avocado oil for 12 weeks had no positive effects on the lipid profile or atherogenic indices in patients with MetS compared with soybean oil consumption. Some factors may have been crucial in the results obtained, such as the lack of diet control, high number of medications used by the participants, duration of the intervention and the supplemented dose. Therefore, future studies that pay attention to these methodological issues are needed.

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Contributors

Azevedo ACSF participated in data collection, analysis and interpretation, and in writing the study. Lima MFC and Ramos ELL participated in the idealization of the study design; in the collection, analysis and interpretation of data; in the writing of the study and in the final review and approval of the manuscript for submission. Moreira APB participated in the idealization of the study design and in the final review and approval of the manuscript for submission. Souza CT participated in data collection, analysis and interpretation; participated in the writing of the study; in the final review and approval of the manuscript for submission.

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