Effects of Flaxseed Oil on Serum Lipids and Lipoproteins in Hemodialysis Patients

A Randomized Controlled Trial

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Keywords. flaxseed oil, hemodialysis, lipids, lipoproteins, alpha-linolenic acid

Introduction. One of the major risk factors for cardiovascular disease is lipid abnormalities among hemodialysis patients. The present study was designed to investigate the effects of flaxseed oil consumption on serum lipids and lipoproteins in hemodialysis patients.

Materials and Methods. In a randomized double-blinded controlled trial, 34 hemodialysis patients were assigned to either the flaxseed oil or the control group. The patients in the flaxseed oil group received 6 g/d of flaxseed oil for 8 weeks, whereas the control group received 6 g/d of medium chain triglycerides oil. At baseline and the end of week 8, blood samples were obtained after a 12- to 14-hour fast and serum concentrations of triglyceride, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and lipoprotein(a) were measured.

Results. Serum triglyceride concentration decreased significantly up to 23% in the flaxseed oil group at the end of week 8 compared to baseline, and the reduction was significant in comparison with the medium chain triglycerides oil group ($P < .01$). There were no significant differences between the two groups in the mean changes of serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and lipoprotein(a).

Conclusions. This study indicates that daily consumption of 6 g of flaxseed oil reduces serum triglyceride concentration, which is a risk factor for cardiovascular disease in hemodialysis patients, whereas it has no effects on other lipid parameters, especially lipoprotein(a).

IJKD 2016;10:405-12
www.ijkd.org

Original Paper

INTRODUCTION

The most important cause of mortality in patients with chronic kidney failure, including hemodialysis patients, is cardiovascular disease (CVD).[1,2] A marked increase in CVD incidence and death rate has been reported in dialysis patients as compared with an age-matched general population.[1,2] In hemodialysis patients, one of the major risk factors for CVD is lipid abnormalities, including high serum concentrations of triglyceride, very-low-density lipoprotein cholesterol (VLDLC), lipoprotein(a), and low serum concentration of high-density lipoprotein cholesterol (HDLC).[3–5]

At the present time, blood lipid-normalizing drugs such as statins and fibric acid derivatives are used to treat lipid abnormalities and prevent CVD in hemodialysis patients; however, no effective treatment has been known to reduce lipoprotein(a) in these patients so far.[6]

Flaxseed oil is a rich source of plant omega-3

fatty acid alpha-linolenic acid,[7] and in recent years, 2 studies have demonstrated that flaxseed or flaxseed oil consumption could reduce serum triglyceride, total cholesterol, and low-density lipoprotein cholesterol (LDLC), and increase HDLC in hemodialysis patients,[8,9] but serum lipoprotein(a) has not been measured in these two studies.[8,9] In addition, one study in hypercholesterolemic patients indicated that flaxseed consumption significantly decreased serum lipoprotein(a).[10] However, to our knowledge, no studies to date have examined the effects of flaxseed oil on serum lipoprotein(a) in hemodialysis patients. Considering the scarcity of studies on the effects of flaxseed oil consumption on lipid abnormalities, particularly high serum lipoprotein(a) concentration in hemodialysis patients, this study was designed to investigate the effects of flaxseed oil consumption on serum lipids and lipoproteins in hemodialysis patients.

MATERIALS AND METHODS

Participants

This study was a randomized double-blinded controlled trial performed between December 2014 and March 2015. The minimum sample size estimated for each group was 17 at a power of 80% and type 1 error of 0.05 for a 2-arm parallel study with 2-tailed testing, to detect a difference of 27 mg/dL in serum triglyceride concentration with a pooled standard deviation of 28 mg/dL, obtained from the study by Kontogianni and colleagues.[11]

Thirty-eight hemodialysis patients eligible for this trial were selected from the hemodialysis units at Taleghani Hospital and Modares Hospital in Tehran, Iran. The criteria for inclusion were age of 18 years and greater and being on hemodialysis for at least 6 months. Patients enrolled in this study did not have inflammatory and infectious diseases, and none of them received steroidal or nonsteroidal anti-inflammatory drugs or omega-3 fatty acids supplement. In addition, patients who had regularly used flaxseed or flaxseed oil within 1 month prior to the beginning of the study were excluded. In all cases, hemodialysis was performed with polysulfone capillary dialysis membranes and bicarbonate dialysis solution, 3 times a week, 4 hours per session. During the study, the hemodialysis procedure and type of dialysis membrane were not altered for any of the patients.

The study protocol was approved by the Ethics Committee of the National Nutrition and Food Technology Research Institute of Iran. The study was in adherence with the Declaration of Helsinki. Written informed consent was obtained from all patients before initiating the study. This clinical trial was registered at Iranian Registry of Clinical Trials (IRCT201412192716N3).

Protocol

The patients, after stratification based on diabetes mellitus, were randomly allocated to either a flaxseed oil or control group by block randomization. For this block randomization, we chose a block size of 4, and possible balanced combinations with 2 C (control) and 2 F (flaxseed) subjects were calculated as 6 blocks (FFCC, FCFC, FCCF, CFFC, CFCF, CCFF). Then, blocks were randomly chosen, based on a simple random sampling method, to determine the assignment of all patients into the groups. The block randomization was performed by a trained dietician. Patients in the flaxseed oil group received 7 mL/d (or 6 g/d) of flaxseed oil, as 1 Iranian tablespoon of flaxseed oil, for a period of 8 weeks, whereas the control group received 7 mL/d (or 6 g/d) of medium chain triglycerides (MCT) oil. The participants consumed oils with salad at lunch or dinner. The flaxseed oil was provided by Barij Essence Company (Tehran, Iran), and MCT oil was provided by the SHS International Ltd Company (Liverpool, UK). The flaxseed oil had 57.5% alpha-linolenic acid, 17.2% oleic acid, 15.2% linoleic acid, 5.1% palmitic acid, 4% stearic acid, and 1% other fatty acids, whereas MCT oil contained 59.4% caprylic acid, 39.6% capric acid, 0.7% caproic acid, 0.2% lauric acid, and 0.1% myristic acid. The oils were provided in similar dark bottles without any indication of whether the bottle contained flaxseed oil or MCT oil. The taste of flaxseed oil was different from MCT oil, but none of hemodialysis patients had used flaxseed oil or MCT oil before the start of this study and therefore they did not have any experience of the taste of flaxseed oil or MCT oil.

Blinding was performed by a trained dietician, and the patients and researchers were kept blinded to the allocation. The participants were advised not to change their dietary habits, physical activities, and drug regimens. In addition, the study protocol did not change after the trial was commenced. At baseline and the end of the 8th week, 7 mL of

blood was obtained from each patient after a 12- to 14-hour fast. Blood samples were kept at room temperature (20°C to 25°C) for 20 minutes. After clotting, the samples were centrifuged at 2000 rpm for 10 minutes. The samples of serum were separated into small aliquots and were frozen at -70°C, until they were used.

Measurements

The primary outcomes were serum triglyceride, total cholesterol, HDLC, LDLC, and lipoprotein(a). Serum concentrations of triglyceride, total cholesterol, HDLC, creatinine, and urea were assessed using various colorimetry methods by commercial kits (Pars Azemoon, Tehran, Iran) with the aid of a Selectra 2 Autoanalyzer (Vital Scientific, Spankeren, The Netherlands). Intra-assay coefficients of variation for serum triglyceride, total cholesterol, HDLC, creatinine, and urea were less than 3%. As serum triglyceride concentration in all participating patients was less than 400 mg/dL, serum LDLC was estimated using the Friedwald equation.[12]

The participants were weighed after hemodialysis, to determine dry body weight (or postdialysis weight), at baseline and at the end of weeks 4 and 8. In addition, the dietary intakes of the participants were assessed using a 2-day dietary recall (1 dialysis day and 1 nondialysis day) in weeks 1, 4, and 8. Patients' diets were analyzed by Nutritionist IV software (N Squared Computing, San Bruno, CA, USA).

At baseline and the end of week 8, dialysis adequacy based on KT/V index was determined for each patient by a KT/V calculator software using information recorded in patient files, including predialysis blood urea nitrogen concentration, postdialysis blood urea nitrogen, the dialysis session length, postdialysis weight, and ultrafiltration volume.[13]

Adherence

For the ascertainment of patients' adherence, we provided each patient with a fixed volume of oils and instructions to return the unused oils at the end of the study. The degree of adherence for each patient was determined according to the volume of returned oils. The adherence of all patients was more than 90 % and no adverse events were reported.

Statistical Analysis

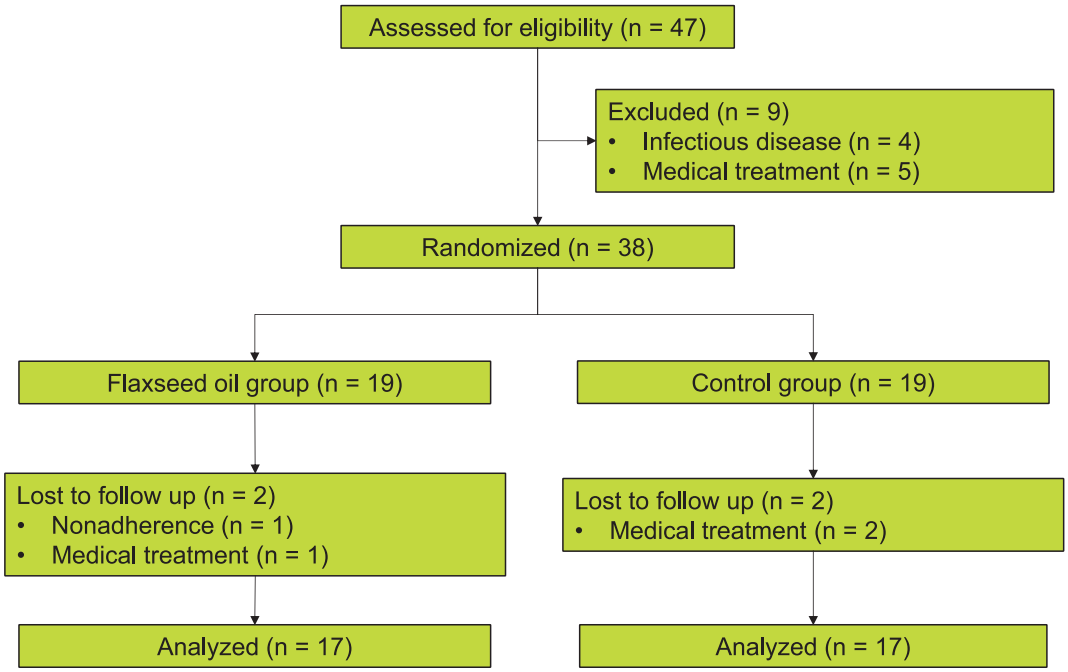
Statistical analysis of data was performed using the SPSS software (Statistical Package for the Social Sciences, version 20.0, SPSS Inc, Chicago, IL, USA). The chi-square test was used to compare qualitative variables between the two groups. Since all quantitative parameters had normal distributions according to the Kolmogorov-Smirnov test, we used the *t* test and paired *t* test to compare parameters between and within groups, respectively. In addition, because dietary and anthropometric parameters were measured 3 times during the study, the analysis of variance for repeated measurements was used to compare data among these time points. The results are expressed as mean ± standard error. Differences were considered significant at a *P* value less than .05.

RESULTS

Of the 38 hemodialysis patients eligible for this trial, 2 in the flaxseed oil group and 2 in the MCT oil group were withdrawn because of nonadherence or medical treatments (Figure). No adverse events were reported. The baseline characteristics of the patients did not differ significantly between the two groups (Table 1). There was no significant difference in dialysis adequacy between the two groups at baseline and the end of week 8 (Table 1).

There were no significant differences in the mean dietary intake of energy, protein, carbohydrate, fiber, total fat, monounsaturated fatty acids, ω6-polyunsaturated fatty acids, cholesterol, vitamin E, and vitamin C between the two groups at weeks 1, 4, and 8. In addition, these factors did not significantly change within each group during the study (Table 2). The mean dietary intake of saturated fatty acids was significantly higher in the MCT oil group compared with the flaxseed oil group at weeks 1 and 4 (Table 2); whereas, the mean dietary intake of ω3-polyunsaturated fatty acids was significantly higher in the flaxseed oil group compared with the MCT oil group at weeks 1, 4, and 8 (Table 2).

Serum triglyceride concentration reduced significantly in the flaxseed oil group at the end of week 8 compared to baseline, whereas no significant change was observed in the MCT oil group. The reduction of serum triglyceride concentration in the flaxseed oil group was significant in comparison



Summary of the study flow diagram.

with the MCT oil group (Table 3).

No significant changes were observed in serum total cholesterol, LDLC, HDLC, and lipoprotein(a) within each group during the study (Table 3).

DISCUSSION

Hypertriglyceridemia is one of the most common lipid abnormalities in hemodialysis patients.[3,5] In our study, at baseline, approximately 32% of hemodialysis patients had serum triglyceride levels higher than normal (≥ 150 mg/dL according to the

Table 1. Baseline Characteristics of Patients in the Flaxseed Oil Group and the Medium Chain Triglycerides (MCT) Oil Group*

Characteristics	Flaxseed Oil Group (n = 17)	MCT Oil Group (n = 17)
Age, y	68.0 ± 3.0	59.0 ± 4.0
Duration of dialysis, y	4.4 ± 1.0	4.6 ± 1.0
Serum urea, mg/dL	144.0 ± 10.0	129.0 ± 7.0
Serum creatinine, mg/dL	10.0 ± 0.7	9.5 ± 0.4
Sex		
Male	12 (71.0)	10 (59.0)
Female	5 (29.0)	7 (41.0)
Smokers	3 (18.0)	3 (18.0)
Diabetes	5 (29.0)	4 (23.5)
Intake of supplements		
Vitamin E	8 (47.0)	5 (29.0)
Vitamin C	8 (47.0)	4 (23.5)
L-carnitine	2 (12.0)	2 (12.0)
Intake of drugs		
Gemfibrozil	0 (0.0)	0 (0.0)
Atorvastatin	5 (29.0)	6 (35.0)
Dialysis adequacy (KT/V)		
Baseline	1.2 ± 0.1	1.3 ± 0.1
Week 8	1.3 ± 0.1	1.2 ± 0.1

*Values are mean ± standard error or frequency (percentage).

Table 2. Anthropometric and Dietary Factors in the Flaxseed Oil Group and the Medium Chain Triglycerides (MCT) Oil Group*

Factors	Week 1	Week 4	Week 8
Weight, kg			
Flaxseed oil group	70.0 ± 3.0	71.0 ± 3.0	71.0 ± 3.0
MCT oil group	63.0 ± 3.0	63.0 ± 3.0	63.0 ± 3.0
BMI, kg/m^2			
Flaxseed oil group	26.0 ± 1.0	26.5 ± 1.0	26.5 ± 1.0
MCT oil group	25.0 ± 1.5	25.0 ± 1.5	25.0 ± 1.5
Energy, kcal/d			
Flaxseed oil group	1372.0 ± 86.0	1365.0 ± 86.0	1405.0 ± 112.0
MCT oil group	1483.0 ± 91.0	1495.0 ± 88.0	1340.0 ± 166.0
Protein, g/d			
Flaxseed oil group	54.0 ± 5.0	56.0 ± 5.0	63.0 ± 4.0
MCT oil group	55.0 ± 4.0	59.0 ± 5.0	58.0 ± 8.0
Carbohydrate, g/d			
Flaxseed oil group	183.0 ± 15.0	177.0 ± 13.0	162.0 ± 14.0
MCT oil group	206.0 ± 13.0	205.0 ± 12.0	166.0 ± 24.0
Fiber, g/d			
Flaxseed oil group	9.0 ± 1.0	9.0 ± 1.0	8.0 ± 1.0
MCT oil group	10.0 ± 1.0	10.0 ± 1.0	7.0 ± 1.0
Fat, g/d			
Flaxseed oil group	48.0 ± 2.0	49.0 ± 4.0	56.0 ± 8.0
MCT oil group	49.0 ± 4.0	50.0 ± 5.0	49.5 ± 6.0
SAFA, g/d			
Flaxseed oil group	14.0 ± 1.0	15.5 ± 2	20.0 ± 4.0
MCT oil group	20.0 ± 1.5†	23.0 ± 2.0†	23.0 ± 3.0
MUFA, g/d			
Flaxseed oil group	17.0 ± 1.0	17.0 ± 1.5	21.0 ± 3.5
MCT oil group	16.5 ± 1.5	16.5 ± 2.0	16.0 ± 2.0
ω6-PUFA, g/d			
Flaxseed oil group	8.6 ± 0.6	8.5 ± 0.9	8.5 ± 1.4
MCT oil group	9.0 ± 0.9	7.6 ± 0.9	7.3 ± 1.0
ω3-PUFA, g/d			
Flaxseed oil group	4.0 ± 0.05‡	4.2 ± 0.09‡	4.0 ± 0.09‡
MCT oil group	0.6 ± 0.09	0.7 ± 0.12	0.4 ± 0.06
Cholesterol, mg/d			
Flaxseed oil group	192.0 ± 26.0	217.0 ± 33.0	257.0 ± 43.0
MCT oil group	146.0 ± 21.0	162.0 ± 24.0	200.0 ± 29.0
Vitamin E, mg/d			
Flaxseed oil group	10.0 ± 2.0	9.0 ± 1.0	8.0 ± 1.5
MCT oil group	10.0 ± 0.1	7.5 ± 1.0	8.0 ± 1.0
Vitamin C, mg/d			
Flaxseed oil group	38.5 ± 8.0	32.0 ± 4.0	35.0 ± 8.0
MCT oil group	47.0 ± 10.0	44.0 ± 7.0	49.0 ± 10.0

*Values are mean ± standard error.
†P < .05 versus the flaxseed oil group
‡P < .01 versus the MCT oil group
BMI indicates body mass index; SAFA, saturated fatty acids; MUFA, monounsaturated fatty acids; ω6-PUFA, ω6-polyunsaturated fatty acids; and ω3-PUFA, ω3-polyunsaturated fatty acids.

National Cholesterol Education Program criteria).[14]

In our study, daily consumption of 6 g of flaxseed oil, a rich source of plant omega-3 fatty acid alpha-linolenic acid, significantly reduced serum triglyceride concentrations up to 23% during 8 weeks. To our knowledge, few studies have examined the effects of flaxseed or flaxseed oil on serum triglyceride concentration in hemodialysis patients. In agreement with our study, Lemos and coworkers showed that daily consumption of 2 g of flaxseed oil for 3 months reduced serum triglyceride in hemodialysis patients and this reduction was

Table 3. Serum Concentrations of Lipids and Lipoproteins in the Flaxseed Oil Group and the Medium Chain Triglycerides (MCT) Oil Group*

Parameters	Baseline	Week 8	Change
Triglyceride, mg/dL			
Flaxseed oil group	183 ± 38	141 ± 25†	-42 ± 18‡
MCT oil group	122 ± 16	144 ± 17	22 ± 8
Total cholesterol, mg/dL			
Flaxseed oil group	140 ± 9	145 ± 12	5 ± 7
MCT oil group	152 ± 9	159 ± 11	7 ± 6
LDLC, mg/dL			
Flaxseed oil group	73 ± 7	76 ± 10	3 ± 7
MCT oil group	87 ± 7	89 ± 9	2 ± 5
HDLC, mg/dL			
Flaxseed oil group	35 ± 2	38 ± 2	3 ± 2
MCT oil group	41 ± 2	42 ± 2	1 ± 3
Lipoprotein(a), mg/dL			
Flaxseed oil group	29 ± 2#	27 ± 1	-2 ± 2
MCT oil group	22 ± 2	24 ± 2	2 ± 1

*Values are mean ± standard error.
†$P < .05$ versus baseline
‡$P < .01$ versus the MCT oil group
#$P < .05$ versus the MCT oil group
LDLC indicates low-density lipoprotein cholesterol and HDLC, high-density lipoprotein cholesterol.

marginally significant.[8] Khalatbari-Soltani and colleagues indicated that the consumption of 40 g/d of ground flaxseed, for 8 weeks, significantly decreased serum triglyceride in hemodialysis patients.[9] In addition, Devarshi and coworkers showed that flaxseed oil consumption reduced serum triglyceride in diabetic rats.[15] In contrast, Bloedon and colleagues indicated that daily consumption of baked products containing 40 g of ground flaxseed, for 10 weeks, did not change serum triglyceride concentration in hypercholesterolemic patients.[10] Also, some animal studies showed that flaxseed oil consumption had no effect on serum triglyceride concentration.[16,17] These contradictory findings may be due to the baseline serum triglyceride concentration, the duration and the amount of flaxseed, or flaxseed oil consumption.

It has been shown that omega-3 fatty acids, including alpha-linolenic acid, inhibit hepatic synthesis of fatty acids and triglycerides by suppressing gene expression of sterol regulatory element-binding proteins and consequently gene expression of enzymes involved in fatty acid synthesis, which are acetyl-coenzyme A carboxylase and fatty acid synthetase complex.[18-20] In addition, omega-3 fatty acids increase β-oxidation of fatty acids and consequently decrease the synthesis of triglycerides by upregulating the key transcription factor peroxisome proliferator-activated receptor-α.[15]

In our study, flaxseed oil consumption had no significant effects on serum total cholesterol and LDLC. In agreement with these findings, some studies showed that flaxseed oil consumption caused no changes in serum total cholesterol and LDLC.[15-17, 21] In contrast, some other studies have indicated that flaxseed or flaxseed oil reduces serum concentrations of total cholesterol and/or LDLC.[8-11,21,22] In our study, the majority of hemodialysis patients had serum total cholesterol and LDLC within the normal ranges; therefore, we cannot expect flaxseed oil consumption to reduce serum total cholesterol and LDLC in these patients.

In hemodialysis patients, serum HDLC concentration is lower than the normal range.[4,5] In our study, at baseline, mean serum HDLC concentration was 35 mg/dL and 41 mg/dL in the flaxseed oil and control groups, respectively. Low serum HDLC concentration in hemodialysis patients may be due to decreased activities of lipoprotein lipase, hepatic lipase, lecithin-cholesterol acyl transferase, and reduced synthesis of apoprotein AI.[4,5] In our study, flaxseed oil consumption did not affect serum HDLC. In agreement with this finding, most previous studies have shown that flaxseed oil consumption causes no change in serum HDLC.[8,11,16,17,21,22] In contrast, few studies have indicated that flaxseed or flaxseed oil increases serum HDLC.[9,10,15] These contradictory findings may be due to the baseline serum HDLC, the duration and the amount of flaxseed or flaxseed oil consumption.

Hyperlipoprotein(a) is a common lipid disorder in hemodialysis patients. [3,5] Serum lipoprotein(a) concentration higher than 30 mg/dL constitutes a major risk factor for CVD.[23] Hyperlipoprotein(a) in hemodialysis patients may be due to increased hepatic synthesis of lipoprotein(a) following loss of amino acids through hemodialysis.[24,25] In our study, flaxseed oil consumption had no significant effect on serum lipoprotein(a). We found no study on the effects of flaxseed oil consumption on serum lipoprotein(a), in hemodialysis patients, to compare with the results of our study. However, Bloedon and associates indicated that daily consumption of baked products containing 40 g of ground flaxseed, for 10 weeks, significantly decreased serum lipoprotein(a) in hypercholesterolemic patients.[10] The disagreement of Bloedon and

associates' finding with that of our study may be due to the consumption of ground flaxseed instead of flaxseed oil. Flaxseed, but not flaxseed oil, is the richest known source of lignans, a class of phytoestrogens.[10,26] It has been shown that estrogen may reduce serum lipoprotein(a) by 20% and therefore flaxseed phytoestrogens may have a role similar to that of estrogen in reducing serum lipoprotein(a).[27]

The most important strength of our study was its design as a randomized controlled trial. We did not measure serum concentrations of apoproteins (such as apoproteins AI and B100), and this was a limitation of our study.

CONCLUSIONS

This study indicates that daily consumption of 6 g of flaxseed oil reduces serum triglyceride concentration, which is a risk factor for CVD in hemodialysis patients, whereas it has no effects on other lipid parameters especially lipoprotein(a).

ACKNOWLEDGMENTS

The authors thank the staff of the Hemodialysis Units at Taleghani Hospital and Modares Hospital in Tehran, Iran, for their invaluable assistance, and the staff of the research laboratory of the Research Institute for Endocrine Sciences and the Nutrition Research Laboratory of the Faculty of Nutrition and Food Technology for their technical assistance.

FINANCIAL SUPPORT

This study was supported by the National Nutrition and Food Technology Research Institute of Iran.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Bravo-Jaimes K, Whittembury A, Santivañez V. High Prevalence of Cardiovascular Disease in End-Stage Kidney Disease Patients Ongoing Hemodialysis in Peru: Why Should We Care About It? Int J Nephrol. 2015; 2015:568702.
2. Coric A, Resic H, Celik D, et al. Mortality in hemodialysis patients over 65 years of age. Mater Sociomed. 2015; 27:91-4.
3. Pandya V, Rao A, Chaudhary K. Lipid abnormalities in kidney disease and management strategies. World J Nephrol. 2015;4:83-91.
4. Vaziri ND. Altered lipid metabolism and serum lipids in kidney disease and kidney failure. In: Kopple JD, Massry SG, Kalantar-zadeh K, editors. Nutritional management of renal disease. 3rd ed. Amsterdam: Academic Press; 2013. p. 31-48.
5. Cheung AK. Is lipid control necessary in hemodialysis patients? Clin J Am Soc Nephrol. 2009;4 Suppl 1:S95-101.
6. Wanner C. Altered lipid metabolism and serum lipids in renal disease and renal failure. In: Kopple JD, Massary SG, editors. Kopple and Massary's nutritional management of renal disease. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 42-55.
7. Bloedon LT, Szapary PO. Flaxseed and cardiovascular risk. Nutr Rev. 2004;62:18-27.
8. Lemos JR, de Alencastro MG, Konrath AV, Cargnin M, Manfro RC. Flaxseed oil supplementation decreases C-reactive protein levels in chronic hemodialysis patients. Nutr Res. 2012;32:921-27.
9. Khalatbari Soltani S, Jamaluddin R, Tabibi H, et al. Effects of flaxseed consumption on systemic inflammation and serum lipid profile in hemodialysis patients with lipid abnormalities. Hemodial Int. 2013;17:275-81.
10. Bloedon LT, Balikai S, Chittams J, et al. Flaxseed and cardiovascular risk factors: results from a double blind, randomized, controlled clinical trial. J Am Coll Nutr. 2008;27:65-74.
11. Kontogianni MD, Vlassopoulos A, Gatzieva A, et al. Flaxseed oil does not affect inflammatory markers and lipid profile compared to olive oil, in young, healthy, normal weight adults. Metabolism. 2013;62:686-93.
12. Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of Low- density lipoprotein cholesterol in plasma without use of the preparation ultracentrifuge. Clin Chem. 1972;18:499-502.
13. Daugirdas JT, Stone JCV. Physiologic principles and urea kinetic modeling. In: Daugirdas JT, Blake PG, Ing TS, editors. Handbook of dialysis. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 15-45.
14. Raymond JL, Couch SC. Medical nutrition therapy for cardiovascular disease. In: Mahan LK, Escott-Stump S, Raymond JL, editors. Krause's food and the nutrition care process. 13th ed. Missouri: Elsevier/Saunders; 2012. p. 746.
15. Devarshi PP, Jangale NM, Ghule AE, Bodhankar SL, Harsulkar AM. Beneficial effects of flaxseed oil and fish oil diet are through modulation of different hepatic genes involved in lipid metabolism in streptozotocin-nicotinamide induced diabetic rats. Genes Nutr. 2013;8:329-42.
16. Lee P, Prasad K. Effects of flaxseed oil on serum lipids and atherosclerosis in hypercholesterolemic rabbits. J Cardiovasc Pharmacol Ther. 2003;8:227-35.
17. Rosa DD, Sales RL, Moraes LFS, et al. Flaxseed, olive and fish oil influence plasmatic lipids, lymphocyte migration and morphometry of the intestinal of Wistar rats. Acta Cir Bras. 2010;25:275-80.
18. Jump DB, Botolin D, Wang Y, Xu J, Christian B, Demeure O. Fatty acid regulation of hepatic gene transcription. J Nutr. 2005;135:2503-6.
19. Foretz M, Guichard C, Ferre P, Foufelle F. Sterol

regulatory element binding protein-1c is a major mediator of insulin action on the hepatic expression of glucokinase and lipogenesisrelated genes. Proc Natl Acad Sci U S A. 1999;96:12737-42.

20. Shimano H, Yahagi N, Amemiya-Kudo M, et al. Sterol regulatory element-binding protein-1 as a key transcription factor for nutritional induction of lipogenic enzyme genes. J Biol Chem. 1999;274:35832-9.
21. Akpolat M, Kanter M, Topcu-Tarladacalisir Y, Aydogdu N. Protective effect of flaxseed oil on renal injury in hyperlipidaemic rats: the effect of flaxseed oil on hyperlipidaemia. Phytother Res. 2011;25:796-802.
22. Gillingham LG, Gustafson JA, Han SY, Jassal DS, Jones PJ. High-oleic rapeseed (canola) and flaxseed oil modulate serum lipids and inflammatory biomarkers in hypercholesterolaemic subjects. Br J Nutr. 2011;105:417-27.
23. Superko HR. Did grandma give you heart disease? The new battle against coronary artery disease. Am J Cardiol. 1998;82:34Q-46Q.
24. Enkhmaa B, Anuurad E, Berglund L. Lipoprotein (a): Impact by ethnicity, environmental and medical conditions. J Lipid Res. 2016;57:1111-25.
25. Yang WS, Kim SB, Min WK, Park S, Lee MS, Park JS. Atherogenic lipid profile and lipoprotein(a) in relation to serum albumin in haemodialysis patients. Nephrol Dial Transplant. 1995;10:1668-71.
26. Ingram AJ, Parbtani A, Clark WF, et al. Effects of flaxseed and flax oil diets in a rat-5/6 renalablation model. Am J Kidney Dis. 1995;25:320-9.
27. Su W, Campos H, Judge H, Walsh BW, Sacks FM. Metabolism of Apo (a) and ApoB100 of lipoprotein (a) in women: effect of postmenopausal estrogen replacement. J Clin Endocrinol Metab. 1998;83:3267-76.

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Received April 2016
Revised May 2016
Accepted May 2016