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HEMODIALYSIS-ASSOCIATED DYSLIPIDEMIA: EFFECT OF VIRGIN ARGANE OIL CONSUMPTION

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AUTHORS' CONTRIBUTIONS
This work was carried out in collaboration between all authors. Author FZB managed patients and collected all the data. Author TSH designed the study and revised the manuscript. Authors KAS, HA, SD, KAB and MA managed patients. Author ME designed the protocol, wrote the manuscript, did statistical data analysis and coordinated the study. All authors read and approved the final manuscript.

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ABSTRACT

Background and Aims: Most Hemodialysis patients suffer from dyslipidemia-associated cardiovascular events. Targeting blood lipids with Virgin Argane Oil consumption as a lipid-modulatory mean is the scope of the present study.
Methods: Among 86 patients of our hemodialysis facility, 47 patients were eligible and were randomly assigned to either control group or to Argane Oil consumption group during 5 weeks study. Clinical and blood biochemistry exams were obtained before and after Argane Oil consumption.
Results: Most hemodialysis patients included in the present study have dyslipidemia. They have, respectively, 95.55%, 51.11% and 53.33%, low blood levels of HDLc, high triglycerides and high LDLc blood levels. Furthermore, between 79.54% and 89.47% of patients have high lipid atherogenic incides. When compared to control group of patients, those who were on Argane Oil treatement for five weeks experienced a statistically significant decrease of LDLc and apolipoprotein B, and an increase of HDLc. Furthermore, when compared to control group, argane oil consumption induced an important and statistically significant decrease of all lipid atherogenic indices.
Conclusion: Consumption of Virgin Argane oil is safe and efficient to positively modulate blood lipids in hemodialysis patients with dyslipidemia. Results of the present clinical study support the daily consumption of Virgin Argane Oil as a practical application against dyslipidemia-associated cardiovascular and cerebrovascular complications.

Keywords: Hemodialysis; LDLc; HDLc; virgin argane oil.

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ABBREVIATIONS

HD: Hemodialysis; BMI: Body Mass Index.

1. INTRODUCTION

HD patients suffer from heavy brain and cardiovascular events [1,2] that cause high mortality and morbidity. The latters are associated with several risk factors such as dyslipidemia, hyperglycemia and hypertension, which are added to the general inflammatory state and malnutrition [3,4] usually found in hemodialysis patients. Many clinical studies have shown that HD patients have abnormal lipid and lipoproteins status [5,6] that play an important role in atheroma formation and cardiovascular events. On the other hand, generation of oxidized LDLc and HDLc is a key factor in plaque formation [7]. Hence, targeting dyslipidemia in HD patients is one of the therapeutic strategies toward reducing cardiovascular events. Statins are among those drugs that interfere with cholesterol metabolism and lipoprotein's synthesis [8,9]. Other therapeutic strategies are based on dietary interventions, and some of them were studied in HD patients such as anti-oxidants [10] and omega-3 polyunsaturated fatty acids [11] which proved to be able to manage dyslipidemia in cardiovascular protection [12]. In the last two decades, quality of hemodialysis process was ameliorated by introducing new brands of biocompatible dialysis membranes [13,14] and high quality dialysis water [15]. Despite these improvements, HD patients with dyslipidemia are at high risk for cardiovascular and brain events. Virgin Argane Oil (VAO) is known in Moroccan traditional medicine as an effective therapeutic tool in many health conditions such as skin and osteoarthritis issues [16]. It is believed that consumption of VAO has beneficial effects on human health through its capacity to improve cholesterol metabolism and to enrich the human body with anti-oxidant molecules [17,18], as VAO is rich in oleic and linoleic acids, tocopherols, sterols and polyphenol molecules [19,20]. VAO is extracted from nuts of Argania spinosa, an endemic tree of south eastern Morocco. The rational of our current clinical study, is that VAO as a lipid modulator, it could benefit to patients who have abnormal lipid status. In a concomitant clinical study on a another group of HD patients, we have found that consumption of VAO could improve anti-oxidant status and HDLc levels [18].

2. PATIENTS AND METHODS

Our prospective study (january or april 2013) included 86 HD patients, who were 18 years old or over. Patients signed an informed consent and the study was approved by a local ethic committee at our university hospital. Inclusion criteria of patients were as follow: HD therapy more than six months, patients aged 18 years or older, and a constant blood volume. Exclusion criteria were as follow: infectious episodes over 15 days previously to the study; smoking habit, patients under insulin, anti-oxidants or under lipid lowering therapy during the last six months before starting the study, and malnourished patients (blood albumin below 35 g/L and BMI below 18.5 Kg / m^2). Patients were considered to have dyslipidemia, when they have one of the following levels of blood lipids: total cholesterol levels above 4.78 mmol/L, triglyceride levels above 1.69 mmom/L, LDLc levels above 2.39 mmo/L and HDLc levels below 0.96 mmol/L. Three weeks after beginning the study, two patients from VAO group were excluded from the study (One sudden death, and one acute coronary syndrome). Clinical and biologic data of patients were obtained before and after five weeks of VAO consumption (30 ml every morning at breakfast).

Blood samples: Venous blood was collected after 12 h of fasting. Blood lipids: total cholesterol, TG, high-density lipoproteins (HDL) and low-density lipoproteins (LDL) were analyzed using fresh blood samples. LDL levels were calculated using Fridewald's formula. Other blood assays were of routine procedures. Blood analysis were performed at the Central Laboratory of Hassan II University Hospital of Fez.

Hemodialysis: Patients received three dialysis sessions per week, using Helixon® (Fx8) dialysis membrane (Fresenius Medical Care). Bicarbonate buffer was used, pompe flow rate was set at more than 300 ml /min (Kt/V above 1.2), and used sodium heparin as anti-coagulant.

Body fat tissue and body fluids contents were determined with the technique of body bioimpedance spectroscopy using a "Body Composition Monitor" apparatus from Fresenius Medical Care.

VAO was purchased from women cooperative of VAO production in the southwest of Morocco, with a main composition as follows: oleic acid (47%), linoleic acid (32%) and tocopherols (44 mg / 100 g).

2.1 Statistical Analysis

Data (mean ± S.D) were analyzed with Office Excel (2003) and SPSS (IBM categories Mai 2010) using ANOVA one factor, Paired t-test was used to compare data of each group before and after argane oil consumption period.

3. RESULTS

According to our inclusion and exclusion criteria, 47 patients of our HD center (mean age 49.44±14 years., sex ratio (M/W: 0.55) were enrolled in the study and were randomly assigned to either a control group (without any treatment) or to a group that received VAO for every morning consumption during five weeks (Fig. 1).

Age distribution and cause of nephropathy are shown in Fig. 2.

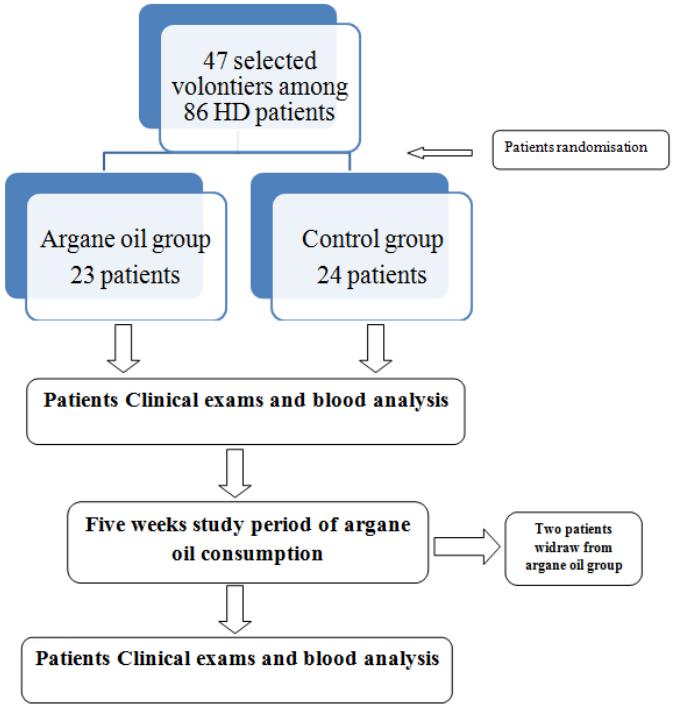

Fig. 1. Flow chart of argane oil study in hemodialysis patients

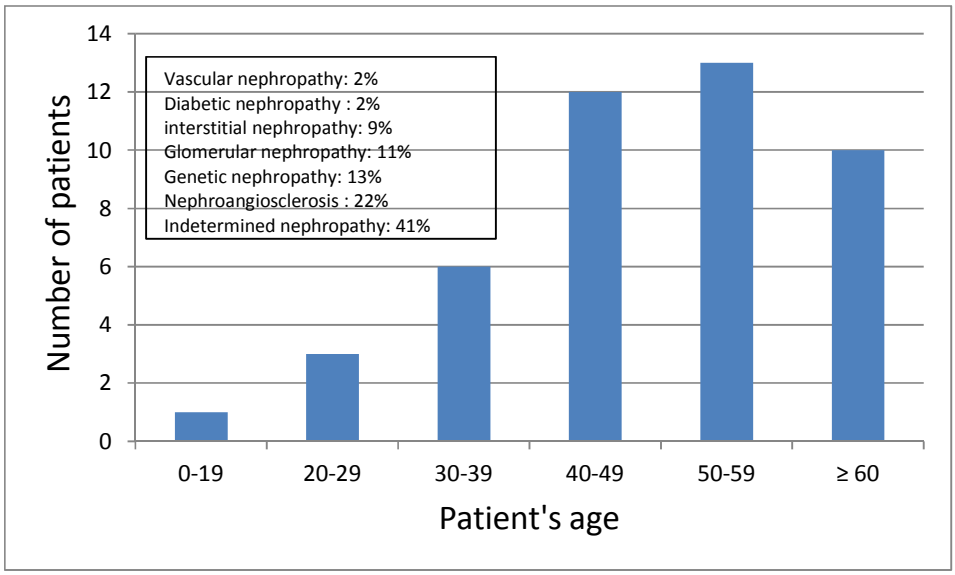

Fig. 2. Age distribution and type of nephropathy (boxed text) in the VAO study on hemodialysis patients

Clinical characteristics of patients are shown in Table 1, and biological characteristics of patients are shown in Table 2. Upon randomisation of patients to be included in control or in argane oil group, and following clinical exams and determination of blood biological parameters of patients, comparison of the data (mean ± SD and p values) showed no statistically significant difference between control and argane oil group of patients, as shown in Tables 1 and 2.

Lipid profiles of all patients as well as those of control and VAO group are shown in Table 3. Comparison of the data (mean ± SD and p values) showed no statistically significant difference between control and argane oil group of patients, as shown in Table 3.

95.55% of the 47 patients of our study have hypo HDLc levels (less than 0.96 mmol/L), 51.11% of them have hyper TG levels (above 1.69 mmol/L) and 53.33% of them have hyper LDLc levels (above 2.39 mmol/L). When we considered the following atherogenic indices Cholesterol/HDL, TG/HDL and LDL/HDL above 5, 3.75 and 2.5 respectively, as higher limits, we found that 84% of our population study has higher cholesterol/HDL ratio, 89.47% of it has higher TG/HDL ratio, and 79.54% of it has higher LDL/HDL ratio. From the above data, our HD patients enrolled in the present study can be considered as mostly dyslipidemic.

Upon five weeks of VAO treatment (Table 4), there was a significant decrease of LDLc in VAO group (from 2.57±0.84 to 2.18±0.62 mmol/L, p=0.001). VAO group experienced a significant and more important increase of HDL levels when compared to control group (Table 4). Lipoprotein B levels decreased significantly mainly in VAO group, however, the most important and significant changes were found in the atherogenic indices (Table 4), where all of them went towards lower trends (Table 4) mainly in the VAO group compared to control group. A little but a non significant decrease of total cholesterol and triglyceride levels were also observed in VAO group.

Blood pressure and BMI of patients were not significantly modified upon the five weeks study period of argane oil study (Table 5).

Table 1. Clinical characteristics of patients of argane oil study. Data of patients of control group and argane oil group were compared and p value are given in the table

	Study population	Control group	Arganeoil group	p value
Sex (M/W)	16/29	11/13	5/16	
Age (years)	49.44±14.58 (18 to 82 years)	49.87±14.12 (18 to 82 years)	48.95±15.42 (22 to 66 years)	0.835
Weight (Kg)	60.95±11.16	63.43±11.61	58.23±10.23	0.124
Years on hemodialysis therapy	7.84±4.46 (1 to 21 years)	7.70±4.42 (1 to 21 years)	8.23±4.63 (1 to 16 years)	0.698
BMI (Kg/m2)	23.12±4.36	23.71±4.14	22.47±4.58	0.350
Mid-upper arm circumference (cm)	25.57±3.73	25.75±3.65	25.38±3.91	0.745
Calf circumference (cm)	28.80±4.41	29.31±4.06	28.21±4.81	0.409
Waist circumference (cm)	92.04±10.83	94.45±8.94	89.28±12.29	0.110
SBP (mmHg)	126.62±19.38	127.45±17.19	125.66±22.02	0.765
DBP (mmHg)	78.71±11.22	79.45±9.03	77.85±13.48	0.647
Cardiothoracic ratio	0.512±0.049	0.502±0.046	0.524±0.052	0.137
Fat tissue Impedance (%)	27.70±8.19	29.67±6.43	26.15±9.13	0.165
Non fat hydric tissue Impedance (%)	59.79±5.83	61.05±4.64	58.33±6.78	0.128

Table 2. Biologic characteristics of patients of argane oil study. Data of patients of control group and argane oil group were compared and p values are given in the table

	Study population	Control group	Arganeoil group	p value
Urea (mmol/L)	45.34±13.92	48.91±0.39	41.05±13.20	0.065
Creatinine (micromol/L)	899.11±234.61	961.70±226.74	855.71±192.71	0.101
Uric acid (micromol/L)	365.56±69.11	383.11±75.24	345.51±56.68	0.063
Albumine (g/L)	37.06±3.43	36.75±3.05	37.41±3.87	0.527
Alkali reserve (mmoL/L)	21.50±3.55	21.16±4.09	21.90±2.82	0.487
Parathormone (ng/L)	1123.3±803.4	1183.20±922.9	1054.89±656.66	0.590

Table 3. Blood lipid profil and atherogenic ratios of patients of argane oil study. Data of patients of control group and argane oil group were compared and p values are given in the table

	Study population	Control group	Arganeoil group	p value
Cholesterol (mmol/L)	4.23±0.77	4.22±0.77	4.22±0.77	0.956
Triglycerides (mmol/L)	2.00±0.77	2.05±0.70	1.94±0.85	0.622
LDLc (mmol/L)	2.53±0.75	2.53±0.69	2.56±0.82	0.901
HDLc (mmol/L)	0.72±0.20	0.68±0.17	0.72±0.18	0.342
Apolipoprotein A1 (micromol/L)	3.73±0.51	3.57±0.42	3.92±0.53	0.086
Apolipoprotein B (micromol/L)	3.22±0.68	3.14±0.64	3.28±0.71	0.496
Cholesterol / HDL	6.01±1.93	6.22±1.32	5.89±1.09	0.483
Triglycerides / HDL	7.27±2.69	7.27±2.69	6.75±3.63	0.629
LDLc / HDLc	3.57±0.95	3.67±0.93	3.54±0.91	0.808
ApoB / ApoA1	0.88±0.16	0.86±0.27	0.81±0.14	0.119

Table 4. Blood lipids and atherogenic ratios of hemodialysis patients before and after five weeks of argane oil consumption. In each group of patients, data before and after the five weeks study period were compared, and p values are given in the table for each group

	Control group			Argane oil group		
	Before	After	p value	Before	After	p value
Cholesterol (mmol/L)	4.22±0.77	4.37±0.82	0.129	4.23±0.78	3.83±0.90	0.088
TriglycTriglycerids (mmol/L)	2.05±0.70	1.92±0.79	0.337	1.94±0.85	1.87±0.70	0.612
LDLc (mmol/L)	2.54±0.72	2.51±0.67	0.782	2.57±0.84	2.18±0.62	0.001
HDLc (mmol/L)	0.72±0.12	0.84±0.19	0.000	0.72±0.18	0.94±0.27	0.000
Apolipo A1 (micromol/L)	3.58±0.47	3.44±0.53	0.085	3.95±0.55	3.71±0.40	0.332
Apolipo B (micromol/L)	3.19±0.61	2.85±0.71	0.000	3.35±0.72	2.62±0.73	0.001
Cholesterol / HDL	6.01±1.93	5.30±2.15	0.038	5.89±1.09	4.38±0.92	0.000
Triglycerides / HDL	7.27±2.69	6.42±2.90	0.058	6.75±3.63	5.30±2.64	0.025
LDLc / HDLc	3.55±1.41	3.11±1.32	0.071	3.53±0.96	2.39±0.66	0.000
ApoB / ApoA1	0.86±0.27	0.87±0.23	0.072	0.81±0.13	0.78±0.16	0.001

Table 5. Clinical characteristics of patients upon argane oil consumption. In each group of patients, data before and after the five weeks study period were compared, and p values are given in the table for each group

	Control group			Argane oil group		
	Before	After	p value	Before	After	p value
SBP (mmHg)	127.45±17.19	134.45±26.03	0.362	125.66±22.03	133.66±38.92	0.276
DBP (mmHg)	79.45±9.03	79.94±14.66	0.655	77.85±13.48	80.90±19.53	0.441
BMI (Kg/m^2)	23.71±4.14	23.15±3.53	0.923	22.47±4.58	22.64±4.57	0.330

4. DISCUSSION

Chronic renal failure patients and those on dialysis, are known to have a high incidence of cardiovascular-related mortality and morbidity, which are closely associated with blood lipid's abnormalities [5-7], high blood pressure and hyperglycemia. There is a close relationship between dyslipidemia and cardiovascular events in HD patients, hence, in these patients dyslipidemia represents a target for both pharmacotherapy [8,9] and complementary nutritional interventions. Our present clinical study was inspired by Morocco's folk medicine, where many health conditions such as skin, respiratory and rheumatologic diseases are treated with VAO. Though, very few clinical trials were reported on VAO consumption and its possible therapeutic benefits [16]. Most of VAO clinical and animal studies have focused on the property of this oil to improve blood lipid profile and to ameliorate the anti-oxidant status in man and animals [17]. In parallel to the present clinical study, we have conducted a similar study in Rabat's Military Hospital, on a group of HD patients who rather have regular blood lipid status, and the finding was that consumption of VAO lead to better HDLc levels and an improvement of anti-oxidant status [18]. In the present study, a population of HD patients with dyslipidemia have consumed VAO during five weeks, and clearly ameliorated their blood lipid profiles through an increase of HDLc and a decrease of LDLc

on one hand, on the hand, concentrations of apolipoprotein B was modified toward a better trend upon VAO consumption. Most importantly, all lipid atherogenic indices in our study were significantly ameliorated in VAO group of patients compared to the control one. This result is of a very significant relevance for the possible prevention of cardiovascular and cerebrovascular events in HD patients. These results confirm the capacity of VAO consumption to modulate blood lipids [17,18], and prove that an important cardiovascular risk factor, namely dyslipidemia and atherogenic indices, can be targeted by VAO consumption. The mechanism of action of VAO on dyslipidemia in man is not clear, however, the presence of sterols in this oil could play a role as possible modulator of cholesterol absorption and/or metabolism that lead to decreasing blood LDLc and increasing HDLc in our hemodialysis patients. Our hypothesis is supported by clinical evidences which reported that plant sterols consumption reduced LDLc and may prevent cardiovascular events [21,22]. In the present study, a significant increase of HDLc was obtained upon argane oil consumption as compared to control patients, though, control patients also experienced an improvement of HDLc levels, and the latter result might be due to a possible effect of other unknown patients diet conditions, such as consumption of olive oil in Moroccan traditional cuisine, since olive oil is mainly consumed in Fez area, and this oil is known for its lipid-modulatory effect in man, that is related to its high composition in oleic acid, sterols and polyphenols. The other possible explanation of HDLc increase in control group could be that patients were aware of their high blood lipid concentration before beginning the study, and that they might have reduced their diet fat consumption. This result on HDLc increase in VAO group is encouraging as HDLc are known to have antiatherogenic properties [23-25]. The anti-oxidant properties of VAO [16,18] could also play a role in protecting LDLc and HDLc from being oxidized and in this way, it could be antiatherogenic, as VAO is rich in tocopherols, carotenoïds and polyphenols. Oleic acid was shown to be responsible for lowering blood pressure in olive oil-treated volunteers [26]. VAO is known to have high oleic acid concentrations as well (19), however, in our present study, no major effect was observed on blood pressure of patients upon VAO consumption.

5. CONCLUSION

Our results bring new data on the ability of VAO consumption to improve blood lipid profile and ameliorate lipid atherogenic indices in dyslipidemic HD patients. The present study supports the use of VAO as an alternative and a natural complementary therapeutic tool against dyslipidemia-associated cardiovascular and cerebrovascular events in HD patients, and should encourage other clinical studies in the field of dyslipidemia-asociated diseases in man.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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