Coll. Antropol. **34** (2010) Suppl. 1: 181–188
Original scientific paper

Are Lipoprotein Disturbances in Chronic Hemodialyzed Patients only Renal Failure Related?

Marko Jakić[1], Vesna Lovčić[2], Dragan Klarić[3], Dubravka Mihaljević[1], Lada Zibar[1], Marijana Jakić[4] and Ivana Marić[5]

[1] Departmant of Internal Medicine, University Hospital Center Osijek, Osijek, Croatia
[2] General Hospital Bjelovar, Bjelovar, Croatia
[3] General Hospital Zadar, Zadar, Croatia
[4] Public Health Institute of the Osijek-Baranya County, Osijek, Croatia
[5] Department of Mineral Metabolism, School of Medicine, University »J. J. Strossmayer«, Osijek, Croatia

A B S T R A C T

Chronically hemodialyzed (HD) patients frequently suffer from quantitative and even more often qualitative serum lipids disorders. Mostly they have increased triglycerides and VLDL-cholesterol, slightly increased or normal total and LDL-cholesterol and decreased HDL-cholesterol concentrations. The study compared lipid profile between two groups of chronic HD patients coming from regionally distinct areas, the continental and the maritime one. The aim was to examine the hypothetic influence of their different dietary habits on lipid profile. The study included 72 patients from continental region (39 men) and 50 from maritime part of the country (30 men). Patients suffering from diabetes mellitus, hypothyroidism, liver disease, alcoholics as well as sevelamer treated patients were not included. Prior to a HD session the patients were determined fasting total cholesterol, triglycerides, HDL- and LDL-cholesterol, total proteins, albumins and C-reactive protein serum concentrations. All patients were undergoing bicarbonate hemodialysis with polysulphone dialysers of low permeability. The continental group of patients were somewhat older, undergoing HD for longer period of time, of lower height, greater weight, greater body mass index, higher total (4.70±0.91: 4.42±1.02 mmol/L), and LDL-cholesterol (2.78±0.74:2.66±0.75 mmol/L) concentrations, while lower triglycerides (1.72±0.84:1.81±0.83 mmol/L) and HDL-cholesterol (1.13±0.42:1.16±0.54 mmol/L). However, all the differences were without statistical significance. Chi-square test showed that the continental group of patients consumed more often pork, bacon, smoked and cured meats, margarine, butter, walnuts, almonds, garlic, cream and full-fat cheese than fish. They prepare food more often with lard and sunflower oil. Almost every fourth continental patient received statins, while only every 25th in the maritime group of patients. There were not any statistically significant Chi-square values for differences in frequencies of patients with total cholesterol greater than 5.2 mmol/L, triglycerides above 1.6 mmol/L, HDL-cholesterol less than 1.1 mmol/L, LDL-cholesterol greater than 2.6 mmol/L, obesity and malnutrition between the two groups. Based on the results of this study we have concluded that diet has significant influence on lipid profile of HD patients. Even though the continental and the maritime groups of patients differed significantly in diet, they were similar in plasmatic lipoprotein concentrations. However, this similarity was ascribed only to statin treatment, which was more frequent in the continental group of patients. The influence of ESRD and HD as a method of renal replacement therapy on lipid profile was not more dominant than diet.

***Key words**: plasmatic lipoproteins, cholesterol, triglycerides, hemodialysis, dietary habits*

Introduction

Final stage chronic renal failure patients very often suffer from quantitative (hyperlipoproteinemia), and even more frequently from qualitative disorders of plasma lipoproteins (dyslipoproteinemia or dyslipidemia). Mostly they have increased triglycerides (TGC) and VLDL-cholesterol (VLDL-C), slightly increased or normal total

Received for publication January 15, 2010

(TC) and LDL-cholesterol (LDL-C) and decreased HDL--cholesterol (HDL-C) concentrations[1–4]. This represent a characteristic feature of renal failure itself, although additional influences are displayed by the basic renal disease, as well as the cause of renal failure and the method of treatment. For that reason, there are differences in plasma lipoprotein disorders between hemodialyzed patients and those treated by peritoneal dialysis. Those differences occur early, following the decrease of glomerular filtration below 50 mL/min/1.73 m^2 of body surface area[5]. Numerous studies showed that 20% of hemodialyzed patients and 5% of patients treated by peritoneal dialysis have total cholesterol (TC) above 6.2 mmol/L, 30% i.e. 45% LDL-C above 3.4 mmol/L, 45% i.e. 50% TGC above 2.3 mmol/L and 50% i.e. 20% of them HDL-C below 0.9 mmol/L[6,7]. According to data from American Society of Nephrology approximately 25% of hemodialyzed and 60% of patients treated by peritoneal dialysis have TGC above 2.26 mmol/L, 70% i.e. 76% LDL-C above 2.60 mmol/L, and 50% of hemodialyzed patients has non-HDL-C above 3.4 mmol/L.[8] They occur due to decreased activity of three key enzymes, important for lipid metabolism, lipoprotein lipase (LPL), hepatic triglyceride lipase (HTGL) and lecithin cholesterol acyltranferase (LCAT)[9–11].

Plasma lipoprotein disorders are firmly correlated with cardiovascular diseases, which are the leading cause of death for this group of patients[12]. It has been estimated that 40–50% of dialyzed patienst die from cardiovascular accidents[13] and that the mortality of patients with final stage of CRF from myocardial infarction, heart failure and stroke is 10–20 times greater when compared to the mortality in general population of comparable age and gender[14–16]. There are numerous studies which prove that the treatment of plasma lipoprotein disorders in patients without CRF[17–19], especially hypercholesterolemia, leads to the decrease not only of the mortality from cardiovascular accidents, but also to the decrease of general mortality, for both the patients with diagnosed[17,18] and the patients without diagnosed cardiovascular diseases[19,20]. Although the relationship between cholesterol and atherosclerosis in patients with CRF is less clear than in general population, Selger et al.[21] has established that the treatment of plasma lipoprotein disorders significantly decreases both the mortality from cardiovascular diseases and general mortality of dialyzed patients. Namely, during 1000 years of dialysis treatment 143 patients treated with statins, and 202 patients not treated with statins have died. The difference is statistically significant. The use of statins decreased the relative mortality risk by 32%. Similar was also the effect on cardiovascular mortality (during 1000 years of dialysis treatment 61 patients who had been using statins and 88 patients who have not been using this medication, died). The authors conclude that statins in these groups of patients exhibit protective influence regardless whether they have or do not have elevated levels of total cholesterol and LDL-C. After having performed the analysis of statin influence on treatment outcome for a large group of hemodialyzed patients (longitudinal follow up of approximately 30,000 patients, successively included in the period 1996–2005, in more than 300 centres for dialysis, in 12 countries on 4 continents – Dialysis Outcomes and Practise Patterns Study – DOPPS), Mason et al.[22] have concluded that every increase in frequency of statin use by 10% decreases the general mortality rate by 5%. However, the correlation between the risk of coronary disease emergence and cholesterol level in hemodialyzed patients is not linear as is in general population. Hemodialyzed patients with total cholesterol below 2.6 mmol/L have 4.3 times greater mortality than the patients with total cholesterol between 5.2 and 6.5 mmol/L[23].

There are three steps in treating plasma lipoprotein disorders, and they are applied almost independently to the cause which provoked them[24]. Those are: adequate diet, workout and pharmacological medications which influence the level of plasma lipoproteins. Adequate diet is the one poor with saturated fatty acids. Workout, if tolerated and performed by patients over a longer period of time, definitely improves lipid profile, as well as glucose tolerance in selected group of patients[25–27]. Nevertheless, it is not known whether the workout decreases mortality in this group of patients[24]. Hemodialyzed patients have decreased ratio of subcutaneous and increased ratio of visceral adipose tissue compared to body mass index (BMI)[28]. The best survival rate is observed among hemodialyzed patients with BMI between 27.5 i 30.0 kg/m^2 body surface area[29,30]. The goal of the treatment was to accomplish the level of LDL-C below 2.6 mmol/L, TGC below 2.0 mmol/L and total cholesterol (TC) above 3.9 mmol/L[24]. The recommendation is that the treatment with hydroxy-beta-methyl-glutaryl coenzyme A *(*HMG--CoA*)*, i.e. statins, should start if target levels of specific plasma lipoproteins[24] have not been achieved after a 3-month diet and workout. If the level of LDL-C remains above 2.6 mmol/L after a 6-week statin therapy, the statin dosage is being gradually increased over another 6-week period. Should the LDL-C level remain above 2.6 mmol/L after that period of time, there is indication for introduction of nicotinic acid[31] or sevelamer hydrochloride[32], phosphate binder, which decrease LDL-C by 5–25%[31], i.e. by 20–30%[32], Patients with TGC between 2.0 i 5.7 mmol/L are recommended to use inhibitors HMG-CoA reductase, those with TGC above 5.7 and 9.0 mmol/L analogs of fibric acid, and to those with TGC above 9.0 mmol/L fish oil and low-molecule heparin[24].

In this paper we compared lipoprotein profile of two groups of hemodialyzed patients, from continental and maritime region, whose dietary habits differ significantly in types of food they consume as well as in the methods of food preparation. Patients from the continental group often eat pork, and they prepare the food using lard or sunflower oil. Patients from maritime group, on contrary, very often eat fish, and prepare their food either without oil or with olive oil. Our goal was to determine whether the patient groups in our study differ in lipoprotein profile and to what extent are possible differences influenced by their dietary habits.

Subjects and Methods

The study included 122 patients (53 females, 69 males) suffering from final stage CRF undergoing bicarbonate dialysis with polysulphone dialysers of low permeability three times a week (surface area 1.5–2.0 m^2, ultrafilatration index 9.8–13.7 mL/mmHg of transmembrane pressure/hour), usual blood flow rate (250–350 mL/minuti) and dialysate (500 mL/minute). To prevent blood coagulation in extracorporeal dialytic circuit all patients received classical sodium heparin. Patients included in the study were treated in three Centres for Dialysis. Two Centres were located in the continental region and one was located in the maritime part of Croatia. The patients from two continental Centres made up the continental group of patients (n=72), and the patients from the maritime Centre made up the maritime group of patients (n=50). Patients suffering from diabetes mellitus, hypothyroidism, liver disease, alcoholics as well as sevelamer treated patients were not included.

Along with the basic data (age, gender, the date of the hemodialysis treatment start), before their regular hemodialysis, each fasting patient was tested for a set of laboratory parameters: total cholesterol (CHOD PAP method – reference values 3–5.2 mmol/L), triglycerides (GPO PAP method – reference values 0.6–1.7 mmol/L), HDL-cholesterol (precipitation with phosphowolframate and magnesium ion – reference values for women above 1.6 mmol/L, and for men above 1.4 mmol/L), LDL-cholesterol (for triglyceride values below 3.0 mmol/L it was calculated mathematically using Friedewald formula[33], and for triglyceride values above 3.0 mmol/L it was calculated using precipitation method with polyvinil sulphate– reference values up to 3.5 mmol/ l), total proteins (Cologel method– reference values 64–82 g/L), albumin (BCG method – reference values 35–52 g/L), hemoglobin (automated cell counter – reference values 119–157 g/L for women, 138–175 g/L for men) and C-reactive protein – immunoturbidimetric method, Boehringer, Manheim – reference values up to 5.0 mg/L), body weight (kg) and body height (cm). Body Mass Index (BMI)[34] was calculated from body weight and body height.

All patients anonymously filled out a questionnaire requesting data about their dietary habits. Basically, patients were asked to answer whether they consume: 1. pork, 2. bacon, 3. smoked and cured meat, 4. fish, 5. margarine, 6. butter, 7. coffee, 8. walnuts, almonds, hazelnuts, peanuts, 9. garlic, 10. cream and full-fat cheese a) daily b) every other day, c) twice a week d) once a week or e) even less frequently. They were also asked if they used lard, sunflower oil, olive oil or any other vegetable oil in food preparation. From patients' medical records as well as interviews we have learned which one of them take hypolipemic medications, β-blockers, diuretics and erythropoietin.

The obtained individual results were expressed as arithmetic means, standard deviations and percentages. They have been analyzed by means of Student's t-test for independent samples and χ^2-test. The level of statistical significance was set from 1 and 5% ($p<0.01$ and $p<0.05$)[35].

TABLE 1
BASIC CHARACTERISTICS OF THE TWO GROUPS OF HEMODIALYZED PATIENTS (A – CONTINENTAL GROUP, B – MARITIME GROUP)

	A n=72		B n=50		t-test
	$\bar{X}$±SD	range	$\bar{X}$±SD	range	
Age (years)	59.68±15.83	24–84	58.89±15.24	26–81	0.28
HD (months)	75.48±60.54	3–261	65.28±49.19	9–204	1.02
Gender (f/m)	33/39		20/30		[a]0.21
Height (cm)	167±10	150–190	168±12	140–192	0.48
Weight (kg)	68.18±14.32	43.50–115	65.59±12.74	38–91	1.05
BMI (kg/m^2)	24.46±4.20	16.28–38.54	23.18±3.49	14.29–31.62	1.83
Tot.-C (mmol/L)	4.70±0.91	2.92–6.54	4.42±1.02	2.04–6.59	1.56
TGC (mmol/L)	1.72±0.84	0.64–6.22	1.81±0.89	0.68–4.07	0.56
HDL-C (mmol/L)	1.13±0.42	0.62–3.70	1.16±0.54	0.55–3.98	0.33
LDL-C (mmol/L)	2.78±0.74	1.39–4.49	2.66±0.75	0.93–4.20	0.87
Haemoglobin (g/L)	98.25±7.12	70–127	96.42±6.85	68–123	1.43
Tot. proteins (g/L)	67.99±4.76	55.70–77	69.11±5.04	60–81.40	1.23
Albumin (g/L)	41.47±3.44	33.3–49.8	41.21±2.67	36.6–48.50	0.47
CRP (mg/L)	8.94±10.58	1.30–46.70	7.61±10.86	1.50–68	0.67
Heparin (UI)	3590±1319	2000–7000	3296±946	2000–5500	1.78

[a] χ^2-test; BMI – body mass index, Tot.-C – total cholesterol, TGC – triglycerides, HDL-C – HDL-cholesterol, LDL-C – LDL-cholesterol, CRP – C-reactive protein

Results

The patients from the continental group (n=72; females 33, males 39) compared to the patients from the maritime group (n=50; females 20, males 30) were somewhat older, undergoing HD for longer period of time, of lower height, greater weight, greater BMI, higher TC (4.70±0.91:4.42±1.02 mmol/L) and LDL-C (2.78±0.74: 2.66±0.75 mmol/L), haemoglobin, C-reactive protein and albumin, and lower TGC (1.72±0.84:1.81±0.83 mmol/L), HDL-C (1.13±0.42:1.16±0.54 mmol/L) and total proteins. According to Student's t-test differences were not statistically significant (Table 1). According to χ^2-test statistically significant was the fact that the patients from the continental group consumed more often pork, bacon, smoked and cured meat, margarine, butter, walnuts, almonds, garlic, cream and full-fat cheese, and rarely fish. It is also significant that they more frequently prepared

TABLE 2
BASIC DATA ON THE FREQUENCY OF CONSUMPTION OF CERTAIN FOODS AND ON THE METHODS OF FOOD PREPARATION IN THE TWO GROUPS OF HEMODIALYZED PATIENTS (A – CONTINENTAL GROUP, B – MARITIME GROUP) AND THEIR STATISTICAL SIGNIFICANCE

	A n=72					B n=50					χ^2-test
	Consumption frequency										
Food	a	b	c	d	e	a	b	c	d	e	
1.Pork	2	12	22	22	14	0	0	1	15	34	40.17**
2. Bacon	1	6	12	8	46	0	0	2	0	46	18.89**
3. Smoked and cured meat	8	12	8	10	34	0	6	13	12	19	11.68**
4. Fish	0	4	6	40	22	1	4	25	17	3	30.51**
5. Butter	8	8	18	2	36	0	2	2	1	45	22.50**
6. Margarine	20	16	14	6	16	1	2	11	7	29	29.26**
7. Black coffee	42	4	8	6	12	30	4	2	0	14	8.05
8. Walnuts, almonds, hazelnuts, peanuts	4	4	2	10	52	0	0	0	0	50	16.61**
9. Garlic	4	10	6	10	42	0	4	13	4	29	10.48**
10. Cream and cheese	6	14	14	20	18	0	0	2	0	48	60.64**
	Methods of foods preparation										
	aa	bb	cc	dd	aa	bb	cc	Dd			
Number of patients	8	24	62	6	50	0	1	2			111.57**

TABLE 3
BASIC DATA ON SOME OF THE EXAMINED PARAMETERS IN THE TWO GROUPS OF HEMODIALYZED PATIETNS (A – CONTINENTAL GROUP, B – MARITIME GROUP) AND THEIR STATISTICAL SIGNIFICANCE

	A n=72	B n=50	χ^2-test
Tot. cholesterol above 5.20 mmol/L	22	10	0.73
Triglycerides above 1.60 mmol/L	42	27	0.08
HDL-cholesterol below1.10 mmol/L	41	32	0.35
LDL-cholesterol above 2.60 mmol/L	44	28	0.05
CRP above 5 mL/L	36	15	3.30
Males	39	30	0.21
BMI above 25 kg/m^2	27	13	1.29
BMI above 30 kg/m^2	7	3	0.16
BMI under 20 kg/m^2	7	11	2.63
BMI 20–25 kg/m^2	38	13	1.29
Treatment with statins	17	2	**7.20
Erythropoietin therapy	28	43	0.05

CRP – C-reactive protein, BMI – body mass index

TABLE 4
BASIC CHARACTERISTICS OF TWO SUBGROUPS OF PATIENTS WITHOUT STATINS MEDICATION (A – CONTINENTAL GROUP, B – MARITIME GROUP) AND THEIR STATISTICAL SIGNIFICANCE

	A n=55		B n=48		t-test
	$\overline{X}$±SD	range	$\overline{X}$±SD	range	
Tot.-C (mmol/L)	4.52±0.81	2.92–6.06	4.34±0.96	2.04–6.59	1.02
TGC (mmol/L)	1.59±0.87	0.64–6.22	1.79±0.86	0.68–4.07	1.17
HDL-C (mmol/L)	1.16±0.45	0.62–3.70	1.17±0.55	0.55–3.98	0.10
LDL-C (mmol/L)	2.64±0.69	1.39–4.34	2.61±0.72	0.93–4.20	0.22

Tot.-C – total cholesterol, TGC – triglycerides, HDL-C – HDL-cholesterol, LDL-C – LDL-cholesterol

TABLE 5
BASIC CHARACTERISTICS OF TWO SUBGROUPS OF PATIENTS FORMED ACCORDING TO THE STATINS MEDICATION (A – PATIENTS WITH STATINS MEDICATIONS, B – PATIENTS WITHOUT STATINS MEDI-CATIONS) AND THEIR STATISTICAL SIGNIFICANCE

	A n=19		B n=103		t-test
	$\overline{X}$±SD	range	$\overline{X}$±SD	range	
Tot-C (mmol/L)	5.40±0.99	3.79–6.54	4.43±0.88	2.04–6.59	3.99**
TGC (mmol/L)	2.18±0.71	1.06–3.78	1.68±0.87	0.64–6.22	2.72**
HDL-C (mmol/L)	1.05±0.27	0.66–1.68	1.16±0.50	0.55–3.98	1.39
LDL-C (mmol/L)	3.29±0.74	2.07–4.49	2.63±0.70	0.93–4.34	3.60**

Tot-C – total cholesterol, TGC – triglycerides, HDL-C – HDL-cholesterol, LDL-cholesterol
** $p<0.01$

food using sunflower oil and lard (Table 2). Almost every fourth patient form the continental group received statins (n=17; 23.61%), in comparison to only every twenty-fifth from the maritime group(n=2; 4%). There was not any statistically significant difference in frequency of taking β-blockers, diuretics and erythropoietin.

According to χ^2-test there was not any statistically significant difference between groups of patients concerning the frequency of patients with TC above 5.2 mmol/L, TGC above 1.6 mmol/L, HDL-C below 1.10 mmol/L, LDL-C above 2.60 mmol/L, those with BMI above 25 or 30 as well as those under 20 kg/m^2 (Table 3).

When the patients receiving statins were excluded from the studied groups of patients it has been observed that the differences in mean values of TC, TGC, HDL-C and LDL-C in new formed groups (continental n=55, maritime n=48) were even smaller for 3 out of 4 observed parameters (Table 4). Mean TC of the patients from the continental group receiving statins (n=17) was 5.29±0.97 mmol/L, TGC was 2.16±0.70 mmol/L, HDL-C 1.05±0.27 mmol/L, and LDL-C 3.21±0.73 mmol/L. Mean values of the above-mentioned parameters for two patients from the maritime group were 6.35±0.08, 2.38±1.87, 1.06±0.02, 3.95±0.23 mmol/L, respectively. According to Student's t-test it is statistically significant that the patients receiving statins, compared to the patients who were not receiving statins, have higher mean values of 3 out of 4 observed lipoproteins (Table 5). They did not differ significantly solely in the level of HDL-C.

Discussion

In this study we compared lipoprotein profile of two groups of hemodialyzed patients, continental and maritime. Our goal was, as previously mentioned, to determine whether the studied groups differ in plasma lipoprotein profile or not, and to what extent could those differences be explained by differences in their dietary habits. Nevertheless, adequate diet is the first step in treatment of primary and secondary disorders of lipid metabolism.

The results of the retrospectively conducted research on selected hemodialyzed patients have shown that the patients from the continental and maritime group significantly differ in types of food they consume, as well as according to the methods of food preparation. Accoriding to χ^2-test it is statistically significant that the patients from the continental group eat more often pork, and prepared their food using lard or sunflower oil. Significant was the fact that the patients from the maritime group statistically more frequently eat fish and prepared their food by cooking it or with olive oil (so-called »mediterranean cuisine«) (Table 2). Despite the significant differences in their dietary habits, statistically, acoording to Student's

t-test the two groups of patients did not differ significantly in mean values of TC, TGC, LDL-C i HDL-C (Table 1). However, statistically, according to χ^2-test, there were significantly more hemodialyzed patients from the continental group receiving statins (Table 3).

Svensson and associates[36] have explored the influence of frequency in food consumption on lipid profile of 206 patients receiving hemodialysis for a period longer than 6 months. According to frequency of fish consumption, they were divided into three groups. In the first group there were patients who consumed fish rarely, in the second group those who consumed it moderately often, and in the third those who consumed it very often. The more frequently patients consumed fish, the more often they had higher serum concentrations of two unsaturated fatty acids, eicosapentaenoic (EPA) and docosahexaenoic (DHA) acid, as well as lower values of TGC and higher of TC, LDL-C i HDL-C. Introduction of omega-3 fatty acids, comprising 45% EPA and 37.5% DHA, has resulted in minimal decrease of TGC, TC and LDL-C as well as increase of HDL-C; introduction of olive oil has resulted in minimal decrease of TC and LDL-C, as well as increase of TGC and HDL-C. Although fatty acids from fish oil can lead to doubling of bleeding time, the use of fish oil has not been followed by significant risk of bleeding[37].

Cano et al.[38] have studied the influence of olive oil and soja oil administered in the form of lipid emulsion on the nutritional status of a small group of patients undergoing dialysis for longer than 6 months. They included patients with BMI under 20 kg/m^2 body surface area, with albumins below 35 g/L, prealbumin below 300 mg/L, daily protein catabolic rate (nPCR) under 1 g/kg of body weight, as well as those who manged to reduce their weight by at least 10% during 6 months. After 5 weeks in both groups there was a significant increase in TC and LDL-C, and non-significant increase in TGC snd HDL-C. However, regular intake of 25 mL of olive oil on daily basis did not have any significant influence on lipid profile of healthy subjects[39].

By studying the influence of diet on body weight increase in hemodialyzed patients, Özdemir et al.[40] have concluded that patients (n=194) on Mediterranean diet rich in seafood and vegetables significantly less increase their body weight (2.47±0.94 kg) between two cycles of hemodialysis in comparison to continental group of patients(n=508) (3.08±0.94 kg), whose food is rich in proteins and carbohydrates. A group of Greek authors has investigated the influence of Mediterranean diet on total mortality, as well as mortality from coronary and malignant diseases in total population. According to the types of food they consume as well the frequency of consumption, the subjects were divided into those that accept Mediterranean diet partially and those that accept it almost completely. They have found that the subjects who almost completely accept Mediterranean diet have by 25% lower total mortality, by 33% lower mortality rate from coronary diseases, and by 24% lower mortality rate from malignant diseases, compared to the subjects who accept Mediterranean diet only partially (n=22043; follow-up period: 44 months).

By researching possible influence of erythropoietin on plasma lipid profile of dialyzed patients (n=33; females

TABLE 6
MEAN TOTAL, LDL- AND HDL-CHOLESTEROL SERUM CONCENTRATIONS IN THE TWO HEMODIALYSIS PATIENTS GROUP (A – CONTINENTAL GROUP, B – MARITIME GROUP) WITH PRESUMED CHANGE FOLLOWING STATINS MEDICATION AND THEIR STATISTICAL SIGNIFICANCE

	A n=72	B n=50	t-test	p
Tot. cholesterol – mmol/L	4.70±0.91	4.42±1.02	1.56	0.061
Decrease 10%	4.84±0.95	4.45±1.07	*2.07	0.020
Decrease 15%	4.92±0.99	4.46±1.13	*2.32	0.011
Decrease 20%	5.01±1.05	4.48±1.18	*2.55	0.006
Decrease 25%	5.12±1.09	4.50±1.23	*2.87	0.003
LDL – C – mmol/L	2.78±0.74	2.66±0.75	0.87	0.193
Decrease 10%	2.87±0.78	2.68±0.79	1.31	0.097
Decrease 15%	2.92±0.81	2.69±0.82	1.53	0.065
Decrease 20%	2.97±0.85	2.70±0.86	*1.71	0.045
Decrease 25%	3.04±0.89	2.71±0.90	*2.00	0.024
Decrease 30%	3.11±0.93	2.73±0.94	*2.22	0.014
Decrease 35%	3.19±0.96	2.75±0.97	*2.47	0.007
HDL – C – mmol/L	1.13±0.42	1.16±0.54	0.33	0.629
increase 10%	1.11±0.45	1.16±0.54	0.54	0.703

HDL-C – HDL-cholesterol, LDL-C – LDL-cholesterol
* statistical significant

22, males 11), Allegra et al.[42] have found out that TC, TGC, LDL-C and apolipoprotein B were increased only in those patients (n=19) who during erythropoietin treatment increased their daily calorie intake by more than 10%, due to increased intake of proteins, fats and carbohydrates. Hence, the influence of diet on plasma lipoprotein profile of dialyzed patients can be stronger than the influence of chronic renal failure itself and its methods of treatment. Why such an influence has not been observed in our study?

Analyses show that our two studied groups of patients do not distinguish themselves only in dietary habits, but also according to frequency of statin taking. The results of numerous studies have indicated that statins decrease LDL-C by 25–40% in patients suffering from final stage CRF[43–47], similar as in patients without CRF[20,48]. In the famous »4 S Study«, which included 4444 patients with TC between 5.5 and 8.0 mmol/L, the treatment with simvastatin has resulted in mean decrease of TC by 25%, LDL-C by 35%, as well as increase of HDL-C by 8%[17]. Statins do not normalize plasma lipoproteins in all patients who take them. For that reason, 19 of our patients treated with statins statistically have significantly higher mean values of TC, TGC and LDL-C compared to patients who did not receive statins. Their HDL-C is indeed lower, but statistically not significantly lower (Table 5).

Under presumption that statins were equally efficient in our patients who received them, as they were for »4 S Study«[17] patients, then, without them, patients from the continental group would have TC 5.12±1.09 mmol/L, LDL-C 3.19±0.96 mmol/L, and HDL-C 1.11±0.45 mmol/L. The patients from the maritime group would have TC 4.50±1.23 mmol/L, LDL-C 2.75±0.97 mmol/L, and HDL-C 1.16±0.54 mmol/L. According to t-test statistically there should be significant differences in mean values of TC and LDL-C, but not of HDL-C (Table 6). Or, to paraphrase it: statin-caused TC decrease by 10% and LDL-C by 20% is enough to eliminate value differences when comparing two groups of patients.

When analyzing both of our groups together, it is obvious that almost every 7th subject takes statins (13.93%). For the purpose of comparison, it should be stated that according to Seliger and associates[21] less than 10% of their dialyzed patients received statins at the beginning of the treatment using this method; which is significantly more compared to our patients from the maritime group (4%), and significantly less compared to our patients from the continental group (23.61%). In DOPPS, already mentioned in Introduction, during the year 2000 in 7 countries 11.80% of dialyzed patients have received statins; from 3.5–5% in Italy and Japan to 12–17% in Germany, France and United States of America[22].

In the conclusion, based on the results obtained from our study, we can state that diet significantly influences the lipid profile of dialyzed patients. Namely, the patients from the continental group plasma lipoprotein values similar to the patients from the maritime group, from which they significantly differ in dietary habits, only thanks to significantly more frequent taking of statins. The influence of final stage CRF and hemodialysis as method of treatment are not more dominant in comparison to dietary habits.

REFERENCES

1. MOORHEAD JF, Am J Kidney Dis, 17 (1991) 65. — 2. KEANE WE, Kidney Int, 57 (2000) 27. — 3. ATTMAN PO, ALAUPOVIC P, Kidney Int, 39 (1991) 16. — 4. MONZANI G, BERGESIO F, CIUTI, R, ROSATI A, FRIZZI V, SERRUTO A, VITALI D, BENUCCI A, TOSI PL, BANDINI S, SALVADORI M, Blood Purif, 14 (1996) 262. — 5. ATTMAN PO, SAMUELSSON O, ALAUPOVIC P, Am J Kidney Dis, 21 (1993) 573. — 6. KASISKE BL, Am J Kidney Dis, 32 (1998) 8. — 7. ELISAF MS, BAIRAKTARI HT, TZIALLOS CS, GERMANOS NK, SIAMOPOULOS KC, Dial Transplant, 24 (1995) 642. — 8. National Kidney Foundation: K/DOQI Clinical practice guidelines for managing dyslipidemias in chronic kidney disease, Am J Kidney Dis, 41 Suppl 3 (2003) 1. — 9. ATTMAN PO, KNIGHT-GIBSON C, TAVELLA M, SAMUELSSON O, ALAUPOVIC P, Nephrol Dial Transplant, 13 (1998) 2833. — 10. SHOJI T, NISHIZAWA Y, NISHITANI H, YAMAKAWA M, MORII H, Kidney Int, 41 (1992) 1653. — 11. HAVEL RJ, HAMILTON RL, Hepatology, 8 (1988) 1689. — 12. MASSY ZA, KEANE WF, Management of hyperlipidemia in chronic dialysis patients. In: NISSENSONS AR, FINE RN (Eds) Dialysis therapy, 3rd edition (Hanley and Belfus inc., Philadelphia, 2002). — 13. MURPHY SW, PARFREY PS, Management of ischemic heart disease, heart failure and pericarditis in hemodialysis patients. In: NISSENSONS AR, FINE RN (Eds) Dialysis therapy, 3rd edition. (Hanley and Belfus inc., Philadelphia, 2002). — 14. BROWN JH, HUNT LP, VITES NP, SHORT CD, GOKAL R, MALLICK NP, Nephrol Dial Transplant, 9 (1994) 1136. — 15. FOLEY RN, PARFREY PS, SARNAK MJ, Am J Kidney Dis, 32(2) (1998) 12. — 16. CHEUNG AK, SARNAK MJ, YAN G, DWYER JT, HEYKA RJ, ROCCO MV, TEEHAN BP, LEVEY AS, Kidney Int, 58 (2000) 353. — 17. SCANDINAVIAN SIMVASTATIN SURVIVAL STUDY GROUP, Lancet, 344 (1994) 1383. — 18. SACKS FM, PFEFFER MA, MOXE LA, ROULEAU JL, RUTHERFORD JD, COLE TG, BROWN L, WARNICA JW, ARNOLD JM, WUN CC, DAVIS BR, BRAUNWALD E, N Engl J Med, 335 (1996) 1001. — 19. SHEPHERD J, COBBE S, FORD I, ISLES CG, LORIMER AR, MACFARLANE PW, MCKILLOP JH; PACKARD CJ, N Engl J Med, 333 (1995) 1301. — 20. DOWNS JR, CLEARFIELD M, WEIS S, WHITNEY E, SHAPIRO DR, BEERE PA, LANGENDORFER A, STEIN EA, KRUYER W, GOTTO AM, JAMA, 279 (1998) 1615. — 21. SELIGER SL, WEISS NS, GILLEN DL, KESTENBAUM B, BALL A, SHERRARD DJ, STEHMAN-BREEN CO, Kidney Int, 61 (2002) 297. — 22. MASON NA, BAILIE GR, SATAYATHUM S, BRAGG-GRESHAM JL, AKIBA T, AKIZAWA T, COMBE C, RAYNER HC, SAITO A, GILLESPIE BW, YOUNG EW, Am J Kidney Dis, 45 (2005) 119. — 23. LOWRIE EG, LEW NL, Am J Kidney Dis, 15 (1990) 458. — 24. EUROPEAN BEST PRACTISE GUIDELINES FOR HAEMODIALYSIS, Nephrol Dial Transplant, 17 (2002) 88. — 25. HARTER HR, GOLDBERG AP, Med Clin North Am, 69 (1985) 159. — 26. GOLDBERG AP, HAGBERG JM, DELMEZ JA, HAYNES ME, HARTER HR, Kidney Int, 18 (1980) 754. — 27. GOLDBERG AP, GELTMAN EM, GAVIN JR, CARNEY RM, HAGBERG JM, DELMEZ JA, NAUMOVICH A, OLDFIELD MH, HARTER HR, Nephron, 42 (1986) 311. — 28. ODAMAKI M, FURUYA R, OHKAWA S, YONEYAMA T, NISHIKINO M, HISHIDA A, KUMAGAI H, Nephrol Dial Transplant, 14 (1999) 2427. — 29. FLEISCHMANN E, TEAL N, DUDLEY J, MAY W, BOWER JD, SALAHUDEEN AK, Kidney Int, 55 (1999) 1560. — 30. HAKIM RM, LOWRIE E, Kidney Int, 55(4) (1999) 1580. — 31. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), J Am Med Assoc, 285 (2001) 2486. — 32. CHEROW GM, BURKE SK, DILLON MA, SLATOPOLSKY E, Nephrol Dial Transplant, 14 (1999) 2907. — 33. FRIEDEWALD WT, LEVY RI, FREDRICKSON DS, Clin Chem, 18 (1972) 499. — 34. DENKE M, WILSON JD, Assessment of nutritional status. In: FAUCI AS, BRAUNWALD E, ISSELBACHER KJ, KASPER DL, HAUSER SL, LONGO DL, JAMESON JL (Eds) Harrison's Principles of internal medicine, 14th edition (Megraw Hill, New York-London-Toronto, 1998)

448. — 35. BOŽIKOV J, IVANKOVIĆ D, KERN J, KOPJAR B, LUKOVIĆ G, VULETIĆ S, Osnove statističke analize za medicinare, (Medicinska knjiga, Zagreb, 1991). — 36. SVENSSON M, SCHMIDT EB, JORGENSEN KA, CHRISTENSEN JH, Nephrol Dial Transplant, 23 (2008) 2918. — 37. DONNELLY SM, ALI MA, CHURCHILL DN, J Am Soc Nephrol, 2 (1992) 1634. — 38. CANO NJ, SAINGRA Y, DUPUY AM, LOREC--PENET AM, PORTUGAL H, LAIRON D, CRISTOL JP, COME A, LE BRUN A, ATLAN P, LEVERLE XM, British J Nutrition, 95 (2006) 152. — 39. BONDIA-PONS I, SCHRÖDER H, COVAS MI, CASTELLOTE AJ, KAIKKONEN J, POULSEN HE, GADDI AV, MACHOWETZ A, KIESEWETTER H, LOPEZ-SABATER MC, J Nutrition, 137 (2007) 84. — 40. ÖZDEMIR FN, AKCAY A, ELSURER R, SEZER S, ARAT Z, HABERAL M, J Renal Nutrition, 15 (4) (2005) 371. — 41. TRICHOPOULOU A, COSTACOU T, BAMIA C, TRICHOPOULOS D, N Engl J Med, 348 (2003) 2599. — 42. ALLEGRA V, MARTIMBIANCO L, VASILE A, Nephrol Dial Transplant, 12 (1997) 924. — 43. MATTHYS E, SCHURGERS M, LAMBERIGTS G, LAMEIRE N, VANDECASTEELE N, LABEUR C, BEISIEGEL U, ROSSENEU M, Atherosclerosis, 86 (1991) 183. — 44. NISHIKAWA O, MUNE M, MIYANO M, NISHIDE T, NISHIDE I, MAEDA A, KIMURA K, TAKASHAKI T, KISHINO M, TONE Y, OTANI H, OGAWA A, MAEDA T, YUKAWA S, Kidney Int, 57 (71) (1999) 219. — 45. NISHIZAWA Y, SHOJI T, EMOTO M, KAWASAKI K, KONISHI T, TABATA T, INOUE T, MORII H, Clin Nephrol, 43 (1995) 268. — 46. WALKER RJ, SUTHERLAND WHF, WALKER HL, MAC MAHON S, ROBSON R, Nephrol Dial Transplant, 12 (1997) 87. — 47. WANNER C, HORL WH, LULEY CH, WIELAND H, Kidney Int, 39 (1991) 754. — 48. SACKS FM, PFEFFER MA, MOYE LA, ROULEAU JL, RUTHERFORD JD, COLE TG, BROWN L, WARNICA JW, WUN CC, DAVIS BR, BRAUNWALD E, N Engl J Med, 335 (1996) 1001.

M. Jakić

Ukrinska 21, 31 000 Osijek, Croatia
e-mail: mjakic1@gmail.com

JESU LI POREMEĆAJI LIPOPROTEINA PLAZME HEMODIJALIZIRANIH BOLESNIKA POSLJEDICA SAMO BUBREŽNOG ZATAJENJA?

S A Ž E T A K

Hemodijalizirani bolesnici imaju često kvantitativne, a još češće kvalitativne poremećaje serumskih lipida. Najčešće su im povišeni trigliceridi i VLDL-kolesterol, mini-malno povišen ili normalan ukupni i LDL-kolesterol i snižen HDL--kolesterol. U ovom radu uspoređivali smo lipidni profil dvije skupine hemodijaliziranih bolesni-ka, jedne iz kontinentalnog, a druge iz primorskog dijela zemlje. Cilj nam je bio odrediti je li na njihov lipidni profil utječu razlike u njihovoj prehrani. U istraživanje su uključena 72 bolesnika iz kontinentalnog (m-39) i 50 iz primorskog dijela zemlje (m-30). Nisu bili uključeni šećerni bolesnici, bolesnici s hipotireozom, jetrenim bolestima, alkoholičari i bolesnici liječeni sevelamerom. Svakom bolesniku, uz osnovne po-datke, određen je natašte, prije redovite hemodijalize, niz laboratorijskih parametara. Svi su bolesnici dijalizirani bikarbonatnom hemodijalizom polisulfonskim dijalizatorima niske permeabilnosti. Bolesnici kontinentalne skupine bili su nešto stariji, dulje liječeni ponavljanim hemo-dijalizama, niži, teži, većeg indeksa tjelesne mase, višeg ukupnog (4,70±0,91:4,42±1,02 mmol/L) i LDL-kolesterola (2,78±0,74:2,66±0,75 mmol/L), a nižih triglicerida (1,72±0,84:1,81±0,83 mmol/L) i HDL-kolesterola (1,13±0,42:1,16±0,54 mmol/L), ali bez statistički značajne razlike. Prema χ^2-testu češće su jeli svinjsko meso, slaninu, suhomesnate proizvode, margarin, maslac, orahe, bademe, češnjak, vrhnje i punomasne sireve, a rijeđe ribu. Hranu su značajno češće pri-premali na svinjskoj masti i suncokretovom ulju. Skoro svaki 4. bolesnik kontinentalne skupi-ne uzimao je statine, a samo svaki 25. iz primorske skupine bolesnika. Prema χ^2-testu u pod-skupinama bolesnika nije bilo razlike udjela onih sa ukupnim kolesterolom iznad 5,20 mmol/L, trigliceridima iznad 1,60 mmol/L, HDL-kolesterolom ispod 1,10 mmol/L, LDL kolesterolom iznad 2,60 mmol/L, pretilih, a ni pothranjenih bolesnika. U zaključku možemo, na osnovi rezultata dobivenih našim ispitivanjem reći da prehra-na ipak bitno utječe na lipidni profil hemodijaliziranih bolesnika. Naime, bolesnici kontinen--talne skupine imaju lipoproteine plazme vrlo slične lipoproteinima plazme bolesnika primor-ske skupine, od koji se značajno razlikuju po prehrani, samo zahvaljujući značajno češćem uzimanju statina. Utjecaj završnog stadija KBZ i hemodijalize kao metode liječenja nije dominantniji od prehrane.