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Atherogenic lipids and apolipoprotein parameters in hemodialysis and CAPD patients

The lipoprotein metabolism is altered in patients with chronic renal insufficiency, as well in patients on maintenance hemodialysis patients (1,5,8). Lipid abnormalities often persist or aggregate during the renal replacement treatment. The aim of our study was the comparison of lipid parameters between hemodialysis (HD) patients, and continuous peritoneal dialysis (CAPD) patients.

MATERIAL AND METHODS

CAPD patients. A total of 30 patients (17 female, 13 male: mean age 52.2±15.1, ranging from 26 to 80 years) receiving CAPD were studied. The average duration of CAPD treatment was 23±18.4 months (ranging from 3 to 62 months).

Underlying renal disease in the patients included chronic glomerulonephritis (n=16), diabetic nephropathy (n=9), chronic interstitial nephritis (n=5), polycystic kidney disease (n=2), obstructive nephropathy (n=2), and Wegener granulomatosis (n=1). The patients were dialyzed continuously using 2-L or 2.5 L plastic bags of Baxter. The prescribed daily dialysate volume was 8 liters in 16 patients, 10 liters in 8 patients, 12.5 liters in 5 patients, and 6 liters in one patient. Solution containing 1.36% or 3.86% glucose was administered depending on the individual need for ultrafiltration. The urine volume was 530±480 ml/24h (range 0–2000 ml/24h), seven patients were anuric. Fourteen patients suffered from coronary diseases. Nine patients suffered from thyroid or liver disease, and all patients under study were free of peritonitis. No patients were treated with any lipid-lowering drugs. The majority of the patients were given calcium carbonate, multivitamins and antyhypertensive medications, either calcium channel blockers or converting antagonists.

HD patients. We studied 40 stable patients on HD (19 female, 21 male) with an average age of 47.9 years (range 20 to 70 years). The mean duration of HD 22.5 months (range 5 to 68 months). The underlying cause of chronic renal failure included chronic glomerulonephritis in 16 patients, diabetic nephropathy in 3 patients, nephrosclerosis in 2 patients, polycystic kidney disease in 3 patients, obstructive nephropathy in 6 patients, chronic interstitial nephritis in 8 patients, and miscellaneous in 2 patients.

Hemodialysis was performed 4 hours per session, three times per week, all using polysulfone hollow fibre dialyzers with bicaronate containing dialysate. The mean urine volume was 460 ml/24 h (range 0–1000 ml/24 h). Nine patients were anuric. Patients received no other medication except polyvitamins, phosphate binders and calcitriol. In hypertensive dialysis patients angiotensin enzyme inhibitors, calcium channel blockers or both were also given. Twenty seven hemodialysis patients were on erythropoietin. The control subjects were 30 healthy individuals matched

for age (mean age 51.7±8.6 years) and gender (15 female and 15 male) who had no known disease and who were not taking any medication.

Blood samples were taken from patients and controls after a 14-hour overnight fast for the determination of lipid parameters. Following parameters were estimated in plasma total cholesterol (TC), triglicerides (TG), high density lipoprotein cholesterol (HDL-C), apolipoprotein A (Apo AI), and apolipoprotein B (Apo B). The TC/HDL-C ratio, LDL-C/HDL-C ratio, Apo AI/ApoB ratio, LDL-C/ApoB ratio, and HDL-c/Apo AI ratio were also evaluated.

Routine laboratory parameters such as the level of urea, uric acid, creatinine and albumin were determined by using Roche Cobas Integra Analyser, and electrolyte concentrations with ionoselective electrodes Kone analyser. The results of routine laboratory parameters are shown in Table 1. Lipids and lipoproteins were also determined on Cobas Integra analyzer. Total cholesterol was determined by enzymatic-colorimetric method (cholesterol CHOD – PAP, Roche). HDL-cholesterol were determined after precipitation with phosphotungstic acid and magnesium ions, and LDL-cholesterol was calculated according to the friedewald formula. Triglicerides were determined enzymatically by Roche Kit. Apo AI and Apo B were also measured using turbidimetric methods with Roche Kit. All results were subjected to analysis of variance and Tukey's test. The relationships among the lipoprotein parameters were determined by the linear correlation coefficient.

RESULTS

Lipid and lipoprotein in the control group as well as in the CAPD patients are summarized in table 2. Blood urea nitrogen, creatinine, and uric acid levels in the CAPD patients were lower than those in the HD patients. A significant difference was found in serum albumin level between the controls, HD and CAPD patients (Table 1). Both groups of dialysis patients had increased serum triglycerides and decreased levels of HDL-C and Apo A1 compared to the controls. Moreover, the risk ratios TC/HDL-C and LDL-C/HDL-C were significantly higher, and the ratio Apo AI/Apo B was significantly lower in both group of patients in comparison to the normal subjects. Both groups of dialysis patients exhibited decreased ratio of HDL-C/Apo AI suggesting the presence of compositional lipoprotein changes. CAPD patients displayed heightened atherogenic lipid profile compared to hemodialysis patients. They exhibited higher levels of TC, LDL-C and Apo B as well as of the ratios TC/HDL-C and LDL-C?HDL-C, and lower levels of the ratio Apo AI/ApoB compared to hemodialysis patients.

Table 1.The clinical and routine laboratory parameters in controls, HD and CAPD patients
$p< 0.05$, a – versus controls, b – versus HD

	Controls (n=30)	HD (n=40)	CAPD (n=30)
Na (mmol/l)	139.90 ±1.17	137.38 ± 3.23^{a}	140.80 ± 3.50^{b}
K (mmol/l)	4.35 ± 0.19	5.17 ± 0.69^{a}	4.41 ± 0.55^{b}
Cl (mmol/l)	99.14 ± 23.00	112.19 ± 7.27^{a}	98.00 ± 3.60^{b}
P (mmol/l)	3.16 ± 0.50	6.96 ± 2.17^{a}	6.04 ± 1.34^{ab}
Urea (mg/dl)	24.40 ± 5.68	150.46 ± 32.96^{a}	109.29 ± 37.53^{ab}
Creatinine (mg/dl)	0.82 ± 0.11	10.91 ± 2.11^{a}	9.49 ± 0.94^{ab}
Uric acid (mg/dl)	3.98 ± 1.03	6.42 ± 1.24^{a}	5.24 ± 0.57^{ab}
Albumin (g/dl)	4.74 ± 0.25	4.42 ± 0.35^{a}	3.93 ± 0.58^{ab}
Kt/V	-	1.21 ± 0.32	2.16 ± 0.31^{b}

Table 2. Serum lipoproteins parameters in controls, HD and CAPD patients

	Controls (n = 30)	HD (n = 40)	CAPD (n = 30)
TG (mg/dl)	94.26±41.9	168.74±82.17[a]	218.19±99.7[ab]
TC (mg/dl)	177.27±21.20	170.58±42.6	213.04±41.40[ab]
LDL-C (mg/dl)	100.83±21.7	103.34±31.59	133.65±34.4[ab]
HDL-C (mg/dl)	55.14±10.69	34.80±10.52[a]	37.79±9.60[a]
Apo AI (mg/dl)	152.00±19.90	124.26±20.05	132.67±19.37[a]
Apo B (mg/dl)	92.32±12.75	94.58±24.43	115.57±22.63[ab]
TC/HDL-C	3.33±0.70	5.22±2.09[a]	5.96±1.79[a]
LDL-C/HDL-C	1.94±0.65	3.24±1.58[a]	3.74±1.25[a]
ApoAI/ApoB	1.77±0.42	1.38±0.33[a]	1.18±0.24[ab]
HDL-C/ApoAI	0.36±0.04	0.28±0.05[a]	0.29±0.05[a]

$p < 0.05$, a – versus controls, b – versus HD

The significant correlation coefficients among various serum lipoprotein parameters in CAPD patients are summarise in Table 3. The significant correlation coefficients among various serum lipoprotein parameters in HD patients are summarisedin Table 4. The length of the CAPD treatment (more or less than 24 months) did not make any noticeable difference in any of the measured parameters.

Table 3. The significant correlation coefficients among various serum lipoproteins parameters in CAPD patients (r and p)

	TG	TC	LDL	HDL	ApoAI	ApoB	TC/ HDL-C	LDL-C/ HDL-C	ApoAI /ApoB	HDL-C/ ApoAI
Albumin		0.73 (0.001)	0.70 (0.001)			0.69 (0.001)			-0.46 (0.05)	
TG	-						0.56 (0.05)			
TC		-	0.95 (0.001)		0.45 (0.05)	0.94 (0.001)		0.47 (0.05)	-0.66 (0.01)	
LDL-C			-			0.95 (0.001)		0.54 (0.05)	-0.71 (0.001)	
HDL-C				-	0.77 (0.001)		-0.73 (0.001)	-0.64 (0.01)		0.83 (0.001)
ApoAI					-		-0.48 (0.05)			
ApoB						-		0.54 (0.05)	-0.76 (0.001)	
TC/ HDL-C							-	0.96 (0.001)	0.80 (0.001)	-0.78 (0.001)
LDL-/ HDL-C								-	-0.85 (0.001)	-0.74 (0.001)
ApoAI/ B									-	0.48 (0.005)
HDL-C/ ApoAI										-

Table 4. The significant correlation coefficients among various serum lipoproteins parameters in HD patients (r and p)

	TG	TC	LDL	HDL	ApoAI	ApoB	TC/ HDL-C	LDL-C/ HDL-C	ApoAI/ ApoB	HDL-C/ ApoAI
Albumin	0.39 (0.05)					0.38 (0.05)	0.38 (0.05)			
TG	-	0.66 (0.001)	0.49 (0.001)			0.70 (0.001)	0.72 (0.001)	0.50 (0.01)	-0.72 (0.001)	-0.48 (0.01)
TC		-	0.92 (0.001)		0.47 (0.01)	0.93 (0.001)	0.61 (0.001)	0.55 (0.01)	-0.59 (0.001)	
LDL-C			-			0.91 (0.001)	0.70 (0.001)	0.74 (0.001)	-0.65 (0.001)	
HDL-C				-	0.82 (0.001)		-0.61 (0.001)	0.55 (0.01)	0.54 (0.01)	0.82 (0.001)
ApoAI					-					0.40 (0.05)
ApoB						-	0.76 (0.001)	0.71 (0.001)	-0.80 (0.001)	
TC/ HDL-C							-	0.90 (0.001)	-0.86 (0.001)	-0.73 (0.001)
LDL-C/ HDL-C								-	-0.80 (0.001)	-0.64 (0.001)
ApoAI/ ApoB									-	0.53 (0.01)
HDL-C/ ApoAI										-

DISCUSSION

Cardiovascular disease remains the most common cause of death in maintenance dialysis patients (7,12). Lipid disturbance is one of the most important risk factors for atherosclerotic cardiovascular disease. The lipoprotein metabolism is altered in patients with chronic renal insufficiency as well as in patients on maintenance dialysis and CAPD patients (5,8). The cause of dyslipidemia in hemodialysis and CAPD is multifactorial. The main metabolic abnormality of the lipoprotein profile is a delayed catabolism of triglicerydes-rich Apo B containing lipoproteins. It results from the decreased activity lipolytic enzymes such as lipoprotein lipase (LPL), and hepatic triglyceride lipase (3,11). The activity of the lecitin-cholesterol acyl transferase (LCAT), an enzyme responsible for cholesterol escerification, may also be reduced in uremia (13).

Our patients had increased serum triglycerydes and decreased HDL-C levels compared to control subjects. Low levels of HDL cholesterol are most likely due to hypertriglyceridemia, as there is a good inverse correlation between triglycerides and HDL cholesterol levels. Low HDL cholesterol levels in uremic patients could also be attributed to other mechanism such as decreased hepatic lipase activity and LCAT, and decreased Apo AI synthesis (9). Apo AI levels were decreased in our hemodialysis and CAPD patients when compared to the controls, the ratio of HDL/Apo AI was also significantly lower. These findings imply the existence of qualitative changes in the composition of the HDL-C. The total and LDL cholesterol levels were not different in our HD patients and the controls. Our CAPD patients had a more atherosclerotic lipid profile compared to hemodialysis patients. It has been suggested that increased lipid synthesis contributes to the hyperlipidemia in CAPD patients (10). Such synthesis may result from glucose load to which these patients are exposed as well as from the continuous loss of albumin through the peritoneal membrane, which may result in a non-specific stimulation of hepatic protein synthesis including apolipoproteins, causing increased lipoprotein levels.

A loss of protein into the dialysate, growing higher as the molecular weight decreases, results in preferential loss of high-density lipoprotein (HDL) (6). Loss of carnitine, which plays an important role in facilitating the transport of fatty acid through the inner mitochondrial membrane prior to B-oxidation, may also contribute to their hypertriglyceridemia (4).

Bloembergen et al. (2) showed that five causes of death including myocardial infarction and cerebrovascular disease, were significantly higher in peritoneal dialysis treated patients, compared with hemodialysis treated patients. According to our study, no difference was found between groups of patients who were on renal replacement therapy for long or a short period of time.

CONCLUSIONS

1. HD and CAPD patients have abnormal serum lipids and lipoprotein profile.
2. Dyslipidemia may contribute to the high incidence of cardiovascular disease observed in this population.
3. CAPD patients exhibited more atherogenic lipid profile than the HD patients.
4. Changes in lipoprotein metabolism associated with CAPD appear early during the course of treatment.

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SUMMARY

Lipid abnormalities often complicate chronic renal failure and they persist or aggravate during renal replacement treatment. Serum lipid and apolipoprotein profiles including triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDLC), apolipoproteins (Apol and Apo B) were determined in 30 CAPD patients, 47 HD patients and 30 healthy subjects. The TC/HDL-C ratio, LDL-C/ HDL-C ratio, ApoAI/ApoB ratio, LDL-C/ApoB ratio, and HDL-C/ApoAI ratio in these three groups were also evaluated. There was a significant increase in TG ($p<0.001$), TC/HDL-C, LDL-C/HDL-C and decrease in HDL-C, ApoAI and ApoB and HDL-C/ApoAI ratios comparing HD patients to the control group. There were increased TG, TC, LDL, ApoB, TC/HDL-C ratio and LDL-C/HDL-C ratio and LDL-C/HDL-C ratio, and decreased HDL-C, ApoAI and ApoAI/ApoB, HDL-C/Apo AI ratios in CAPD patients as compared to normal subjects. Otherwise, there were significantly higher TG, TC, LDL-C, ApoB and LDL-HDL-C ratio in CAPD patients as compared to those of HD patients. There was a significant inverse correlation between TG and HDL-C ($r=-0.48$ $p<0.01$). No differences were observed in the values of the lipid parameters between patients who were on hemodialysis or CAPD for either more or less than 20 months. We conclude that dyslipidemia may contribute to high incidence of cardiovascular disease observed in this population. CAPD patients exhibit a more atherogenic lipid profile than that of HD patients.

Parametry lipidowe i apolipoproteiny u pacjentów hemodializowanych i leczonych CADO

Zaburzenia lipidowe często wikłają przewlekłą niewydolność nerek i są obecne lub nasilają się w czasie leczenia nerkozastępczego. Oznaczano osoczowy profil lipidów, obejmujący trójglicerydy (TG), całkowity cholesterol (TC), lipoproteiny o wysokiej gęstości (HDL-C), lipoproteiny o małej gęstości (LDL), apolipoproteiny (Apo AI i ApoB) u 30 pacjentów leczonych CADO, 47 HD pacjentów i 30 osób zdrowych. Określano stosunek TC/HDL-C, LDL-C/ HDL-C, ApoAI/ApoB, LDL-C/ApoB i HDL-C/ApoAI we wszystkich trzech grupach. Stwierdzono u HD pacjentów w porównaniu ze zdrową grupą istotny statystycznie wzrost stężenia TG ($p< 0,001$) TC/HDL-C, LDL-C/HDL-C i spadek stężenia HDL-C, ApoAI i ApoB oraz stosunku HDL-C/ApoAI. U pacjentów leczonych CADO w porównaniu z grupą zdrową stwierdzono wzrost stężenia TG, TC, LDL, ApoB, stosunku TC/HDL-C, LDL-C/HDL-C i LDL-C/HDL-C i spadek stężenia HDL-C, ApoAI i stosunku ApoAI/ApoB oraz HDL-C/Apo AI. Poza tym stwierdzono istotnie wyższe stężenie TG, TC, LDL-C, ApoB i stosunku LDL-C/HDL-C u pacjentów dializowanych CADO w porównaniu z pacjentami HD. Stwierdzono istotnie statystycznie odwrotną korelację między TG i HDL-C ($r= - 0,48$ $p< 0,01$). Nie obserwowano różnic między wartościami parametrów lipidowych zarówno wśród pacjentów hemodializowanych, jak leczonych CADO dłużej, jak i mniej niż 20 miesięcy. Wnioskujemy, że dyslipidemia może powodować wysoką zapadalność na choroby serca, obserwowaną w populacji pacjentów leczonych CAPD. Pacjenci leczeni CADO mają bardziej miażdżycowy profil lipidowy niż pacjenci leczeni HD.