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Hyperlipidaemia in Uraemic Patients under Chronic Haemodialysis

Correlation with Serum Lipoprotein Lipase and Insulin Levels

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Hyperlipidaemia is implicated in vascular complications of uraemic patients on haemodialysis. In this work serum lipids, serum lipoprotein lipase (LPL) and insulin levels were measured in 45 chronic uraemic patients on haemodialysis and 44 healthy volunteers. A significant rise in total lipids (TL), cholesterol and triglycerides (TG) was detected in the haemodialysis patients, but no changes were found in either serum phospholipids or high density lipoprotein cholesterol (HDL-chol.). The rise in TL, TG and cholesterol was positively correlated with the duration of dialysis but not with age or sex. On the other hand, a significant rise was also observed in serum LPL and insulin levels but with no correlation between any of them and the lipid levels. From this study it may be apparent that other factors rather than LPL abnormalities may be implicated in hyperlipidaemia in uraemic patients under haemodialysis.

Introduction

Hyperlipidaemia has been recognized in patients with renal disease for over a century. In some chronically uraemic patients, large light-scattering triglyceride-rich fat particles may accumulate in sufficient numbers to cause plasma lactescence [1]. However, ethnic or geographical difference might exist in the lipid patterns of dialysis patients [2]. The precise mechanism(s) causing hypertriglyceridaemia in patients with renal failure remains unknown [3].

The aim of this work was to study the serum lipid changes in Egyptian chronic uraemic patients on haemodialysis. In addition, circulating insulin level and serum lipoprotein lipase were estimated in an attempt to study some of the possible mechanisms underlying these changes.

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Material and methods

The study included 45 chronic uraemic patients under chronic haemodialysis treatment in the Urology and Nephrology Center, Mansoura University. Their age varied between 14 and 42 years. In addition, 44 healthy volunteers of nearly the same age and sex distribution were taken as a control group.

After an overnight fasting, blood samples were taken and centrifuged to separate the serum. Serum samples were subjected to total lipids (TL), triglycerides (TG), phospholipids, high density lipoprotein-cholesterol (HDL-chol.) and serum lipoprotein lipase (LPL) determinations [4, 5, 6, 7, 8]. Cholesterol estimation was done by an enzymatic method using bioMerieux Kit (Ref. 61224), while the immunoreactive insulin was determined by an immunoassay method using Wako Kit, Code No. 228-88909.

Statistical analysis was done by both the standard *t*-test and Spearman's rank correlation coefficient [9].

Results

Serum total lipids (TL) (Table 1)

In the control group the mean value was 473 ± 121 mg/100 ml and in the haemodialysis group it was 722 ± 475 mg/100 ml. This rise was statistically highly significant ($P < 0.005$).

Table 1

Serum TL, cholesterol, TG, phospholipids and HDL-chol. levels in haemodialysis patients and the control group

Group	TL (mg%)	Cholesterol (mg%)	TG (mg%)	Phospholipids (mg%)	HDL-chol. (mg%)
Control					
Mean ± S.D.	473±121	173±56	179±93	174±53	22.2±12.7
No.	23	27	29	34	22
Ch. R. F. on haemodialysis					
Mean ± S.D.	722±475	256±158	413±614	184±59	25.5±20.2
No.	34	29	24	23	31
T	3.22	3.02	1.88	1.60	0.95
P	<0.005	<0.005	<0.05	>0.05	>0.05

TL = total lipids
TG = triglycerides
HDL-chol. = high density lipoprotein cholesterol
Ch. R. F. = chronic renal failure

Serum triglycerides (TG) (Table 1)

The mean value was 179 ± 93 mg/100 ml in the control group and 413 ±614 mg/100 ml in the haemodialysis group. The difference was also statistically significant ($P < 0.05$).

Serum cholesterol (Table 1)

The mean value was 173 ± 56 mg/100 ml in the control group and 256 ±158 mg/100 ml in the haemodialysis group. The difference was statistically significant ($P < 0.005$).

Serum phospholipids (Table 1)

The mean value was 174 ± 53 mg/100 ml in the control group and 184 ± 59 mg/100 ml in the dialysis group. The difference was statistically insignificant.

Serum high density lipoprotein cholesterol (HDL-chol.) (Table 1)

The mean value was 22.24 ± 12.7 mg/100 ml in the control group and 25.5 ± 20.2 mg/100 ml in the haemodialysis group. The difference was statistically insignificant.

Serum lipoprotein lipase (LPL) (Table 2)

The mean value was 61.67 ± 24.29 U/l in the control group and 197.53 ± 155.71 U/l in the haemodialysis group. The difference was statistically highly significant ($P < 0.005$).

Table 2

Lipoprotein lipase (LPL) and insulin levels in haemodialysis patients compared to controls

Group	Lipase (U/2)	Insulin (NU/2)
Control		
Mean ± S.D.	61.67±24.29	39.64±17.39
No.	18	9
Ch. R. F. on haemodialysis		
Mean ± S.D.	197.53±155.71	63.24±36.16
No.	24	18
T	4.35	3.78
P	<0.005	<0.005

Serum insulin level (Table 2)

The mean value was 39.64 ± 17.39 NU/ml in the control group and 63.24 ± 36.16 NU/ml in the haemodialysis group. The difference was statistically significant ($P < 0.005$).

Correlative study (Tables 3–6)

No correlation was detected between the different lipoproteins studied in this work and either the LPL or the serum insulin levels. Also, no correlation was found between the lipoprotein lipids involved in this study and the patient's age or sex. However, there was a strong positive correlation between the duration of dialysis and TL ($P < 0.02$); TG ($P < 0.002$) and serum cholesterol ($P < 0.01$).

Table 3

Spearman's rank correlation coefficient (r_s); relationship between different lipoprotein lipid levels and plasma lipoprotein lipase in haemodialysis patients

	TL	Cholesterol	TG	Phospholipid	HDL-chol.
r_s	0.01	0.2	0.19	0.057	0.05
No.	19	12	7	16	12

Table 4

Spearman's rank correlation coefficient (r_s); relationship between different lipoprotein lipid levels and plasma lipoprotein lipase in haemodialysis patients

	TL	Cholesterol	TG	Phospholipid	HDL-chol.
r_s	0.224	−0.03	0.103	−0.109	−0.334
No.	14	14	12	14	8

Table 5

Spearman's rank correlation coefficient (r_s); relationships between either the patient's age or the duration of dialysis and the lipoprotein lipid levels in haemodialysis patients

	Age			Duration of haemodialysis		
	TL	Cholesterol	TG	TL	Cholesterol	TG
r_s	0.02	−0.023	0.241	0.467*	0.557**	0.673***
No.	27	22	19	27	22	19

* $P < 0.02$
** $P < 0.01$
*** $P < 0.002$

Table 6

Lipoprotein lipids levels in male and female patients

	Total lipids		Cholesterol		Triglyceride	
	M	F	M	F	M	F
Mean	708.65	766.250	245.20	253.90	341.2	226.0
No.	26	8	22	9	10	6
S.D. ±	529.92	247.193	179.02	83.59	438.0	93.8
T	1.024		0.33		1.2	
P	>0.05		>0.05		>0.05	

M = males
F = females

Discussion

Cardiovascular diseases are common in patients with chronic renal failure treated by dialysis and transplantation. Considerable attention has been paid to the factors involved in this process, with a view both to reducing the morbidity and mortality of chronic uraemia and to throw light on the cause of the atherosclerotic process itself. One of the most important possible factors is hyperlipidaemia that frequently occurs in chronic renal failure [10, 11].

In our study, significant hyperlipidaemia was seen in haemodialysis patients in comparison with the control group; also the TL level as well as the serum TG and serum cholesterol were not correlated with the patient's age or sex. However, the lipid levels TL, TG and cholesterol correlated significantly with the duration of dialysis ($P < 0.02$; $P < 0.002$ and $P < 0.01$, respectively). This is against the observation of Rapoport et al. [11] that there is apparently no relationship between the length of dialysis and hyperlipidaemia.

Carlson and Bottiger [12] found that in general the risk of developing ischaemic heart disease increased with increasing fasting plasma TG concentration. In the present study a highly significant rise of TG was detected in haemodialysis patients in comparison with the control group.

Another important risk factor for developing ischaemic heart disease is the rise in plasma cholesterol level [12, 13]. In our work, significant hypercholesterolaemia was observed in haemodialysis patients in comparison with the control group, and this is in agreement with the finding of other workers [14]. On the other hand, no significant difference was found in serum phospholipids between the two groups, which was previously reported by Reinold et al. [15].

Epidemiologic studies have shown that plasma HDL concentration is negatively correlated with the risk of acquiring ischaemic heart disease [16]. In the majority of the previous works low levels of HDL-cholesterol were detected in

uraemia and haemodialysis patients [11, 17]. In our study, no significant changes in HDL-cholesterol were found in haemodialysis patients. However, qualitative abnormalities were previously reported in the distribution of aproproteins in HDL in haemodialysis patients and this abnormal HDL composition may be a major factor in atherosclerosis of these patients [11].

The precise mechanism(s) causing hypertriglyceridaemia in renal failure remain unknown [3]. It could be due to either increased TG production by the liver and/or reduced peripheral removal.

It was suspected that increased hepatic synthesis may be a factor causing hypertriglyceridaemia. Kinetic studies, however, indicated that in most renal failure patients the TG production is not increased [10]. In the present study the rise of the insulin level was more significant in the haemodialysis than in the control group, but the insulin level was not correlated with lipoprotein lipid levels. In addition, the finding that elevated insulin levels in some uraemic patients result from a disproportionate increase of proinsulin [18] make the hypothesis of insulin-TG synthesis less tenable.

It is well established that both qualitative and quantitative abnormalities in LPL, the tissue enzyme system which mediates TG removal, are present in renal failure patients [1]. Very low plasma lipolytic activity levels in dialysis patients was previously described [19]. However, in a total of 110 patients with chronic renal failure, Sommer et al. [20] found hyperlipidaemia in 46.4% of cases and the degree of reduction of renal function was positively correlated to the frequency of hyperlipidaemia as well as to the elevation of the lipase activity in serum. In the present study a significant rise was observed in serum LPL in haemodialysis patients in comparison to the control group, and the level of LPL was not correlated with the lipoprotein lipid levels. However, in addition to the qualitative abnormalities in LPL which was previously reported, other factors also appear to compromise LPL functionally in uraemia [10, 11].

From the above data it may be apparent that the predominant mechanism responsible for hyperlipidaemia in haemodialysis patients is a defective removal rather than increased synthesis; there is also a relationship between the length of dialysis and hyperlipidaemia. It may be apparent that other factors rather than LPL abnormalities may play a role in defective TG removal. A great deal of attention has recently been directed toward the possibility that an impairment in the cellular oxidation of fatty acids resulting from carnitine deficiency also might contribute to hyperlipidaemia in uraemic patients treated by dialysis. This carnitine deficiency is especially found in long-term haemodialysed patients [21] and this may explain the relationship between the length of dialysis and the degree of hyperlipidaemia observed in this study. There are recent reports of successful improvement of lipid abnormalities in haemodialysis patients by L-carnitine supplementation [22, 23] and this may be a point for further investigations.

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