LIPID ABNORMALITIES IN CHRONIC RENAL FAILURE ASSOCIATED WITH SPINAL CORD INJURY

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Abstract. Serum lipid fractions were studied in ten patients with chronic renal failure (CRF) associated with long-standing spinal cord injury (SCI). A group of age-and-sex-matched patients with long-standing SCI but normal renal function were included for comparison. Serum triglycerides were markedly elevated in SCI-CRF patients. Both SCI groups exhibited moderate hypocholesterolemia. High density lipoprotein (HDL) cholesterol was severely reduced in the SCI-CRF group and moderately reduced in the SCI-control group. Chronic renal failure, reduced physical activity and several other factors may be operative in the genesis of hypertriglyceridemia and reduced HDL-cholesterol levels in this condition. Further investigations are necessary to examine the possible effect of these lipid abnormalities on the cardiovascular system in these patients.

Key words: Spinal cord injury; Chronic renal failure; Hemodialysis; Lipid disorders.

Introduction

LIPID metabolism is abnormal and mortality from cardiovascular disease is increased in patients with chronic renal failure treated with dialysis or transplantation (Lindner *et al.*, 1974; Lowrie *et al.*, 1974; Bierman & Brunzell, 1978). Elevated serum triglycerides, normal or reduced total cholesterol, increased triglyceride-rich very low density lipoprotein (VLDL), increased high density lipoprotein (HDL)-triglycerides and reduced HDL-cholesterol have all been demonstrated in ambulatory dialysis patients (Lewis *et al.*, 1966; Bagdade *et al.*, 1968; Losowsky & Kenward, 1968; Brons *et al.*, 1972; Ibels *et al.*, 1975; Daubresse *et al.*, 1976; Bagdade *et al.*, 1976; Brunzell *et al.*, 1977; Bagdade *et al.*, 1977; Vaziri *et al.*, 1980). Long-term physical exercise programs have been shown to lower serum total triglycerides and VLDL-triglycerides and increase HDL-cholesterol in dialysis patients (Goldberg *et al.*, 1979) as well as the nonuremic individuals (Holloszy *et al.*, 1964; Lopez *et al.*, 1974; Gyntelberg *et al.*, 1977; Erklens *et al.*, 1978).

Long-standing spinal cord injury (SCI) can cause chronic renal failure (CRF) due to the associated neuropathic bladder dysfunction, chronic pyelonephritis, urolithiasis and secondary amyloidosis. In addition to uremia, several other factors can potentially influence lipid metabolism in this setting. These include relative physical hypoactivity, possible systemic amyloidosis, peculiar nature of renal pathology and characteristics of residual renal function to mention a few. To our knowledge, data on lipid metabolism in CRF associated with SCI are lacking. Here we report our data on the subject.

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Patients and Methods

Ten paraplegic men with advanced chronic renal failure aged 59 ± 12 years were studied (Table I). Patients with diabetes mellitus, hypothyroidism, discernible liver disease and alcoholism were excluded. Five of the ten patients had creatinine clearances between 4 and 8 ml/minute and required maintenance hemodialysis. These patients received dialysis treatment for 4 hours, 2 to 3 times a week. A single-pass dialysate delivery system, a glucose-free acetate-based

TABLE I
Clinical Data

Patients	Age (yrs.)	Level of SCI	Duration of SCI (yrs.)	Duration dialysis (months)	Creatinine clearance (ml/min)	Serum albumin (g/dl)	24-hr Urine protein (g/day)	Blood pressure (mmHg)
1	71	C5	36	9	6.0	2.3	1.0	168/110
2	62	T5	37	6	5.0	2.7	3.1	125/65
3	69	T12	22	4	4.0	3.2	1.0	145/90
4	57	C5-6	23	3	6.0	2.9	2.1	170/85
5	68	C5-6	28	18	4.0	3.2	0.7	135/70
6	57	C4-5	21	—	10.0	3.1	1.4	168/95
7	46	C5	18	—	22.0	3.5	0.4	120/75
8	60	C5-6	34	—	12.0	3.2	1.1	185/80
9	32	C5	13	—	17.0	3.5	0.6	165/85
10	68	C5	36	—	18.0	3.5	0.9	145/83

dialysate, and hollow fibre or parallel flow dialysers with 1.2-2.5 m surface areas² were used. The remaining five patients had creatinine clearances ranging from 10 to 22 ml/minute and did not require dialysis. Dietary restrictions were limited to sodium, potassium and fluid intakes as needed to control fluid overload and hyperkalemia. No protein or caloric restrictions were imposed. Aluminium carbonate was prescribed to control hyperphosphatemia and multivitamin, folic acid, pyridoxine and oral or parenteral iron supplements were administered.

The etiology of chronic renal failure was presumed to be chronic pyelonephritis with or without amyloidosis. Urinary protein excretion ranged from 0.4 to 3.1 g/day. All patients had chronic pyuria and bacteriuria. They were free of acute illnesses and stress at the time of the study and for several weeks previously.

A control group of age- and sex-matched patients with spinal cord injury, but without significant renal failure (creatinine clearance = 86 ± 14 ml/min) were included for comparison. The lipid values from the SCI patients with and without renal failure were compared with those previously reported on normal population and hypertriglyceridemic individuals (Goldstein *et al.*, 1973; Albers *et al.*, 1976).

Venous blood samples for lipid analyses were obtained following a 14-hour fasting period. In patients undergoing maintenance dialysis blood samples were drawn before the dialysis session which was preceded by the longest interdialytic interval (3 to 4 days). Serum cholesterol and triglyceride concentrations and HDL-cholesterol were measured as previously described (Goldstein *et al.*, 1973; Albers *et al.*, 1976).

Linear regression and a *t*-test were used in statistical analysis of the data. All data are expressed as mean $\pm$ standard deviation.

Results

The results are displayed in Table II. Serum total triglyceride concentration in the SCI patients with chronic renal failure (180 ± 96 mg/dl) was significantly ($P < 0.05$) higher than the values obtained in the SCI patients without renal failure (100 ± 22 mg/dl), and those previously reported in the age- and sex-matched normal individuals (104 ± 4 mg/dl; $P < 0.05$). There was no significant difference in the serum triglyceride levels between the SCI patients without renal disease and their age- and sex-matched normal control individuals.

There was no significant difference in serum cholesterol between the SCI patients with renal failure (152 ± 56 mg/dl) and SCI patients without renal failure (142 ± 18 mg/dl). However, serum cholesterol levels in both SCI groups were significantly lower than those established for their age- and sex-matched normal control individuals (224 ± 12 mg/dl).

HDL-cholesterol was significantly ($P > 0.001$) lower in the SCI patients with renal failure (12 ± 8 mg/dl) than that found in the SCI patients without renal failure (31 ± 9 mg/dl). HDL-cholesterol levels in both SCI groups were significantly lower than those found in their age- and sex-matched normal control

TABLE II

Comparison of the lipid data in SCI patients with chronic renal failure, SCI patients without renal failure, and age- and sex-matched normal control group

Patients	Triglycerides mg/dl	Cholesterol mg/dl	HDL-Cholesterol mg/dl
1	130	133	10.0
2	174	164	31.5
3	164	163	8.3
4	142	97	7.5
5	162	149	6.8
6	73	69	7.5
7	158	140	11.7
8	185	164	8.0
9	167	158	18.0
10	440	284	83.0
Mean $\pm$ SD	180 ± 96	152 ± 56	12 ± 8
SCI Control Group	100 ± 22	142 ± 18	31 ± 9
Normal Control	104 ± 4	224 ± 12	49 ± 4
<i>P</i> values:			
SCI-CRF			
v.			
SCI-Control	< 0.05	N.S.	< 0.001
SCI-CRF			
v.			
Normal Control	< 0.05	< 0.01	< 0.001
SCI-Control			
v.			
Normal Control	N.S.	< 0.001	< 0.02

individuals (49 ± 4 mg/dl). Since the SCI-CRF patients had marked hypertriglyceridemia, which is known to lower HDL-cholesterol, we compared their HDL-cholesterol levels with these established in hypertriglyceridemic but otherwise normal individuals. HDL-cholesterol in the SCI group was significantly lower ($P < 0.001$) than that of the control hypertriglyceridemic individuals (37 ± 1.3 mg/dl).

Within the SCI group with chronic renal failure, no significant difference was found between the dialysed and undialysed patients with respect to the serum lipid fractions studied.

Systolic blood pressure in the study group (159 ± 21 mmHg) was significantly ($P < 0.02$) higher than the control SCI group (135 ± 18 mmHg). The respective values for diastolic blood pressure (82 ± 10 and 77 ± 11 mmHg), however, were not significantly different.

Discussion

Serum triglyceride level in the SCI patients with chronic renal disease was significantly higher than those found in the SCI patients without renal failure and the age- and sex-matched normal individuals. This observation is consistent with the expected influence of uremia on triglyceride metabolism (Bagdade *et al.*, 1968; Brons *et al.*, 1972; Daubresse *et al.*, 1976; Vaziri *et al.*, 1980). Increased synthesis and reduced peripheral clearance of triglycerides associated with the reduced tissue lipoprotein lipase activity have been proposed as possible mechanisms.

In the SCI patients, additional factors such as reduced physical activity, the tubulointerstitial and medullary origin of renal pathology, and proteinuria may also contribute to the genesis of hypertriglyceridemia. Physical exercise has been shown to improve hypertriglyceridemia in patients with renal failure (Goldberg *et al.*, 1979) and those with other conditions (Holloszy *et al.*, 1964; Lopez-s *et al.*, 1974; Erklens *et al.*, 1978). Reduced physical activity due to the associated paralysis and uremia may therefore contribute to hypertriglyceridemia in SCI-CRF patients.

The underlying renal pathology associated with SCI is chronic obstructive pyelonephritis in which tubulointerstitial and medullary lesions are predominant. Severe hyperlipidemia has been recently reported in analgesic nephropathy which too is primarily tubulointerstitial and medullary in nature (Helber *et al.*, 1980). Moreover, the rise in serum triglyceride level after a fat load has been shown to be considerably higher in patients with chronic pyelonephritis than in those with glomerulopathies (Kokot *et al.*, 1971). These observations demonstrate the increased propensity to severe hypertriglyceridemia in patients with advanced renal disease due to tubulointerstitial and medullary damage. Deficiency of a lipid-lowering factor(s) associated with renal medulla has been considered to be responsible for this phenomenon (Kokot *et al.*, 1971). Nephrotic syndrome with heavy proteinuria is known to be associated with hyperlipidemia. Only one of our patients (No. 2) had nephrotic range proteinuria (> 3.0 g/day). Moreover, the predominant lipid abnormality associated with nephrotic syndrome is hypercholesterolemia which was generally lacking in our patients.

Although no significant difference in serum cholesterol concentration was found between the SCI patients with renal disease and those without renal failure, the values observed in both SCI groups were significantly lower than those established in the sex- and age-matched normal population. The mechanisms of the observed hypocholesterolemia are unclear. Reports on serum cholesterol concen-

tration in ambulatory dialysis patients are contradictory. Both normal (Losowsky & Kenward, 1968; Brons *et al.*, 1972; Ibels *et al.*, 1975; Daubresse *et al.*, 1976) and reduced (Brunzell *et al.*, 1977; Vaziri *et al.*, 1980) levels have been reported previously. Our findings in the SCI-CRF patients are consistent with those of Brunzell *et al.* (1977) and Vaziri *et al.* (1980) in ambulatory CRF patients.

Serum HDL-cholesterol in the SCI-CRF patients was significantly lower than those found in the SCI control group, the sex- and age-matched normal individuals and those with hypertriglyceridemia. This finding is suggestive of the possible etiologic role of advanced renal disease in the pathogenesis of reduced HDL-cholesterol observed in our patients. When compared with the values established in the sex- and age-matched normal controls, serum HDL-cholesterol was abnormally low in the SCI patients without renal failure. This may be partly a reflection of the lower serum total cholesterol level in these individuals. Physical exercise has been shown to increase HDL-cholesterol both in renal failure patients (Goldberg *et al.*, 1979) and in those with other conditions (Gyntelberg *et al.*, 1977; Erklens *et al.*, 1978). Relative physical inactivity associated with paralysis in SCI patients may therefore contribute to the genesis of their reduced HDL-cholesterol levels.

Low serum levels of HDL-cholesterol have been correlated with an increased incidence of cardiovascular disease in nonuremic man (Miller *et al.*, 1975; Castelli *et al.*, 1977; Gordon *et al.*, 1977). Further studies are necessary to assess the effect of reduced HDL-cholesterol as a risk factor for cardiovascular mortality and morbidity in the SCI patients.

No significant difference was noted in the measured lipid fractions between the dialysed and undialysed SCI-CRF patients. This observation tends to rule against a possible contributory role of hemodialysis in the genesis of lipid disorder in these patients. Due to the small size of the population studied, however, such conclusions cannot be made with certainty.

SUMMARY

Ten patients with chronic renal failure (CRF) associated with long-standing spinal cord injury (SCI) were studied. A group of age- and sex-matched patients with long-standing SCI but normal renal function were included for comparison. Serum triglycerides were markedly elevated in SCI-CRF patients. Both SCI groups exhibited moderate hypocholesterolemia. High density lipoprotein (HDL)-cholesterol was severely reduced in the SCI-CRF group and moderately reduced in the SCI-control group. Chronic renal failure, reduced physical activity and several other factors may be operative in the genesis of the observed elevated serum triglyceride and reduced HDL-cholesterol levels in this condition.

RÉSUMÉ

Notre étude porte sur dix patients présentant une défaillance rénale chronique (CRF) associée à une blessure de la colonne vertébrale (SCI) remontant à de nombreuses années. Pour comparer, nous avons inclus un groupe de patients de même âge et sexe ayant une SCI de longue durée, mais avec une fonction rénale normale. Le niveau sérique des triglycérides était considérablement élevé dans le cas des patients souffrant de SCI et de CRF. Les deux groupes exhibaient une hypocholestérolémie modérée. Le niveau de la cholestéroline des lipoprotéines de haute densité (LHD) était sévèrement réduit dans le groupe souffrant de SCI et de CRF, et modérément réduit dans le groupe de contrôle avec SCI. La défaillance rénale chronique, l'activité physique réduite et plusieurs autres facteurs encore peuvent être la cause du niveau élevé du sérum des triglycérides et du niveau réduit de LHD dans cette condition.

ZUSAMMENFASSUNG

Zehn Patienten mit chronischem Nierenversagen (CRF) im Zusammenhang mit langdauernder Wirbelsäulenverletzung (SCI) wurden untersucht. Zum Vergleich wurde eine Gruppe desselben Alters und Geschlechts mit langdauernder SCI, aber normaler Nierenfunktion in die Untersuchung miteinbezogen. Bei den Patienten mit CRF und SCI waren die Serumtriglyzeridwerte beträchtlich erhöht. Beide Gruppen zeigten mäßige Hypcholesterolämie. Die Lipoproteincholesterine von hoher Dichte (LHD) waren bei der CRF-mit-SCI-Gruppe stark reduziert und bei der SCI-Gruppe mäßig reduziert. Als Ursache der beobachteten erhöhten Serumtriglyzeridwerte und der reduzierten LHD-Cholesterinwerte in diesen Fällen können CRF, verminderte körperliche Bewegung und mehrere andere Faktoren gelten.

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