Changes in glucose tolerance, insulin, serum lipids and lipoproteins in patients with renal failure on intermittent haemodialysis

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Summary

Fasting serum lipids and lipoprotein patterns, glucose tolerance and serum insulin response to glucose were investigated in eight patients with renal failure on intermittent haemodialysis and five normal controls. The mean 0.5, 1 and 2 hr blood glucose values were significantly higher in patients compared with controls but there was no significant difference between patients and controls in respect of fasting serum insulin levels or the insulin response to glucose. Six of the eight patients showed hypertriglyceridaemia (hyperprebetalipoproteinaemia).

Introduction

Hyperlipoproteinaemia is a known complication of end-stage renal failure (Bagdade, Porte & Bierman, 1968; Bagdade, Bierman & Porte, 1967). In addition, impaired glucose tolerance has been described in patients with chronic renal failure on intermittent haemodialysis (Losowsky & Kenward, 1968; Bagdade, 1968; Hutchings, Hegstrom & Scribner, 1966).

In the present study, glucose tolerance and insulin response to glucose, and serum lipids with lipoprotein patterns were investigated in an attempt to determine whether there is any consistent relationship between disturbances of carbohydrate tolerance and lipoprotein patterns in patients with end-stage renal failure.

Subjects

Patients—Eight patients with end-stage chronic renal failure on intermittent haemodialysis were studied as in-patients (Table 1). Their mean age was

38 years (range 22–49 years). There were six females and two males. All patients were within 10% of ideal body weight (*Metropolitan Life Insurance Company Statistical Bulletin*, 1959). The creatinine clearance of each patient was less than 1.5 ml/min. The mean duration of dialysis was 25.7 months (range 2–50 months). There was no evidence of any other systemic disease and there was no family history of diabetes mellitus. No patient had evidence of infection of the shunt or elsewhere at the time of study. All patients were dialysed twice weekly (18 hr/week) using a coil dialyser. They were taking 60 g of protein/day and carbohydrate constituted 40–45% of the total calorie intake.

Controls—Five healthy subjects working in the renal unit acted as controls. Their mean age was 29 years (range 21–42 years). There were three females and two males. All were within 10% of ideal body weight.

Methods

Patients and controls were on a 300 g carbohydrate diet for 3 days before each test. Blood samples were taken after a 10-hr overnight fast, in the resting state and without applying a tourniquet, for the estimation of glucose, insulin and serum lipids. Blood samples were taken 0.5, 1 and 2 hr after 50 g of oral glucose for blood glucose and insulin.

Blood glucose was estimated by a glucose oxidase method (Werner, Roy & Weiling, 1970) using an AutoAnalyzer. Serum cholesterol was estimated by a method using the modified Leiberman–Burchard reaction (Abell *et al.*, 1952) and the serum triglycerides were determined by an enzymatic method (Eggstein, 1966). Lipoprotein patterns were assessed qualitatively using an agarose-gel method (Fredrickson, Levy & Lees, 1967).

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TABLE 1. Age, sex, duration of dialysis and serum lipids in patients

Patient	Age (years)	Sex	weight (kg)	% of desirable weight	Diagnosis	Duration of haemodialysis (months)	Serum cholesterol (mg/100 ml) (normal range 190-260)	Serum triglycerides (mg/100 ml) (normal range 95-160)	Lipoprotein pattern (Fredrickson classification)
M.L.	22	F	50	100	Chronic pyelo-nephritis*	50	282	216	Type IV
M.B.	39	F	55	102	Proliferative glomerulo-nephritis	18	205	59	Normal
M.J.	30	F	54	106	Henoch-Schönlein purpura	12	245	110	Normal
D.G.	37	M	70	100	Chronic pyelo-nephritis*	46	280	260	Type IV
R.H.	48	M	54	93	Polycystic kidneys*	36	286	271	Type IV
M.G.	49	F	56	100	Chronic glomerulo-nephritis	20	264	400	Type IV
B.B.	38	F	60	100	Malignant hyper-tension	2	206	284	Type IV
I.B.	45	F	46	93	Chronic glomerulo-nephritis	22	240	226	Type IV

* Anephric.

TABLE 2. Mean blood glucose and mean serum insulin values in eight patients and five controls

Time (hr)	Mean blood glucose (mg/100 ml)			Mean serum insulin (μ U/ml)		
	Patient	Control	P	Patient	Control	P
Fasting	64.23 SE $\pm$ 2.85	65.57 SE $\pm$ 5.20	> 0.1	8.71 SE $\pm$ 1.58	7.85 SE $\pm$ 1.65	> 0.1
0.5	94.15 SE $\pm$ 5.18	77.14 SE $\pm$ 4.97	< 0.05	33.21 SE $\pm$ 5.97	33.71 SE $\pm$ 6.75	> 0.1
1	97.38 SE $\pm$ 5.89	63.00 SE $\pm$ 3.01	< 0.001	37.31 SE $\pm$ 6.02	33.14 SE $\pm$ 10.97	> 0.1
2	82.77 SE $\pm$ 6.08	61.00 SE $\pm$ 4.89	< 0.05	22.84 SE $\pm$ 6.50	14.43 SE $\pm$ 4.24	> 0.1

All the tests were repeated at least once in all the patients and controls.

Results

The mean glucose and serum insulin values during glucose tolerance tests are shown in Table 2, Figs. 1 and 2.

Table 1 shows the results of serum lipids in the patients, and the normal range in our laboratory.

FIG. 1. Mean blood glucose values of eight renal patients (solid line) and five controls (dashed line) following 50 g glucose. Bars indicate standard error of means.

FIG. 2. Mean insulin values of eight renal patients (solid line) and five controls (dashed line) following 50 g of glucose. Bars indicate standard error of means.

Serum cholesterol was within the normal range in five patients and was marginally raised in the other three. The mean serum cholesterol was 227 mg/100 ml (SE $\pm$ 31) as compared with a level of 211.5 mg/100 ml (SE $\pm$ 10.0) in the controls which is not a significant difference ($P > 0.1$).

The serum triglyceride levels were significantly raised in six of the eight patients, the mean in the eight patients being 228 mg/100 ml (SE $\pm$ 31) as

compared with 108.4 mg/100 ml (SE $\pm$ 13.1) in the controls ($P < 0.01$).

The plasma lipoproteins assessed qualitatively from the electrophoretic patterns conformed with the lipid measurements, i.e. the six patients who had hypertriglyceridaemia showed Type IV hyperlipoproteinaemia according to Fredrickson's classification (Fredrickson *et al.*, 1967).

Discussion

Raised fasting immunoreactive insulin levels (Bagdade *et al.*, 1968; Bagdade *et al.*, 1967; Rabinowitz & Zierler, 1968), hypertriglyceridaemia (Bagdade *et al.*, 1968; Losowsky & Kenward, 1968; Hollister, Overall & Snow, 1967), increased insulin levels after glucose (Bagdade *et al.*, 1968; Losowsky & Kenward, 1968; Hutchings *et al.*, 1966; Karam, Grodsky & Forsham, 1963; Kreisberg *et al.*, 1967; Perley & Kepnis, 1963; Yalow & Berson, 1960) and a high frequency of carbohydrate intolerance (Bagdade *et al.*, 1968; Cohen, 1957; Ogilvie, 1935; Perkoff *et al.*, 1958; Cerletty & Engbrung, 1967; Horton, Johnson & Lobovitz, 1968) have been described in patients with uraemia and in obesity. In contrast to those of other workers such as Bagdade *et al.* (1968) all our patients had fasting immunoreactive insulin and fasting blood glucose levels within the normal range. Though 0.5, 1 and 2 hr blood glucose values were significantly higher than in controls, the absolute levels recorded in our patients were much lower than in other series and all the glucose tolerance curves were within the normal range. This may be related to the longer duration (mean 25.7 months) of haemodialysis, as there is evidence of reversibility of glucose intolerance in patients on intermittent haemodialysis (Hampers *et al.*, 1966; Alfrey *et al.*, 1967; Westervelt & Schreiner, 1962). Hutchings' patients however still showed glucose intolerance 4 years after being on haemodialysis (Hutchings *et al.*, 1966).

Hypertriglyceridaemia (hyperprebetalipoprotein-aemia, Type IV Fredrickson's classification) was observed in six of the eight patients in accordance with the findings of other workers (Bagdade *et al.*, 1968; Losowsky & Kenward, 1968; Evens & Ostrander, 1967; Harlan *et al.*, 1967; Hollister *et al.*, 1967). This hypertriglyceridaemia may be due either to increased production or diminished removal of plasma triglycerides, or to a combination of both mechanisms.

Hypertriglyceridaemia resulting probably from increased synthesis of prebetalipoprotein has been shown to be associated with elevated fasting circulating immunoreactive insulin in non-uraemic subjects (Bagdade *et al.*, 1968; Bagdade, 1968; Bierman & Porte, 1968; Reaven *et al.*, 1967). The same relationship between triglycerides and circulating fasting

insulin was shown in haemodialysed patients by Bagdade *et al.* (1968). But the presence of normal fasting insulin levels and a normal insulin response to glucose in our patients suggests that hyperinsulinaemia cannot be a major factor in the pathogenesis of hypertriglyceridaemia seen in patients on maintenance haemodialysis.

Diminished peripheral removal of lipids may play an important part in hypertriglyceridaemia. Subnormal post-heparin lipolytic activity has been demonstrated in uraemia (Bagdade *et al.*, 1968; Boyer & Scheig, 1970) with or without dialysis. This post-heparin lipolytic activity seems to reflect tissue levels of lipoprotein lipase, an enzyme which plays an important part in the removal of triglycerides. This low activity may be either due to true low levels of lipoprotein lipase or the presence of an inhibitor of lipoprotein lipase. The fact that three of our patients who have been haemodialysed for 3 years still showed hypertriglyceridaemia throws doubt on the existence of this inhibitor or it suggests such an inhibitor is not dialysable.

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