HYPERLIPÆMIA IN PATIENTS ON REGULAR DIALYSIS TREATMENT

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Serum of patients on regular dialysis treatment was observed to be lactescent. This led to an
investigation of lipids.

A moderate hyperlipæmia of a specific type was found in the majority of patients treated
by regular haemodialysis as well as in patients with terminal uraemia.

PATIENTS AND METHODS

Ten patients, ranging in age from 16 to 48 years, were studied, who had been dialysed for
periods up to 23 months. Diagnoses were chronic glomerulonephritis (7 patients), subacute
nephritis (2), polycystic kidney disease (1) and probable Alport's syndrome (1). Haemodialysis
was performed twice weekly, for 14 hours overnight, with Kil dialysers, central dialysate
supply and single-pass dialysate flow of 500 ml per minute at a temperature of 39°C. The
glucose concentration of dialysate was rather high: 750 mg/100 ml. The diets contained 50 g
protein, 170 to 280 g carbohydrate and 60 to 130 g fat.

Mean predialysis blood urea levels ranged from 100 to 200 mg/100 ml, postdialysis levels
from 30 to 65 mg. Serum creatinine levels ranged from 10.6 to 16.5 mg/100 ml predialysis
and from 3.5 to 6.6 mg postdialysis. Serum albumin was normal or near normal as soon as
general health had improved.

In addition two patients aged 16 and 20 years, were investigated who had not been
dialysed. Diagnoses were chronic pyelonephritis due to bladder neck constriction, and
subacute glomerulonephritis. Their blood urea levels were 255 and 315, creatinine clearances
less than 1 and 2 ml per minute respectively.

Total lipids were determined by alcohol-petroleum ether or chloroform-methanol extraction
and weighing according to standard procedures. Cholesterol was determined by the Lieber-
mann-Burchard method. Lipid phosphorus was determined by a modified Zinzadse method
(Hooghwinkel and Van Niekerk, 1960). Triglycerides were estimated by subtraction of the
sum of cholesterol and cholesterolesters (being 1.52 × total cholesterol) and phospholipids
from total lipids. The cholesterol to cholesterol-ester ratio in these patients was found to be
normal and to vary within normal limits. The triglyceride data were not corrected for free
fatty acids and other lipids which are normally present only in small amounts. Lipoprotein
electrophoresis was performed with the use of cellogel (Chemtron) in barbital buffer of
pH 8.6 and ionic strength 0.08. Horizontal electrophoresis was carried out for 75 minutes
at 150 Volts with a current of 12.5 to 16 milli-Amperes per strip. After electrophoresis the
strips were stained with Kohn's ozone-Schiff method (Kohn, 1961).

Oral glucose tolerance tests were carried out following the conditions laid down by Fitz-
gerald and Keen (1964), at least 24 hours after the last dialysis. In the days preceding the test
the patients received normal diets, which contained more than 200 grams of carbohydrate.

Insulin was determined by immuno-assay according to Yalow and Berson (1960).
Hyperlipaemia

The majority of patients were found to have elevated total lipids. Data are presented in Table I.

The elevation was mainly due to an increase in triglycerides. Cholesterol and phospholipids were raised to a lesser degree. The lactescence, however, which was found to be most marked postprandially, could not be explained simply by hypertriglyceridaemia. Cellogel electrophoresis showed a broad and dense \( \text{pre-} \beta \)-lipoprotein band in all dialysis patients tested, as well as in the two patients with terminal uraemia mentioned above. An example is shown in the first two samples of Figure 3. Chylomicrons were absent, except in non-fasting sera in two cases. The \( \alpha \)-lipoprotein band appeared normal in all cases.

### TABLE I

**Lipids in patients with end-stage renal disease**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Duration (months)</th>
<th>Total lipids</th>
<th>Cholesterol (mg per 100 ml)</th>
<th>Phospholipids (mg per 100 ml)</th>
<th>Triglycerides (mg per 100 ml)</th>
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<tbody>
<tr>
<td>Me</td>
<td>M</td>
<td>48</td>
<td>23</td>
<td>1905*</td>
<td>450*</td>
<td>351*</td>
<td>852*</td>
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<tr>
<td>Vs</td>
<td>M</td>
<td>31</td>
<td>19</td>
<td>1030*</td>
<td>257*</td>
<td>254</td>
<td>475</td>
</tr>
<tr>
<td>vE</td>
<td>M</td>
<td>45</td>
<td>14(\frac{1}{2})</td>
<td>1098*</td>
<td>273*</td>
<td>214</td>
<td>600</td>
</tr>
<tr>
<td>IJz</td>
<td>M</td>
<td>19</td>
<td>6</td>
<td>1330*</td>
<td>281*</td>
<td>282</td>
<td>779</td>
</tr>
<tr>
<td>Ku</td>
<td>F</td>
<td>37</td>
<td>4</td>
<td>1690*</td>
<td>374*</td>
<td>222</td>
<td>707</td>
</tr>
<tr>
<td>Dr</td>
<td>F</td>
<td>18</td>
<td>4</td>
<td>1020*</td>
<td>286*</td>
<td>286</td>
<td>700</td>
</tr>
<tr>
<td>Do</td>
<td>F</td>
<td>35</td>
<td>3(\frac{1}{2})</td>
<td>1170*</td>
<td>279*</td>
<td>295</td>
<td>681</td>
</tr>
<tr>
<td>Ma</td>
<td>M</td>
<td>21</td>
<td>3</td>
<td>814*</td>
<td>185*</td>
<td>216</td>
<td>589</td>
</tr>
<tr>
<td>Kw</td>
<td>M</td>
<td>16</td>
<td>3</td>
<td>967*</td>
<td>188*</td>
<td>117</td>
<td>542</td>
</tr>
<tr>
<td>Dij</td>
<td>M</td>
<td>20</td>
<td>1 week</td>
<td>975</td>
<td>231</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dij</td>
<td>M</td>
<td>20</td>
<td>0</td>
<td>1120</td>
<td>190</td>
<td>176</td>
<td>701</td>
</tr>
<tr>
<td>Ho</td>
<td>M</td>
<td>16</td>
<td>0</td>
<td>935*</td>
<td>148</td>
<td>159</td>
<td>631</td>
</tr>
</tbody>
</table>

* Mean of three or more determinations.
** Fasting. The other data do not all refer to the fasting state.

Glucose tolerance

In our patients abnormal glucose tolerance tests were a frequent finding, as is shown in Table II. Only one of the patients, Me, had been tested before dialysis treatment. At that time, when the blood urea level was 279 mg/100 ml, the glucose tolerance test was already abnormal.

Glucose and insulin levels during dialysis

At a dialysate glucose concentration of 750 mg/100 ml, the glucose level in the blood outflow line of the dialyser was consistently about 200 mg/100 ml higher than in the inflow line. At usual blood-flow rates this results in a glucose load to the patient of 200 to 250 g during a 14-hour dialysis.

In order to investigate which demands this placed on insulin production glucose and insulin were determined in two patients during dialysis. Figure 1 shows that blood glucose increased rapidly after the beginning of dialysis. Insulin also rose promptly to a level, higher than normal postprandial levels, and was sustained for a period longer than ever occurs physiologically. Both patients became slightly hypoglycaemic one hour after dialysis.

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TABLE II

Glucose tolerance in patients on regular dialysis treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>Glucose tolerance test*</th>
<th>Diabetes in family</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>abnormal</td>
<td>—</td>
</tr>
<tr>
<td>Vs</td>
<td>abnormal</td>
<td>—</td>
</tr>
<tr>
<td>vE</td>
<td>abnormal</td>
<td>—</td>
</tr>
<tr>
<td>IJz</td>
<td>abnormal</td>
<td>+</td>
</tr>
<tr>
<td>Ku</td>
<td>abnormal</td>
<td>—</td>
</tr>
<tr>
<td>Dr</td>
<td>normal</td>
<td>+</td>
</tr>
<tr>
<td>Do</td>
<td>abnormal</td>
<td>+</td>
</tr>
<tr>
<td>Ma</td>
<td>abnormal</td>
<td>+</td>
</tr>
<tr>
<td>Kw</td>
<td>normal</td>
<td>—</td>
</tr>
<tr>
<td>Dij</td>
<td>abnormal</td>
<td>—</td>
</tr>
</tbody>
</table>

* Normal or abnormal according to standards of the British Diabetic Association (Fitzgerald and Keen, 1964).

In a third patient, Me, insulin levels remained low in relation to blood glucose throughout dialysis, as is shown in Figure 2. This patient had a grossly abnormal glucose tolerance test several years previously, as has been mentioned above.

**Lipids during dialysis (fasting)**

In order to determine whether the glucose administered through the dialyser might re-

![Graphs showing blood glucose and insulin levels during dialysis](image)

*Fig. 1. Blood glucose and insulin levels during haemodialysis in two patients. The patients were in the fasting state from 12 a.m. to 8 a.m.*
appear in the patient’s blood as triglycerides, lipids were determined during dialysis, while
the patient did not receive any food by mouth (Fig. 2).

Lipids showed an initial dip, then gradually decreased during dialysis. This was mainly
due to a decrease in triglycerides; cholesterol and phospholipids changed to a lesser degree.
One hour after dialysis lipids had again risen. At least the initial dip was thought to be caused
by lipoprotein lipase activation by heparin. This was corroborated by cellogel electrophoresis
of the same blood samples (Fig. 3). Fifteen minutes and one hour after the beginning of
dialysis a pattern typical of postheparin lipolytic activity was seen: faster travelling of the
lipoproteins over the medium and breaking up of triglycerides as evidenced by the appearance
of fatty acids carried in combination with albumin. This effect was also seen when heparin
was given to patients while they were not being dialysed.

*Lipids during dialysis (non-fasting)*

Lipids were also followed during dialysis when the patient consumed a meal consisting of
approximately 100 g carbohydrate, 40 g protein and 60 g fat (patients are allowed a less

![Graph showing blood glucose, insulin, total lipids, cholesterol and phospholipids during haemodialysis.](image)

*Fig. 2. Blood glucose, insulin, total lipids, cholesterol and phospholipids during haemodialysis. At start of dialysis 25 mg of heparin was given into inflow line of dialyser, followed by regional heparinization by slow infusion of heparin and protamine sulphate to in- and outflow lines. Patient in fasting state throughout.*

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Fig. 3. Cellogel electrophoresis of serum samples taken during the dialysis shown in Fig. 2. Numbers indicate time in hours from start of dialysis.

Fig. 4. Blood glucose, total lipids and triglycerides during haemodialysis (non-fasting). Heparin was given two hours before dialysis.
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restricted diet than usual in the first hours of dialysis) (Fig. 4). A rise in lipids is seen five to six hours after the meal, consisting mainly of a rise in triglycerides.

DISCUSSION

A moderate hyperlipaemia, characterized by an increase in pre-β-lipoproteins, was observed in end-stage renal disease, in patients who had never been dialysed as well as in patients on regular dialysis treatment.

Pre-β-lipoproteins constitute the means of transport for the so-called ‘endogenous’ triglycerides, i.e., the triglycerides derived from ingested carbohydrates or from free fatty acids released by adipose tissue.

Hyperpre-β-lipoproteinaemia may be associated with impaired carbohydrate tolerance (Fredrickson et al., 1967). The finding that the α-lipoprotein band on cellogel electrophoresis appeared normal in our patients is in contrast with the observation of Lewis et al. (1966), who, using paper electrophoresis, in similar patients found low levels of α-lipoproteins.

The lactic acid, frequently observed in the sera of patients treated by regular dialysis, could not be explained only on the basis of hypertriglyceridaemia.

There may be an abnormality of lipoproteins in patients lacking kidney function, which interferes with triglyceride transport. The response of lipids to heparin, glucose administration and feeding appeared to be essentially normal in the patients studied.

Carbohydrate metabolism

Glucose tolerance tests were abnormal in eight out of ten of our patients on regular dialysis treatment. During dialysis glucose passing from dialysate to patient was seen to provoke sustained high insulin levels in two patients. In a third patient insulin levels remained low.

Abnormal carbohydrate metabolism is known to be frequently present in advanced renal disease. In uraemic patients delayed disappearance rate of glucose, despite levels of insulin which normally would have been adequate, and prolonged elevation of insulin after oral or intravenous glucose have been reported by several investigators (Tchobroutsky et al., 1965; Hampers et al., 1966; Briggs et al., 1967; Cerletty and Engbring, 1967).

Sagild (1962) and Hampers et al. (1966) have shown that glucose tolerance improves after correction of uraemia.

After periods of intermittent haemodialysis insulin levels have been found to be increased, both in the fasting state and after glucose (Hampers et al., 1966; Hutchings et al., 1966).

An increase of insulin levels cannot be explained, if the sole effect of dialysis were the removal of a dialysable insulin antagonist.

In the case described by Gutman et al. (1967), glucose loading during dialysis increased the ability to rapidly metabolise glucose, presumably by stepping up insulin production.

Glucose tolerance associated with an exaggerated insulin response to a glucose load has been described in cases of hyperlipaemia (Farquhar et al., 1966) and in obesity, Cushing’s disease and acromegaly, in which cases insulin antagonism may be reversible (Hulsmans et al., 1967).

Patients on regular dialysis treatment, besides suffering from the insulin antagonism of uraemia, during dialysis have an increased stimulus to produce insulin.

Whether the hyperpre-β-lipoproteinaemia and abnormal carbohydrate metabolism observed in severe renal disease are connected cannot be said without further study. The question whether the dialysis procedure provokes certain of the observed abnormalities also requires further investigation.

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REFERENCES


