Effects of Regular Haemodialysis with Glucose and Glucose free Dialysate on Hyperlipaemia

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Marked lipaemia has been described in renal diseases in the presence of excessive proteinuria, in the nephrotic syndrome and in the last years in patients with non nephrotic uraemia (Bagdade et al, 1968; Irsigler & Mengele, 1968; Bagdade, 1970; Bierman, 1970). Several authors have described supernormal plasma concentrations of triglycerides, phosphatides and cholesterol in chronic renal failure and increased levels of free fatty acids and triglycerides in acute renal failure (Losowsky & Kenward, 1968; Reimold et al, 1970). Moreover the uraemic state is characterised by glucose intolerance and basal hyperinsulinism (Reaven et al, 1967; Ford et al, 1968). The close relation between carbohydrate and lipid metabolism and the fact that the impaired glucose tolerance improves with amelioration of the uraemic state initiated this study on the effect of regular haemodialysis with glucose containing and with glucose free dialysate on hyperlipaemia in chronic renal failure. Glucose free dialysate has been used in our centre (L) for nearly two years (Hübner et al, 1971).

MATERIAL AND METHODS

In a joint study from three centres performing dialysis (groups B, M, L) the pre- and postdialysis lipids in the plasma of 62 fasting patients with chronic renal failure treated by regular haemodialysis were investigated. These patients (44 men and 18 women, aged 20 to 54 years) have been dialysed from 2 months up to nearly 6 years. These subjects suffered from chronic glomerulonephritis and interstitial nephritis. Patients with obesity, diabetes mellitus, cachexia, and especially those with a nephrotic syndrome, were excluded. The mean body weight was 90% of ideal body weight. The following parameters of the lipid metabolism were determined: free and total glycerol, triglycerides, phosphatides, cholesterol, \( \beta \)-lipoprotein and free fatty acids.

In addition the influence of glucose and glucose free fluid on the plasma
lipid level during and after dialysis was investigated. The dialysate of the three centres was equal in electrolyte composition (Na\(^+\) 130 mEq/l, K\(^+\) 3 mEq/l, Ca\(^{++}\) 2.8 mEq/l, Mg\(^{++}\) 1 mEq/l, Cl\(^-\) 101 mEq/l) and acetate concentration (30 mEq/l) and differed only in glucose concentration. One group (L) had been dialysed without glucose in the fluid and the patients of the two other centres (B, M) with 4.4 g/l glucose. Heparin was administered in standard concentrations by a timed infusion pump.

The lipids were measured by standard procedures (reagents supplied by Boehringer/Mannheim). In some cases the lipoproteins were analysed by thin layer chromatography on agar-agarose-gel. The statistical evaluation of the data was performed with Student's t-test and the two rank test of Wilcoxon (Goldstein, 1964).

![Graph](image)

**Figure 1.** Decrease of plasma lipids with increase in the duration of regular haemodialysis
RESULTS

In Figure 1 the data of all 62 patients after haemodialysis are classified according to the duration of haemodialysis therapy. There is a decrease of all parameters with an increase in the duration of chronic intermittent haemodialysis. The values of triglycerides, total glycerol, cholesterol, phosphatides and β-lipoprotein are significantly higher in patients being dialysed less than one year compared to those being dialysed more than two years. The decrease of free glycerol and free fatty acids was not significant.

Table I. Serum lipids of 62 patients with chronic renal failure after haemodialysis (\( + = p = 0.01-0.05 \))

<table>
<thead>
<tr>
<th>Haemodialysis centre</th>
<th>L</th>
<th>M</th>
<th>B</th>
<th>normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid (glucose g/l)</td>
<td>3.26†</td>
<td>2.76†</td>
<td>5.80†</td>
<td>0.98</td>
</tr>
<tr>
<td>Age (years)</td>
<td>35.6</td>
<td>36.2</td>
<td>34.8</td>
<td></td>
</tr>
<tr>
<td>Dialysis (months)</td>
<td>22.8</td>
<td>17.9</td>
<td>12.7</td>
<td></td>
</tr>
<tr>
<td>Patients (number)</td>
<td>23</td>
<td>16</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Free Glycerol mg/100ml</td>
<td>3.26†</td>
<td>2.76†</td>
<td>5.80†</td>
<td>0.98</td>
</tr>
<tr>
<td>Total Glycerol mg/100ml</td>
<td>21.0†</td>
<td>14.6</td>
<td>34.8†</td>
<td>12.9</td>
</tr>
<tr>
<td>Triglyceride mg/100ml</td>
<td>186.3†</td>
<td>115.2</td>
<td>315.5†</td>
<td>126.2</td>
</tr>
<tr>
<td>Cholesterol mg/100ml</td>
<td>140.1</td>
<td>184.2</td>
<td>192.4</td>
<td>197.0</td>
</tr>
<tr>
<td>Phosphatide mg/100ml</td>
<td>157.4</td>
<td>173.5</td>
<td>231.1</td>
<td>194.2</td>
</tr>
<tr>
<td>β-Lipoprotein mg/100ml</td>
<td>368.4</td>
<td>432.3</td>
<td>483.9</td>
<td>468.0</td>
</tr>
<tr>
<td>Free Fatty Acid mEq/100ml</td>
<td>0.95</td>
<td>0.89</td>
<td>1.28</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Grouping the patients according to the dialysis centres, as summarised in Table I, the highest values of all parameters were obtained in group B and the lowest in group M. After haemodialysis free glycerol was significantly increased in all groups whereas total glycerol and triglycerides were found to be significantly increased only in group B and L. All other data were not found to be significantly elevated. The free fatty acids showed a small increase in all groups and the phosphatides were elevated only in group B.

Although the mean age of the subjects of the three groups (35 years) is
equal, significant differences can be noted, especially between group B and M on the one hand and between group M and L on the other hand (Figure 2). Group B shows higher levels in all parameters than group M and L. This difference seems to be due to different periods of dialysis therapy in each group. The patients of group B have been in the dialysis programme only for 12.7 months, whereas those of group M for 17.9 and those of group L for 22.8 months. The patients of group L, though having the longest period of treatment, showed higher concentrations of glycerol and triglycerides than the patients from centre M. To explain this difference between the subjects of group L and M the effect of differences in the glucose concentration of the dialysate was examined. The alterations of the lipid concentrations after haemodialysis with glucose (group M) and without glucose in the fluid (group L) are summarised in Table II. There is a significant increase in free glycerol after dialysis in both groups, whereas alterations in the concentrations of cholesterol, phosphatides or β-lipoproteins have not been observed.

The surprising finding of significantly decreased levels of triglyceride and total glycerol after haemodialysis in group M (glucose concentration of 4.4 g/l) compared to group L (without glucose) is documented in Figure 3. These differences may be accounted for by the different glucose concentrations of 169 mg/100 ml in group M, and of only 95 mg/100 ml in the blood of the subjects in group L, without glucose in their dialysate. In addition to

Figure 2. Plasma lipid levels after haemodialysis with glucose and glucose free dialysate in 62 patients in 3 centres.
Table II. Glycerol, Triglyceride and Cholesterol levels before and after haemodialysis with glucose and glucose free fluid

(+ = p = 0.01 - 0.05)

<table>
<thead>
<tr>
<th>Lipids</th>
<th>Centre</th>
<th>Glucose in fluid</th>
<th>Before dialysis</th>
<th>After dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Glycerol</td>
<td>L</td>
<td>0.0</td>
<td>1.71±0.5</td>
<td>3.26±1.2+</td>
</tr>
<tr>
<td>± SD (mg/100ml)</td>
<td>M</td>
<td>4.4 g/l</td>
<td>1.44±0.7</td>
<td>2.78±1.6+</td>
</tr>
<tr>
<td>Total Glycerol</td>
<td>L</td>
<td>0.0</td>
<td>24.3±8.3</td>
<td>21.0±8.5</td>
</tr>
<tr>
<td>± SD (mg/100ml)</td>
<td>M</td>
<td>4.4 g/l</td>
<td>22.7±7.3</td>
<td>14.6±4.7+</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>L</td>
<td>0.0</td>
<td>201.9±34.3</td>
<td>186.3±31.5</td>
</tr>
<tr>
<td>± SD (mg/100ml)</td>
<td>M</td>
<td>4.4 g/l</td>
<td>204.4±36.7</td>
<td>115.2±45.8+</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>L</td>
<td>0.0</td>
<td>159.9±41.0</td>
<td>140.1±36.6</td>
</tr>
<tr>
<td>± SD (mg/100 ml)</td>
<td>M</td>
<td>4.4 g/l</td>
<td>167.2±43.3</td>
<td>184.2±35.1</td>
</tr>
</tbody>
</table>

![Graph showing changes in glucose, triglyceride, and free glycerol levels before and after haemodialysis](image)

Figure 3. Plasma levels of triglycerides and free glycerol before and after haemodialysis with glucose and glucose free fluid
this, higher mean levels of circulating insulin in Group M (22 mU) compared
with group L (15.4 mU) were found.

DISCUSSION

Hypertriglyceridaemia may result from an increase in hepatic triglyceride
secretion rate secondary to elevated insulin levels. This constellation can
be found in patients with endogenous lipaemia and in uraemia (Reaven et al,
1967; Ford et al, 1968). Hyperinsulinism, a well documented consequence
of uraemia (Briggs et al, 1967; Horton et al, 1968) may influence the plasma
triglyceride level by increasing the triglyceride production in the liver and
by maintaining the tissue lipoprotein lipase in a state of reduced activity
(Schnaitz & Williams, 1963).

The assumption of Bagdade (1970) that both the abnormalities of glucose
tolerance and insulin activity in uraemia as described by several authors
(Hampers et al, 1966; Hutchings et al, 1966) and the hypertriglyceridaemia
in the uraemic state may be corrected by frequent haemodialysis could be
confirmed by our data of 62 patients with chronic renal failure. Contrary to
other investigators (Losowsky & Kenward, 1968; Reimold et al, 1970), sig-
nificantly elevated concentrations of cholesterol, phospholipid or β-lipopro-
tein were not found. A significantly increased plasma level of glycerol and
triglyceride was measured only in the subjects with a shorter duration of
RDT. In these cases thin layer chromatography showed the triglyceride-rich,
very low density, and 'pre-β' migrating lipoprotein fraction enlarged. The
finding of a normalisation and a decrease in the uraemic elevation of lipids
in plasma suggest that it is possible that the same underlying mechanism that
is responsible for glucose intolerance and elevated insulin levels in uraemia
also causes the uraemic alterations in lipid metabolism and the hypertrigly-
seridaemia.

With regard to the composition of the dialysis fluid, surprisingly, we
found a decrease of triglycerides in the group with high glucose dialysate
during the time of dialysis. On the other hand, in 8 patients who were dia-
lysed with glucose free dialysate (Figure 4) we found a small but not signifi-
cant increase of triglycerides. Reimold (1970) described in the course of
peritoneal dialysis with high and low glucose concentrations, a small eleva-
tion of triglycerides in the group of patients with normal blood glucose con-
centrations during dialysis. This effect could result from either a greater
glyceride synthesis in the liver as a consequence of relatively more intensive
metabolism of acetate out of the dialysate (Tsaltas, 1970), or a relatively
smaller deficiency of unsaturated fatty acids which is normally seen during
dialysis with glucose containing fluid (Reimold, 1970). A deficiency of un-
saturated fatty acids is thought to be responsible for the consecutive decrease
of triglycerides in the plasma under conditions of carbohydrate feeding.
SUMMARY

We conclude that the use of glucose free fluid for haemodialysis has no favourable acute effect on plasma triglyceride, glycerol and cholesterol levels. This finding, however, does not reduce the usefulness of glucose free fluid in regular haemodialysis, especially with regard to carbohydrate intolerance and its usefulness in diabetic subjects with chronic renal failure. In the long term, regular haemodialysis with glucose-containing or glucose free fluid will both result in an amelioration of glucose intolerance, hyperinsulinism and uraemic lipoaemia.

ACKNOWLEDGMENT

This study was supported by SFB 68, II-2, Deutsche Forschungsgemeinschaft.
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OPEN DISCUSSION

V PARSONS (London): We have dialysed with glucose free dialysate ever since our unit opened: we don’t know quite why, but we have. We’ve never used glucose. Can you tell us about the carbohydrate intake of the different units, L and M? There seemed to be a difference here that might be explained on dietary intake. Is the dietary regime exactly the same in both units?

HUBNER: No, at the beginning of our investigation, it became clear that all patients must have an equal food situation. That is why I presented more values after haemodialysis than before haemodialysis. After haemodialysis all patients in the three centres in the three different cities were in the same conditions: they had had no food and would have been dialysed for 12 hours. If we took the values before dialysis, however, there were many factors altering the statistical data and we had higher standard deviations before dialysis, than after dialysis. Therefore, in Figure 1 and Table I, I presented the figures after haemodialysis.