Serum Lipids in Uraemic Patients on Regular Haemodialysis

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Summary

Measurement of serum lipids in 75 patients on regular haemodialysis showed that they had a higher mean serum triglyceride level than normal subjects. Cholesterol levels were not significantly different. Amongst haemodialysis patients men had higher serum triglycerides than women and women had higher cholesterol levels than men, a situation analogous to that found in normal subjects. In men, serum triglycerides correlated with % body fat and treatment with Sustanon 250(R) intramuscularly weekly caused a significant rise.

Introduction

Recent observations (Lindner et al, 1974; EDTA, 1974) demonstrate that vascular incidents account for just over 50% of all deaths of patients on regular haemodialysis. Hypertension, secondary hyperparathyroidism and hyperlipidaemia are likely factors predisposing these patients to vascular incidents. Hypertriglyceridaemia appears to be the predominant abnormality of uraemic hyperlipidaemia. (Cramp et al, 1975) but the extent of the problem may vary in different dialysis centres (Bischel, 1975). Androgen therapy (Dombeck et al, 1973), diet and dialysate glucose concentration may be important influencing factors (Novarini et al, 1975).

This study was undertaken in an attempt to define the prevalence, severity and other associated features of disturbed lipid metabolism found in patients on regular haemodialysis in Newcastle upon Tyne.

MATERIAL AND METHODS

Seventy-five patients, 41 men and 34 women on regular haemodialysis for periods ranging from one month to 7½ years were included in the study. Blood was withdrawn after a 12-hour fast and always immediately before starting a haemodialysis
session. Patients were dialysed using either a Meltex Multipoint or Kiil dialyser, 6-8 hours trice weekly and a 60g protein diet was recommended. The glucose dialysate concentration was 200mg/100ml and the sodium acetate concentration was 40mEq/L.

Information about age, time on regular haemodialysis, nature of renal disease and drug therapy was obtained from patients' records, while the percentage body fat was calculated from measurements of height and weight according to Womersley et al (1972). A ponderal index was also calculated (Lewis et al, 1974). Serum cholesterol was determined on the Auto-Analyser using Technicon method N-24a. Lipoprotein electrophoresis was carried out in agarose gel using a modification of the method of Noble (1968) and serum triglycerides were determined by the method of Giegel et al (1972). Comparisons with a normal population were made possible by the availability of data from the Whickham Survey, an epidemiological study involving 2,737 men and women living in the North East of England.

RESULTS

Figure 1 shows the different cumulative frequency percentages of serum cholesterol and serum triglycerides in male and female haemodialysis patients. The mean triglyceride concentration for men on haemodialysis was higher than that for women (p < 0.05) and the mean serum cholesterol concentration for women was higher than that for men, (p < 0.01). A similar pattern was encountered in the normal population where men had higher serum triglycerides (p < 0.01) and women had higher serum cholesterol levels (p < 0.001). Compared to normal subjects, both male and female haemodialysis patients had higher serum triglyceride concentrations (p < 0.001 for men and p < 0.01 for women). These differences in serum triglycerides between haemodialysis patients and normals according to age groups are illustrated in Figure 2.

Figure 1. Graphs showing the cumulative frequency % of serum cholesterol and triglycerides in uraemic haemodialysis male and female patients.

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Figure 2. Distribution of serum triglycerides according to age groups in haemodialysis patients ( ——— ) and normal subjects ( ——— ).

Figure 3 shows the relationship between the serum triglycerides of male haemodialysis patients and time on regular haemodialysis. Taking all 41 male patients together a positive correlation was found \( r = +0.3506, p < 0.05 \). However, when these patients were divided into those treated with androgens, i.e. Sustanon 250(R) intramuscularly weekly and those who had not received this therapy, two different populations were found and no correlation with time on dialysis could be demonstrated with either group. Patients having regular Sustanon 250(R) had significantly higher mean serum triglycerides compared to the group of patients who had received no such therapy \( (p < 0.01) \), but they had also been on regular haemodialysis longer. Male triglyceride values correlated with both the percentage body fat \( r = +0.3916, p < 0.02 \) and ponderal index \( r = +0.4453, p < 0.01 \), while female triglyceride values bore no correlation with indices of obesity or length on regular haemodialysis.

Analysis of serum cholesterol values showed that there were no real differences between normal subjects and haemodialysis patients. Serum cholesterol in both male and female haemodialysis patients bore no relationship to the time on dialysis, percentage body fat or ponderal index.
Figure 3. Graph showing the apparent relationship between male triglycerides and time on regular haemodialysis. When the patients are divided into those treated with Sustanon 250(R) and those who never received such therapy, no correlation with length on dialysis was found.

<table>
<thead>
<tr>
<th>Lipoprotein types</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>2a</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>2b</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Imbalance of type 2a and 4

\[ X^2, \text{3 d.f.} = 13.501 \quad p < 0.01 \]

Figure 4. Demonstration of lipoprotein types on regular haemodialysis patients, showing the prevalence of type 2a in female patients and type 4 in male patients.

Figure 4 shows the results of lipoprotein analysis. There was a balance of the normal type and type 2B in the two sexes but an imbalance of type 2 with nine observed in the female group and none in the male group. Conversely there were 17 males (43%) observed in type 4 and only 7 (20%) females. \[ X^2, \text{3 d.f.} = 13.501 \quad p < 0.01 \].

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DISCUSSION

Previous studies on the lipid disorder of haemodialysis patients (Bagdade, 1970; Gutman et al, 1973; Roodvoets, 1974) have shown that hypertriglyceridaemia is the main demonstrable abnormality. The present study confirms this. Both male and female patients showed elevated serum triglycerides and this was more apparent in the younger age groups (Figure 2). At present hypertriglyceridaemia is thought to result from inadequate clearance of serum triglycerides due to reduced lipoprotein lipase activity (Gutman et al, 1973) aggravated by increased hepatic triglyceride synthesis. Of interest, however, is the possible adverse effect of androgen therapy, usually employed in haemodialysis patients in order to improve haemoglobin synthesis. Dombeck et al (1973) showed that oral fluoxymesterone 90mg daily led to a significant increase in their patients' serum triglycerides. They suggested that exogenous androgen therapy potentiated the known effects of uraemia. In the present study male haemodialysis patients receiving intramuscular weekly Sustanon 250(R) had significantly higher triglycerides than patients not treated with Sustanon 250(R) (p < 0.01). Although the Sustanon 250(R)-treated group had also been on haemodialysis longer there was no other evidence to suggest that the rise in triglycerides was related to the length of time on regular haemodialysis. These findings are of interest for they differ from the reported action of androgens in non-uraemic patients as described by Furman et al (1967). Contrary to our findings and those of Dombeck et al (1973) Wardle et al (1974) prescribed nor-ethandrolone, an anabolic androgen, 20mg daily for 10 weeks to 15 uraemic patients and noted a progressive fall in serum triglycerides. No haemodialysis patients were studied and the mean serum creatinine in their patients was 4.6mg/100ml. It is of interest that all 16 male patients who received no Sustanon 250(R) had serum triglyceride levels within the 95% confidence limits found in the Whickham Survey. Their mean serum triglyceride was significantly lower than that of the male patients given Sustanon 250(R) (p < 0.01) and unlike these patients their mean triglyceride was not significantly higher than that of female haemodialysis patients.

Accurate dietary histories were obtained for 26 of the 75 patients. When total calories, percentage protein and percentage fat and carbohydrate were related to serum triglycerides and cholesterol, no significant correlations were found. Dombeck et al (1973) showed that varying the dialysate glucose concentration from 150 to 500mg/100ml had no effect on serum triglyceride concentration. In our series the dialysate glucose concentration was constant at 200mg/100ml.

This study shows that haemodialysis patients, like normal subjects have a different distribution of cholesterol and triglycerides in the two sexes (Figure 1). Amongst male haemodialysis patients serum triglyceride values correlated with percentage body fat and ponderal index. This situation is analogous to that found in normal people and it suggests that attempts to ‘fatten up’ haemodialysis patients may be accompanied by an increased risk of atherosclerotic vascular
disease. The distribution of lipoprotein types also matched that for normal
subjects (Lewis et al, 1974). As Figure 4 shows there were more men with type 4
and more women with type 2a.

It appears that uraemia and regular haemodialysis, while maintaining the
different lipid patterns seen in male and female patients, favour the accumulation
of serum triglycerides and regular androgen therapy aggravates this situation.

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