PART VIII

LIPID METABOLISM

Chairmen: N Alwall
           H E Jorgensen
Serum Lipids and Lipoproteins in Acute Renal Failure

M MYDLÍK, I AHLERS, K DERZSIOVÁ, M TAKÁČ

1st Department of Medicine and Institute of General Biology, University of P J Safarik, Kosice, Czechoslovakia

Summary

Forty-five patients with various forms and phases of acute renal failure without or with haemodialysis treatment were investigated. The concentration of free fatty acids, triglycerides and total cholesterol in serum were determined and separation of lipoprotein classes on agarose gel was performed.

Increase in free fatty acids and triglycerides, decrease in cholesterol concentration in serum characterised the anuric phase. The increase of prebeta fraction, the decrease of alpha and beta lipoprotein fraction were found in the oligoanuric phase. Decrease in triglyceride concentration was observed as a regular effect of haemodialysis. Decrease in prebeta and increase in beta lipoprotein fraction immediately after the termination of haemodialysis occurred. In the polyuric phase of acute renal failure there was a significant decrease in free fatty acids and triglycerides and increase in cholesterol concentration in serum simultaneous with improvement of clinical signs. An increase in prebeta and decrease in beta lipoprotein fraction was noted in the convalescence phase, despite an opposite trend of serum triglycerides and cholesterol concentrations.

Introduction

Carbohydrate and protein changes are the best known metabolic disturbances in renal failure. Not long ago lipid disorders were noted only in the nephrotic syndrome. Some 15-20 years ago several authors published basic information about the serum lipid and lipoprotein changes in patients with chronic non-nephrotic renal failure (Bagdade, 1968; Bagdade et al, 1968; Brøns et al, 1972). In the literature only few experimental (Nitzan, 1971, 1973) and clinical data (Losowsky & Kenward, 1968; Mydlík et al, 1975) can be found on the serum or tissue lipid and that of circulatory lipoprotein disorders in acute renal failure.

We have investigated lipids and lipoproteins in the serum of patients with acute renal failure of various aetiology in relation to the clinical picture and dialysis treatment.
PATIENTS AND METHODS

Forty-five patients (average age 38.5 years) in the anuric phase of acute renal failure (ARF) and when possible in the polyuric and convalescence phase were investigated. The group consisted of 11 women and 34 men (Table I).

TABLE I. Causes of Acute Renal Failure in 45 Patients

<table>
<thead>
<tr>
<th>Event</th>
<th>Number of Patients</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Acute glomerulonephritis</td>
<td>8</td>
<td>—</td>
</tr>
<tr>
<td>2 Rapidly progressive glomerulonephritis</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>(Goodpasture’s syndrome)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 Acute circulatory renal failure</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>4 Acute tubular necrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Carbon tetrachloride poisoning</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>b. Ethyleneglycol poisoning</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>5 Obstructive nephropathy</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>6 Toxaemia of pregnancy</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>7 Unknown aetiology</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td>45</td>
<td>14</td>
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</table>

In fasting patients free (non-esterified) fatty acids (FFA) were measured by a fluorometric method (Dole, 1956); triglycerides were determined by a spectrophotometric method (Eggstein & Kreutz, 1966). Total cholesterol was measured by a spectrophotometric method (Zlatkis et al, 1953), and lipoproteins were examined by the electrophoretic separation on agarose gel (Ahlers et al, 1971).

A control group was compared with the values of patients in the anuric phase before haemodialysis and in the polyuric and convalescence phase of ARF. In the control group the samples were always taken in the morning and in the same season of the year. Patients’ serum samples were taken at different times of the day and in different seasons. Therefore, it is not possible to eliminate the influence of diurnal and seasonal variations of serum lipids in evaluating these two groups.

Forty-three haemodialysis and two peritoneal dialyses were performed in 45 patients using the Czechoslovak (Chepos, Hradec Král ové) or Travenol coil
dialyser, Cuprophane being used always as dialysing membrane. The haemodialyses were of 4-6 hour duration. Dialysis solution contained 200 mg/100 ml of glucose. Peritoneal dialyses persisted 24 hours and dialysis solution was of standard composition (Peridial).

RESULTS

Free fatty acids in the serum of patients in the oligoanuric phase increased to $1752 \pm 119.4 \mu$Eq/L in comparison with the control group $878.5 \pm 46.5 \mu$Eq/L ($p < 0.01$); triglyceride values were also increased to $209.9 \pm 16.4$ mg/100 ml in comparison with the control group $96.5 \pm 7.3$ mg/100 ml ($p < 0.01$). The mean value of total cholesterol was lowered to $149.0 \pm 6.5$ mg/100 ml in comparison with the control group $210.5 \pm 7.6$ mg/100 ml ($p < 0.01$).

The polyuric phase of ARF was characterised by a non-significant decrease of FFA up to values of $1007 \pm 108.2 \mu$Eq/L in comparison with the control group ($p > 0.05$). The mean values of triglycerides decreased to $176.3 \pm 14.7$ mg/100 ml; however, a significant increase persisted. The total cholesterol in the serum began to increase and reached the value $183.6 \pm 8.9$ mg/100 ml; nevertheless this increase was rather low and still presented a significant decrease in comparison with the control group ($p < 0.01$). In the convalescent phase, when patients had a normal glomerular filtration rate, FFA were normalised to values $948.8 \pm 150 \mu$Eq/L ($p > 0.05$), while triglyceride values were still increased $149.1 \pm 20.8$ mg/100 100 ml ($p < 0.01$). The total cholesterol values reached the bottom limit of the control group values $206.3 \pm 14.5$ mg/100 ml ($p < 0.05$) (Figure 1).

![Figure 1. Serum lipids in acute renal failure.](image-url)
Figure 2. Serum lipid changes during haemodialysis.

The influence of haemodialysis on the serum lipids is given in Figure 2. Free fatty acids and the total cholesterol in serum during haemodialysis did not change as can be seen from the following values: serum FFA values before haemodialysis were 1823.0 ± 140.0 μEq/L and after 1647.7 ± 106.4 μEq/L (p > 0.05); the total cholesterol values before haemodialysis were 154.3 ± 6.5 mg/100 ml and after it 144 ± 4.7 mg/100 ml (p > 0.05). During haemodialysis a significant decrease of triglycerides in serum was noted. Triglycerides decreased from predialysis values 219.9 ± 15.8 mg/100 ml to post-dialysis values of 131.7 ± 8.7 mg/100 ml (p < 0.01).

In the control group of people in the age range 20-40 years the following distribution of lipoprotein fractions occurred after electrophoretic separation: beta fraction 43%, prebeta fraction 24% and alpha fraction 33%.

Changes in the lipoprotein spectrum were measured in two patients with different causes of ARF.

1. Patient DT, a 22-year old male, with acute intracapillary proliferative glomerulonephritis, recovered. In the anuric phase the properties of beta fraction decreased to 20%, the alpha fraction to 23%, and the prebeta fraction increased to 57%. Triglyceride values were 279 mg/100 ml and total cholesterol 146 mg/100 ml. The prebeta fraction decreased significantly during haemodialysis to 21%, while beta and alpha fraction increased to 51% and 28%. Triglyceride values in serum were 115 mg/100 ml and total cholesterol 120 mg/100 ml. In the polyuric phase the value of the beta fraction was 52%, that of prebeta fraction 17%, and alpha fraction 32%. The serum triglyceride value reached 187 mg/100 ml and the total cholesterol value 160 mg/100 ml. In the convalescence phase the proportion of beta fraction was 28%, the prebeta fraction value was mildly increased to 37%, and the alpha fraction was 35%. The triglyceride values in serum were 97 mg/100 ml and total cholesterol 138 mg/100 ml (Figures 3 & 4).
2. Patient JS, a 43-year old male, with acute circulatory renal failure and bronchopneumonia, recovered. An electrophoretogram of his lipoproteins before a 4-hour haemodialysis, revealed the following values: beta fraction decreased to 34%, prebeta increased to 41% and alpha fraction decreased to 25%. Serum triglyceride values were 248 mg/100 ml and total cholesterol 197 mg/100 ml. After haemodialysis the prebeta fraction decreased to 18% and beta and alpha fractions increased to 47% and 35%. Triglyceride values were 115 mg/100 ml and total cholesterol 170 mg/100 ml. After haemodialysis the patient received 10 ml protamine sulphate to neutralise the anticoagulant effect of 15,000 units of heparin. After the normalisation of clotting time (Lee-White) the prebeta fraction increased to 31%, while the beta fraction decreased to 34% and alpha fraction showed no change (Figures 5 & 6).
DISCUSSION

The free fatty acid increase in oligoanuric phase was dependent on the severity of the basic illness. After haemodialysis and peritoneal dialysis FFA in serum decreased non-significantly in comparison with the control group. On the contrary an increase was noted in the patients with severe or fatal illness; no relation of FFA kinetics to recovery was found. The cause of the increased values in oligoanuric phase ARF may be in the excessive lipolysis induced by humoral factors, especially catecholamines. This biochemical picture helps to explain the decreased utilisation of glucose in the skeletal muscle of uraemic patients.

Hypertriglyceridaemia in treated patients did not reach the values found in patients during regular dialysis treatment (Bagdale, 1968; Bagdade et al, 1968;
Losowsky & Kenward, 1968). The cause is not yet known. The severity of the illness, increased formation and decreased utilisation of triglycerides (Boyer & Scheig, 1970), the frequency of haemodialysis, and the composition of dialysis solution seem to participate in this biochemical disturbance. The total serum cholesterol decreased both in the oligoanuric and the polyuric phase of ARF. In the convalescence phase cholesterol increased and reached the value of the control group. In the beginning of ARF decreased formation of cholesterol in the liver due to simultaneous damage (hepatorenal syndrome) may occur.

An increase of prebeta fraction, and decrease of alpha and beta lipoprotein fractions were found in the oligoanuric phase, representing a picture of secondary hyperprebetaalipoproteinaemia. No occurrence of more significant amounts of chylomicrons was found. The abundant beta and prebeta fractions improved in some patients. After haemodialysis a decrease in the prebeta fraction and a partial increase of alpha fraction occurred. The most abundant fractions did not change because of haemodialysis. Heparin was always used as an anticoagulant during haemodialysis. Its hydrolysing action upon the low-density prebeta lipoproteins as a co-factor of lipoprotein lipase is well known. After administration of 10 ml protamine sulphate at the end of haemodialysis the proportion of prebeta lipoprotein fraction increased. In the polyuric phase the alpha and prebeta lipoprotein fractions increased, the abundant fractions did not disappear, but prebeta and beta fractions were more clearly separated. In the convalescence phase, the abundant fractions disappeared and the share of prebeta lipoprotein fraction increased definitively.

No relationship was found between the changes of total cholesterol and the beta lipoprotein fraction, or the triglyceride and prebeta lipoprotein fraction values during the study of serum lipid and lipoprotein kinetics. Haemodialysis seems to have been a partial exception in which serum triglycerides and the proportion of prebeta lipoprotein fraction decreased at the same time. The complete opposite was noted in the biochemical picture of convalescence phase of ARF, when triglyceride concentration in the serum decreased and the proportion of prebeta lipoprotein fraction increased.

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Open Discussion

CHAIRMAN (Alwall) Are there any differences in lipids between cases with acute tubular necrosis and obstruction?

MYDLÍK We do not know.

PONTICELLI (Milan) After haemodialysis free fatty acids are raised and triglyceride levels decreased, probably due to heparin which increases lipolytic activity, by hydrolysing triglycerides into glycerol and free fatty acids. How do you explain that free fatty acids do not rise after haemodialysis in your cases?

MYDLÍK We have not found any changes after haemodialysis, but cannot explain why.

VOSNIDES (London) Were any of your acute renal failure patients infected?

MYDLÍK We had no patients with acute nephritis in renal failure in our group. There was no urinary infection.

ROODVOETS (Netherlands) Seven of your patients had carbon tetrachloride poisoning which could very well have caused liver failure. What was the effect of liver failure on the lipids?

MYDLÍK We found no differences between those with and without liver disorders.