Influence of the Type of Membrane and Heparin on Serum Lipid Parameters during a Dialysis Session: A Pilot Study

Konstantinos P. Katopodisa Moses Elisaf a Olga Balaf a
Petros Nikolopoulos a Eleni Bairaktarib Afroditi Katsarakia
Kostas C. Siamopoulos a

aDepartment of Nephrology and bLaboratory of Biochemistry, University Hospital of Ioannina, Ioannina, Greece

Key Words
Lipids · Hemodialysis · Membranes · Heparin

Abstract

Background/Aim: The type of heparin and membrane used might influence the lipids in patients on hemodialysis (HD). However, there are limited and debatable data concerning the lipid changes during an HD session. The aim of our study was to examine the changes in serum lipid parameters during the HD session in relation to the heparin and dialysis membrane used. Methods: Ten patients on HD 3 times/week participated in the study. The study was performed in three phases (A, B, C), each of 1 week’s duration. The types of membranes used were Hemophan (phase A), ethylene vinyl alcohol (phase B) and polyacrylonitrile (phase C), respectively, in a random order. During the midweek session of each phase we used classic heparin, while during the session at the end of the week low molecular weight heparin was administered. Serum total cholesterol, triglycerides, HDL cholesterol, Lp(a), albumin and total proteins were measured before and 5 min after the HD and hourly during the HD session. Results: In all phases, we found a progressive increase in all lipid parameters during the HD session, except Lp(a). This increase, however, was possibly due to hemoconcentration. Conclusions: This pilot study showed that (1) the type of heparin and membrane used does not seem to affect the serum lipid profile during a single HD procedure, and (2) the changes observed in serum lipid parameters are mainly due to hemoconcentration.

Introduction

Dyslipidemia is a common metabolic disorder in patients undergoing hemodialysis (HD). The typical lipid profile (long term) of these patients is characterized by increased serum triglyceride (TG) and Lp(a) levels accompanied by decreased HDL cholesterol (HDL-CHOL) levels [1]. There are data which suggested that the type of heparin [2] and membrane [3] used might influence serum lipid parameters in this population. However, there are limited and debatable data concerning the lipid changes during a single HD session [4–6]. It is worth mentioning that the changes in serum lipid parameters observed during an HD session could reflect underlying abnormalities of lipoprotein metabolism (changes in the...
activity of lipolytic enzymes) that potentially affect the serum lipid profile of HD patients. Therefore, we undertook the present study to examine the changes in serum lipid parameters, including Lp(a), during an HD session in relation to the type of heparin [classic (CH) or low molecular weight (LMWH)] and dialyzer membrane (compatible or noncompatible) used. Moreover, we try to reveal the effect of changes of extracellular volume (hemoconcentration) on the observed alterations of lipid parameters.

**Patients and Methods**

**Patients**

A total of 10 patients (8 male, 2 female) undergoing chronic HD, who were in a stable condition during the last 6 months, were studied. The median age was 52 years (range 31–72 years). No patient had diabetes mellitus or other metabolic or endocrine disorders.

The HD schedule was 4 h 3 times/week, blood flow was 300 ml/min (machine set), dialysate flow was 500 ml/min and bicarbonate was used as dialysate buffer (35 mmol/l). None of the patients received any other medications except calcium carbonate (as phosphate binder), vitamin D (9 patients) and recombinant human erythropoietin (8 patients) in a stable dose (intravenous at the end of the HD session) during the study. In hypertensive patients angiotensin-converting enzyme inhibitors, calcium channel blockers or both were administered.

**Methods**

The study was performed in three phases (A, B, C) of 1 week’s duration in a random order for each patient. We used three different types of dialyzer membranes: Hemophan in phase A, ethylene vinyl alcohol (EVAL) and polyacrylonitrile (PAN) in phases B and C, respectively. The last two HD sessions/week were used for the study. In the midweek HD session an intravenous initial bolus of 5,000 IU of unfractionated heparin (CH) was administered, while at the next HD session an intravenous initial bolus of 3,500 IU of LMWH was used.

Blood samples were taken from the arterial needle after an overnight fast (12 h) for the determination of serum lipid parameters [total cholesterol (T-CHOL), TG, Lp(a), and HDL-CHOL] immediately before (pre-HD) and 5 min after the end of the HD session (post-HD) as well as every hour during the HD session. Total proteins (TPR) and albumin (Alb) were also measured in the above samples.

Blood samples were obtained in the morning after an overnight fast from all subjects before the dialysis session. Serum was isolated by centrifugation at 1,500 g for 15 min and was stored at 4 °C until analysis. Serum samples for Lp(a) measurement were stored at −80 °C until analysis.

Concentrations of T-CHOL and TG were determined enzymatically on an Olympus AU600 Clinical Chemistry analyzer (Olympus Diagnostica, Hamburg, Germany). Our laboratory is currently participating in the Murex Clinical Chemistry Quality Assessment Program. The coefficient of variation values in this programme in the past 2 years ranged between 0.99 and 2.14% for cholesterol, and between 1.73 and 3.36% for TG. HDL-CHOL was determined by a direct assay (Olympus Diagnostica, Hamburg, Germany). Concentrations of TPR and Alb were measured by the biuret method and bromocresol green method, respectively, on an Olympus AU600 analyzer.

Lp(a) was quantified by an enzyme immunoassay (sandwich-ELISA assay, Macra Lp(a), Temuro Medical Corporation, Diagnostic Division, Elkton, Md., USA).

The post-HD and during-HD values were corrected for the presumed change of the extracellular volume (hemoconcentration) according to an equation [7] adjusted for serum lipid parameters.

\[
C(t)_{corr} = C(t) - 0.2 \frac{BW(t)}{BW(t) + UF(t)}
\]

where \(C(t)_{corr}\) = corrected concentration of lipid parameters at any time during dialysis (mg/dl), \(C(t)\) = measured concentration of lipid parameters (mg/dl), \(BW(t)\) = body weight (kg), and \(UF(t)\) = ultrafiltration rate (ml).

**Statistical Analysis**

The laboratory parameters were expressed as mean ± SD. Because of the skewed distribution of Lp(a), their concentrations were given as median.

Statistical analysis was performed by ANOVA for repeated measurements except for Lp(a) values where the Friedman ANOVA was used. Furthermore, analysis of covariance (ANCOVA) was performed taking into account the baseline values of measured parameters as a covariate. Statistical significance was accepted at \(p < 0.05\).

**Results**

Lipid concentrations before \((t_0)\) and after \((t_4)\) HD, with CH or LMWH, using the Hemophan membrane are given in table 1. A statistically significant increase in serum T-CHOL, TG, HDL-CHOL and TPR was noticed after the dialysis session in uncorrected values \((p < 0.05)\) with both types of heparin and all membranes used. However, this increase disappeared when the values were corrected for the degree of ultrafiltration. Lp(a) concentrations remained unchanged after the dialysis session both as uncorrected and corrected values (table 1).

Similar changes in serum lipid parameters were observed using the other types of membranes (EVAL of PAN) regardless of the heparin used (CH or LMWH) (data not shown).

In figures 1 and 2 we can see the alterations of Lp(a) and TG (corrected) values during the dialysis. TG concentrations decreased 1 h after the initiation of dialysis, remained low in the first half of the dialysis session and started to increase in the second half of dialysis (3rd and 4th hour). Lp(a) increased in the first \((t_1)\) and third \((t_3)\) hour of dialysis and returned to the predialysis values in the second \((t_2)\) hour and at the end \((t_4)\) of the dialysis session. The above alterations in these parameters were observed with both types of heparin and all membranes used.
**Discussion**

In this study, we investigated the influence of the type of heparin and the membrane (non- and biocompatible) used on lipid parameters in a single dialysis session. In all cases a significant increase in serum T-CHOL, TG and HDL-CHOL was noticed. However, this increase was possibly due to hemocoagulation, since the percentage changes were parallel to those of TPR and Alb (data not shown). Furthermore, the values were similar to the predialysis ones after correction for the degree of ultrafiltration. Our findings are in agreement with previous studies.

---

**Fig. 1.** Alterations of TG during an HD session using three types of membranes (▲ = Hemophan, ■ = EVAL, ▲ = PAN) and two types of heparin: CH (a) and LMWH (b).

**Table 1.** Serum lipid parameters and TPR before (t₀) and after (t₄) an HD session using Hemophan and CH or LMWH (n = 10)

<table>
<thead>
<tr>
<th></th>
<th>t₀</th>
<th>t₄</th>
<th>p</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>uncorrected</td>
<td>corrected</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-CHOL, mg/dl</td>
<td>228.0 ± 61.1</td>
<td>256.2 ± 75.4</td>
<td>&lt;0.05</td>
<td>231.0 ± 76.5</td>
</tr>
<tr>
<td>TG, mg/dl</td>
<td>250.0 ± 128.0</td>
<td>295.7 ± 123.6</td>
<td>&lt;0.05</td>
<td>245.7 ± 123.6</td>
</tr>
<tr>
<td>HDL-CHOL, mg/dl</td>
<td>36.5 ± 15.8</td>
<td>41.5 ± 17.0</td>
<td>&lt;0.05</td>
<td>37.3 ± 15.5</td>
</tr>
<tr>
<td>Lp(a), mg/dl</td>
<td>13.8</td>
<td>12.8</td>
<td>NS</td>
<td>10.6</td>
</tr>
<tr>
<td>TPR, g/l</td>
<td>7.0 ± 0.6</td>
<td>8.2 ± 1.5</td>
<td>&lt;0.05</td>
<td>7.2 ± 1.7</td>
</tr>
<tr>
<td><strong>LMWH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-CHOL, mg/dl</td>
<td>230.4 ± 50.9</td>
<td>263.8 ± 38.5</td>
<td>&lt;0.05</td>
<td>239.2 ± 52.3</td>
</tr>
<tr>
<td>TG, mg/dl</td>
<td>179.8 ± 52.3</td>
<td>208.9 ± 93.8</td>
<td>&lt;0.05</td>
<td>185.6 ± 60.8</td>
</tr>
<tr>
<td>HDL-CHOL, mg/dl</td>
<td>35.8 ± 12.8</td>
<td>40.8 ± 12.3</td>
<td>&lt;0.05</td>
<td>36.6 ± 11.3</td>
</tr>
<tr>
<td>Lp(a), mg/dl</td>
<td>13.0</td>
<td>11.7</td>
<td>NS</td>
<td>10.9</td>
</tr>
<tr>
<td>TPR, g/l</td>
<td>7.0 ± 0.6</td>
<td>8.2 ± 1.5</td>
<td>&lt;0.05</td>
<td>7.5 ± 1.3</td>
</tr>
</tbody>
</table>

a  Between t₀ and t₄ (uncorrected).

b  Between t₀ and t₄ (corrected).
although the membrane type used was nonbiocompatible and the heparin type was LMWH in one study [4], while no information was given in the other [5].

Interestingly, there was a change in serum Lp(a) levels implying an alteration in Lp(a) metabolism during an HD session. Heparinization could have played a role in this setting, since an increase in serum Lp(a) levels has been reported after heparin administration [4, 6] in patients with chronic renal failure. It can be hypothesized that Lp(a) may be released from the endothelium vascular surface, since Lp(a) is bound to glucosaminoglycans and to plasminogen on the endothelial surface. Heparin can release lipoprotein lipase anchored to the vascular endothelium through glucosaminoglycans into the circulation, thus it is tempting to suggest that a similar mechanism might be involved in the release of Lp(a) into the bloodstream after heparin (either LMWH or unfractionated). However, 1 h after the beginning of the HD session an increase in serum Lp(a) levels was found along with a profound decrease in serum TG (due to the release of lipoprotein lipase), suggesting that heparin-induced changes of serum Lp(a) levels are less possible.

Alternatively, recent reports provide strong evidence that cytokines can alter lipid parameters, indicating a possible role of the immune system in atherosclerosis [8, 9]. The HD procedure results in cytokine release and IL-6 has been reported to be an activator of the synthesis of acute-phase proteins by hepatocytes [10]. Since Lp(a) has been considered an acute phase protein, this possible influence of cytokines on Lp(a) alterations during HD needs further investigation using a large group of dialysis patients, because our results showed similar changes as concerns biocompatibility in serum Lp(a) concentrations irrespective of the type of membrane used. These studies could also reveal the underlying mechanisms of the potential changes in lipid parameters during an HD session, which may play a significant role in the lipid profile of this population.

The small sample size is a limitation of our study, which is, in fact, a pilot study. However, the number used is adequate to detect a clinically relevant difference of 10% change in serum lipid parameters at a two-sided risk of 5% and a statistical power of more than 80%.

We conclude that the HD procedure by either compatible or noncompatible membranes and the type of heparin used does not affect lipid parameters acutely. However, temporary alterations in some of the parameters during the HD session can be observed. Further investigation is needed to delineate whether these alterations can be of benefit or are harmful for the patients.

**Acknowledgment**

The authors wish to thank Mrs. Aleka Papageorgiou for her skilled secretarial assistance.
References