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Effects of Lipoprotein apheresis on the Lipoprotein(a) levels in the long run

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Abstract

Background: Lipoprotein(a) (Lp(a)) is a low density lipoprotein-like particle to which apolipoprotein(a) is bound. It is recognized as an atherosclerosis-inducing risk factor. Up to now a detailed description of the effect of Lipoprotein apheresis (LA) on Lp(a) levels in the long run is lacking.
Methods: We studied 59 patients with elevated Lp(a) levels who were treated with LA at the Lipoprotein Apheresis Center at the University Hospital Dresden. We analyzed Lp(a) concentrations before the start of the LA treatment and during this extracorporeal therapy.
Results: Comparing the Lp(a) levels before the start of LA therapy and pre-apheresis (measured before the LA sessions) Lp(a) levels, we observed a reduction of the Lp(a) levels of about 22.8% in all patients. Lp(a) levels were acutely (comparing post-apheresis with pre-apheresis concentrations) reduced by all 6 available LA methods (by about 70%). A linear regression analysis was performed to differentiate the long term course of pre-apheresis Lp(a) levels. In 30 patients we saw an increase of the pre-apheresis Lp(a) levels over the time, in 15 patients a constancy and in 14 patients a decrease. Patients with a decrease of pre-apheresis Lp(a) levels over the time had significantly higher initial (before the start of the extracorporeal treatment) and pre-apheresis values and they were significantly older. These patients had significantly more severe peripheral arterial disease as well as cardiac valve and carotid stenosis. The patients with the lowest initial Lp(a) levels and an increase of the pre-apheresis Lp(a) levels over the time had the highest percentage of intake of Tredaptive®/Niaspan® though after stopping the intake of these nicotinic acid preparations no clear increase of Lp(a) concentrations was observed. The applied LA systems did not seem to have a significant influence on the course of pre-apheresis Lp(a) levels. In all patients there was a high variability of Lp(a) concentrations between LA sessions which may in part be due to the inaccuracy of the method used to measure Lp(a) concentrations.
Conclusion: Pre-apheresis Lp(a) levels (before the LA sessions) are lower than those before the start of a LA treatment but they behave differently among patients during LA treatment.

Keywords: Lipoprotein apheresis; Lipoprotein(a); Cardiovascular events; Risk factors; Long term effects

1. Introduction

Studies have shown that elevated Lipoprotein(a) (Lp(a)) levels are a strong risk factor for cardio-vascular diseases [1–3]. Extremely high values of Lp(a) (>90th percentile) are associated with a more than doubled risk of myocardial infarction [2,4]. Lipoprotein apheresis (LA) strongly reduces the incidence of cardiovascular events in patients with isolated Lp(a) elevation [1,2,5,6]. Lp(a) levels are acutely lowered by LA by about 70% per session.

Former studies did not pay special attention to the course of pre-apheresis (measured before the LA sessions) Lp(a) levels in the long run. We focused our attention on this problem and studied all patients with elevated Lp(a)

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levels who were treated at the Apheresis Center at the University Hospital Dresden. We wanted to look for factors which may have influenced the course of these pre-apheresis Lp(a) levels like initial Lp(a) concentrations, applied LA systems, acute reduction rates of Lp(a), intervals between LA sessions, gender, age, accompanying risk factors or concomitant drug intake. Post-apheresis (after the LA session) Lp(a) levels and the interval mean Lp(a) values as well as the course of other lipid levels were also taken into consideration. Moreover, we looked into the association of Lp(a) concentrations with cardiovascular diseases (CVD) and cardiovascular events (CVE). The intra- and interindividual variability of Lp(a) concentrations was also analyzed.

2. Patients, methods and statistical analysis

2.1. Patients

59 patients (34 males, 25 females) with an elevated Lp(a) level were treated on a regular weekly or biweekly basis with LA. The mean Lp(a) levels of all patients before the LA therapy started was 1493 mg/L. The mean age was 61 years (range: 31–81 years) at the time of this evaluation. The mean body mass index (BMI) was 27 kg/m^2 (±SD: 4 kg/m^2) and the mean duration of extracorporeal treatment was 5 years (range: 0.5–22 years).

Information about risk factors and CVD were given in the patients' health documents: renal insufficiency (defined by the GFR $<$ 60 ml/min), hypertension (systolic blood pressure $>$ 140 mmHg/diastolic blood pressure $>$ 90 mmHg or antihypertensive drug treatment), diabetes (defined by fasting blood sugar $>$ 7.0 mmol/L, blood sugar after oGTT $>$ 11.0 mmol/L or the intake of antidiabetic drugs), cardiac valve stenosis (echocardiography), peripheral arterial disease (ultrasound), carotid stenosis (ultrasound), cardiac insufficiency (ejection fraction $<$ 55%), arrhythmia and coronary heart disease (coronary angiography, ECG).

We also documented CVE in all patients: myocardial infarction, atrial fibrillation, ventricular fibrillation, percutaneous coronary intervention (with stent implantation), bypass operation, stroke, transitory ischemic attack, subarachnoidal hemorrhage and amputations because of peripheral arterial disease. The observation time of all patients started with their first cardiovascular event before apheresis and ended in December 2013 (end of this study).

The evaluation of the data of the patients has been approved by an ERB and all patients gave their written informed consent.

2.2. Methods

2.2.1. LA methods

The six different LA methods performed in the Apheresis Center at the University Hospital Dresden have been described before [7]: DALI (Fresenius Medical Care GmbH, Bad Homburg, Germany), HELP (B Braun Avitum AG, Melsungen, Germany), Liposorber D (Kaneka Corporation, Japan), Lipidfiltration (Diamed Medizintechnik GmbH, Cologne, Germany), MONET (Fresenius Medical Care GmbH, Bad Homburg, Germany) and TheraSorb® LDL (Miltenyi Biotec GmbH, Bergisch-Gladbach, Germany).

2.2.2. Lipid concentrations

Before the start of the LA treatment, fasting lipid levels have been assessed. During the extracorporeal treatment time, blood (non fasting values) was drawn immediately before and after each LA session. Lp(a) levels were measured by immuno LEIA anti-human Lp(a) Latex Reagent with the coefficient of variation of 11.3%. All the other parameters (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG)) were measured with Modular (Roche). The interval mean values were calculated with the help of the Kroon formula: $c_{mean} = c_{min} + k^*(c_{max} - c_{min})$ where c_{max} is the Lp(a) concentration before the session, c_{min} is the Lp(a) concentration after the session and $k = 0.73$ [6,8].

2.2.3. Statistical analysis

Lipid levels are given as mean ± standard deviations (SD). The evaluation of the course of pre-apheresis Lp(a) levels during LA therapy (based on measurements before the sessions) was done by linear regression analysis ($y = ax + b$), where "a" is the slope of the regression line. All other lipids described in this study were analyzed by linear regression, too. The variability of Lp(a) levels and all other lipid levels over the time was described with the correlation coefficient r^2 (according to Pearson). The correlation coefficient was defined in the following way: if the value of r^2 is near 1 there is almost no variability of the data, if r^2 is near 0 there is a high variability. Considered parameters for this correlation were the number of sessions and the pre-apheresis lipid values in each of these sessions. Statistical calculations were done by the help of Microsoft Excel version 14.0 and SPSS statistical software package standard 22.0 using ANOVA and the post-hoc tests according to Bonferroni for normally distributed data, the Chi^2 – tests to compare frequencies.

3. Results

3.1. Comparison of Lp(a) levels before the start of LA therapy and pre-apheresis Lp(a) levels

First we analyzed the Lp(a) levels before the start of apheresis treatment and the mean pre-apheresis Lp(a) levels during LA therapy. We observed a reduction of the Lp(a) levels of about 22.8% induced by LA in all patients. We paid attention to the fact that pre-apheresis Lp(a) levels behaved differently in the course of the apheresis treatment.

3.2. Classification of patients according to the course of pre-apheresis Lp(a) levels under LA therapy

We noticed that in some patients there was an increase of the pre-apheresis Lp(a) levels over the time, in some there was a constancy and in some patients there was a decrease of these levels. We performed linear regression analysis in each patient and classified the patients in dependence on the slope of this regression line. We defined the limits of the slope "a" like the following: group 1 ($a > +0.5$), group 2 ($+0.5 \geq a \geq -0.5$) and group 3 ($a < -0.5$) (Table 1). The courses of the pre-apheresis Lp(a) levels in these three groups are significantly different ($p < 0.02$). Examples of the course of pre-apheresis Lp(a) levels in the 3 groups are given in Figs. 1–3.

We looked at the mean Lp(a) levels in the 3 groups before the start of the extracorporeal therapy and during this therapy (pre-apheresis values). In group 3 there were the highest initial Lp(a) levels, in the mean of 1824 mg/L. In contrast to that the mean Lp(a) levels in group 1 was 1370 mg/L and in group 2 1286 mg/L. There was a significant difference between groups 2 and 3. Also pre-apheresis Lp(a) values between groups 2 and 3 showed significant differences. There is a big difference between the maximum and minimum levels of the mean pre-apheresis Lp(a) levels in all groups. And even though there is a difference with respect to the course of the pre-apheresis Lp(a) levels during the time of the extracorporeal therapy between the groups, there is still a reduction of the mean pre-apheresis Lp(a) levels compared to the Lp(a) levels measured before the start of apheresis treatment as you can see by the reduction in each group (Table 2). Most patients have their LA sessions once a week, but the interval of apheresis sessions did not show any influence on the course of the pre-apheresis Lp(a) levels in the groups. Also the acute reduction rates induced by the apheresis sessions did not show any distinctions. The pre-apheresis Lp(a) levels are acutely reduced by about 70% in all groups. The interval mean values of Lp(a) showed a significant difference between groups 2 and 3.

The variability of pre-apheresis Lp(a) levels over the time was measured with the help of the correlation coefficient "r^2". In all three groups we observed a high variability of pre-apheresis Lp(a) levels (group 1: $r^2 = 0.15$ (range: 0.0005–0.55), group 2: $r^2 = 0.07$ (range: 0.0001–0.56), group 3: $r^2 = 0.16$ (range: 0.003–0.54)). All other lipid levels had a high variability, too. But there was no significant difference between the groups.

Table 1
Groups of patients – based on the slope (a) of the regression line of pre-apheresis Lp(a) levels.

	Group 1	Group 2	Group 3
	Increase of Lp(a) ($a > +0.5$)	Constancy of Lp(a) ($+0.5 \geq a \geq -0.5$)	Decrease of Lp(a) ($a < -0.5$)
Males	15 (50.0%)	10 (66.7%)	9 (64.3%)
Females	15 (50.0%)	5 (33.3%)	5 (35.7%)
Total number	30	15	14

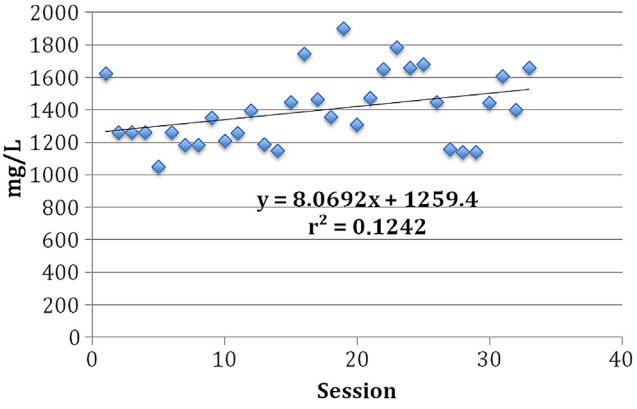

Fig. 1. Example of a patient (Lp(a) levels before single apheresis sessions) out of group 1 with an increase of the Lp(a) levels over the time.

There was no significant difference concerning the distribution with respect to gender or body mass index in all groups. But we observed a significant difference regarding the mean age of the patients (increase of the age from group 1 to 3) (Table 2).

However the treatment with Tredaptive® or Niaspan® showed a significant impact on the Lp(a) levels ($p = 0.035$ between group 1 and 2, $p = 0.05$ between group 1 and 3/ Chi^2-test). In group 1, which had the lowest mean Lp(a) levels before the start of LA treatment, the highest number of patients has been treated with those drugs. The intake of Tredaptive® or Niaspan® continued during LA treatment and stopped in all patients in January 2013 because these drugs were taken off the market. We did not see any significant increase of Lp(a) levels after the cessation of nicotinic acid therapy. The duration of Tredaptive® or Niaspan® intake did not have any influence (Table 3). Also the use of other lipid lowering drugs like statins did not have any impact.

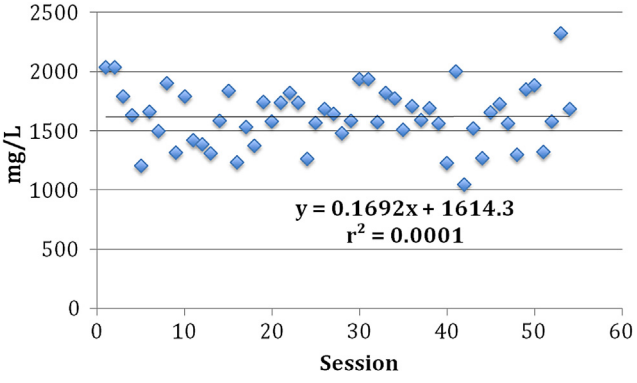

Fig. 2. Example of a patient (Lp(a) levels before single apheresis sessions) out of group 2 with a constancy of the Lp(a) levels over the time.

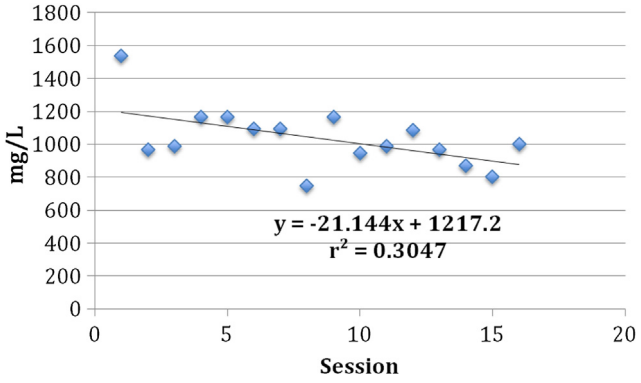

Fig. 3. Example of a patient (Lp(a) levels before single apheresis sessions) out of group 3 with a decrease of the Lp(a) levels over the time.

Another aspect we examined were the different LA methods used in the therapies. All six methods were applied in the groups. In group 1 DALI was the most frequently used method (23%) followed by Liposorber D (20%) and Lipid filtration (20%). In group 2 the mostly used methods were HELP (46%) and DALI (26%), and in group 3 Liposorber D (43%) and MONET (21%). The number of sessions did not have any impact on the different course of the pre-apheresis Lp(a) levels in the three groups. Group 1 had in the mean 198 (range: 11–669) sessions, group 2 had 234 (range: 14–259) and group 3 had 165 (range: 7–524) sessions.

3.3. TC, LDL-C, HDL-C and TG in the subgroups according to the course of pre-apheresis Lp(a) levels under LA therapy

In contrast to the slope of the Lp(a) levels (range: −8.8 to +6.7), the slope of all other lipids is around 0, which means that there were almost no changes of these pre-apheresis lipid levels over the time. We detected no significant difference between the groups. All lipid parameters were found to be acutely reduced by the extracorporeal therapy when evaluated in a similar way (Table 4). The variation of all data, based on the coefficient of determination, showed no significant differences between the groups.

Table 3
The total number of patients treated with Tredaptive®/Niaspan®, (percentages).

Number of patients (%)	Group 1	Group 2	Group 3
Tredaptive®/Niaspan® intake	18 (60.0%)	4 (26.7%)	4 (28.6%)
Duration of intake (months), (range)	15.5 (1–60)	10.5 (1–20)	18.7 (2–25)

3.4. Further risk factors and CVD in the groups according to the course of pre-apheresis Lp(a) levels under LA therapy

With respect to risk factors we observed a significant difference concerning the renal insufficiency between group 1 and 2. Hypertension and diabetes did not show any significant differences between the groups. Considering the CVD in group 3 there was a significantly higher number of patients with either cardiac valve stenosis, peripheral arterial disease or carotid stenosis. The CVD were associated with higher mean Lp(a) levels (pre-treatment and pre-apheresis values) in this group. No differences were detected for heart failure, arrhythmias and coronary heart disease between the three groups (Table 5). There was no difference between the groups considering the number of cardiovascular events before or during the LA treatment. Only the in-group comparison of events before and during the therapy showed the effect of the LA therapy ($p < 0.05$).

4. Discussion

Lp(a) levels measured immediately before the first LA session were similar to those measured previously. This finding is in concordance with data published in the Pro(a) Life study [6]. Once the LA treatment had started, we saw a consistent reduction of pre-apheresis Lp(a) concentrations by 22.8% from baseline in all patients, which is probably due to the LA treatment. In a study by Kassner et al. similar effects were described. After one year of regular LA the mean pre-apheresis levels of Lp(a) were reduced by 22% and after three years a 19% reduction persisted [2].

In the present study we were able to dissect three groups within our cohort with respect to the pre-apheresis Lp(a)

Table 2
Groups of patients – Characteristics.

	Group 1	Group 2	Group 3
Age (years), mean (range), (group 1 vs group 3, p = 0.04)	**58 (31–82)**	61 (49–80)	**67 (45–76)**
BMI (kg/m²)	28 (5.7)	27 (4.6)	27 (4.4)
Lp(a) before the start of LA (mg/L), (group 2 vs group 3, p = 0.002), range	1370 (527), (589–2698)	**1286** (516), (686–2349)	**1824** (900), (819–4068)
Pre-apheresis Lp(a) (mg/L), (group 2 vs group 3, p = 0.001), range	1074 (369), (690–1675)	**908** (349), (564–1432)	**1349** (494), (924–1980)
Difference of pre-treatment Lp(a) and pre-apheresis Lp(a)	−21.6% (12.8%)	−21.5% (10.3%)	−25.4% (20.6%)
Post-apheresis Lp(a) (mg/L)	314 (129)	298 (133)	433 (176)
Lp(a) acute reduction rate per session	−70.3% (5.9%)	−66.4% (6.34%)	−67.8% (5.8%)
Lp(a) interval mean value (mg/L), (group 2 vs group 3, p < 0.05)	869 (300)	**744** (287)	**1102** (403)

Significant differences between the groups are marked as bold values in the table.

Table 4
Groups of patients – Characteristics.

	Group 1	Group 2	Group 3
TC before the start of LA (mmol/L)	5.0 (1.7)	5.8 (1.8)	5.6 (2.2)
Pre-apheresis TC (mmol/L)	4.5 (0.9)	5.1 (1.1)	4.6 (0.9)
Post-apheresis TC (mmol/L)	2.2 (0.4)	2.5 (0.5)	2.3 (0.6)
TC acute reduction rate per session	−50.1% (6.4%)	−50.7% (6.3%)	−49.0% (5.4%)
LDL-C before the start of LA (mmol/L)	3.1 (1.7)	3.9 (1.6)	3.4 (2.0)
Pre-apheresis LDL-C (mmol/L)	2.5 (0.9)	3.0 (0.9)	2.4 (0.6)
Post-apheresis LDL-C (mmol/L)	0.8 (0.3)	0.9 (0.3)	0.8 (0.4)
LDL-C acute reduction rate per session	−70.5% (14.2%)	−66.5% (6.5%)	−67.5% (9.3%)
HDL-C before the start of LA (mmol/L)	1.5 (0.5)	1.4 (0.3)	1.3 (0.3)
Pre-apheresis HDL-C (mmol/L)	1.5 (0.4)	1.4 (0.4)	1.4 (0.4)
Post-apheresis HDL-C (mmol/L)	1.2 (0.3)	1.2 (0.3)	1.2 (0.2)
HDL-C acute reduction rate per session	−16.7% (5.4%)	−14.5% (4.5%)	−15.3% (5.5%)
TG before the start of LA (mmol/L)	1.4 (0.7)	1.5 (0.7)	2.3 (2.6)
Pre-apheresis TG (mmol/L)	1.8 (0.9)	2.2 (0.6)	2.3 (1.5)
Post-apheresis TG (mmol/L)	0.9 (0.6)	1.0 (0.4)	1.0 (0.8)
TG acute reduction rate per session	−47.8% (12.9%)	−51.7% (12.5)	−56.6% (9.1%)

concentrations: group 1 with an increase, group 2 with a constancy and group 3 with a decrease of these levels. For classification of the patients the slope of the regression line was used, we defined values of this slope which clearly represent different tendencies of the pre-apheresis Lp(a) levels. The courses of these values were significantly different between the three groups. In the Pro(a)Life study

Table 5
Risk factors and cardiovascular diseases of the patients, cardiovascular events before and during apheresis treatment.

Risk factors	Group 1	Group 2	Group 3
Hypertension	76.6%	86.6%	78.5%
Diabetes	40.0%	26.6%	64.2%
Renal insufficiency, (group 1 vs group 2, p = 0.05)	**43.3%**	**6.6%**	42.8%
CVD	Group 1	Group 2	Group 3
Arrhythmia	10.0%	13.3%	14.3%
Cardiac insufficiency {20}	20.0%	20.0%	35.7%
Cardiac valve stenosis, (group 2 vs group 3, p = 0.02)	36.6%	**13.3%**	**78.5%**
Coronary heart disease	76.6%	86.6%	85.7%
Peripheral arterial disease, (group 2 vs group3, p = 0.04)	43.3%	**20.0%**	**57.1%**
Carotid arterial stenosis, (group 2 vs group3, p = 0.04)	35.8%	**20.0%**	**57.1%**
CVE per patient/year	Group 1	Group 2	Group 3
before LA	1.12 (0.07–3)	1.4 (0.36–4)	0.45 (0.03–1)
during LA	0.07 (0–1)	0.01 (0–0.09)	0.1 (0–0.54)
reduction rate	−82.4%	−97.4%	−69.3%
time before LA (years)	3.9 (0–17)	2.6 (0–11)	12.8 (0–42)
time since LA (years)	4.1 (0–22)	6 (0–14)	3.1 (0–12)

Significant differences between the groups are marked as bold values in the table.

pre-apheresis Lp(a) levels were observed to be constant during LA treatment, at least in the mean [6]. No details have been reported about the course of these levels in single patients.

On the other hand, Ritter et al. [9], described a slight increase of pre-apheresis Lp(a) values over the time, but compared to the pre-treatment values there was still a reduction by 30%. In their study they only included 13 patients. In a paper by Armstrong et al. [10] a figure shows the data of pre-apheresis Lp(a) concentrations in a child with homozygous familial hypercholesterolemia. In contrast to pre-apheresis LDL-C levels, the pre-apheresis Lp(a) levels tended to increase during LA treatment. One possible explanation for an increase of pre-apheresis Lp(a) levels in group 1 could be the fact that Lp(a) levels obviously do increase in post-menopausal women [11]. The increased production of lipoproteins following the acute reduction after apheresis treatment could be another reason for a long term increase of pre-apheresis Lp(a) levels. It has been found that the Lp(a) concentrations are regulated by production rates, data on the influence of LA sessions on Lp(a) production are not available [12]. Another factor that may have induced an increase in Lp(a) levels could be the deterioration of the kidney function which was seen in some patients [13].

The group with higher initial Lp(a) levels and a decrease of pre-apheresis Lp(a) levels over the time was significantly older and had more severe CVD. The acute reduction rates induced by the apheresis sessions did not show any distinctions. The Lp(a) levels were acutely reduced by about 70% in all groups. The interval mean values of Lp(a) were different between groups 2 and 3. In all 3 groups LP(a) levels were clearly higher than the desirable level of 500 mg/L [3]. Nevertheless LA therapy was effective with respect to reducing CVE.

There was a high intra- and interindividual variability of pre-apheresis Lp(a) concentrations which cannot be fully explained up to now. One possible explanation could be the used laboratory measurement method, which was associated with a rather high coefficient of variation. Observations [14] have shown that with new measurement methods, like "WHO/IFCC International Reference Reagent (SRM2B)", the variability of data is much less than with the method used in this study, which has to be further investigated in subsequent studies. Parhofer et al. [12] measured the fractional catabolic rates and production rates of Lp(a) in 17 patients by fitting a monoexponential function to the rebound of Lp(a) plasma concentration following LA. In eight patients these measurements were repeated. An important finding was that the fractional catabolic rates were concordant (intraclass correlation coefficient), whereas production rates were not. Thus it can be assumed that Lp(a) production may vary leading to variable Lp(a) concentrations. Other factors which could be suspected to have an influence on variability of Lp(a) levels may be inflammatory processes or acute phase reactions after major

events such as myocardial infarction or surgical interventions which increase Lp(a) levels intermittently [15].

Another very interesting aspect is the influence of Tredaptive® or Niaspan® on the Lp(a) levels before extracorporeal therapy and also during. Besides the fact that the patients with the highest intake of these drugs had the lowest initial and pre-apheresis Lp(a) levels, they also had an increase of the pre-apheresis Lp(a) levels over the time during therapy. An explanation for that could be the Lp(a) lowering effect of Tredaptive®/Niaspan® before the therapy started as has already been shown in other studies [16]. The missing effect during therapy after stopping to administer these drugs could be the reason for the increase of pre-apheresis Lp(a) concentrations in group 1. However, we did not see any remarkable increase of pre-apheresis Lp(a) levels after the cessation of nicotinic acid therapy.

Different LA methods had a different effect on the Lp(a) levels over the time, which should be analyzed specifically. We have previously reported that Liposorber D produced the most distinct reduction of Lp(a) concentrations per session [7]. Another study showed different results. Parhofer et al. reported that Lp(a) levels were more effectively reduced by HELP, immunoadsorption and dextran-sulfate apheresis compared with cascade filtration [17]. Evidently different LA methods have different effects on Lp(a) levels per session [18–20]. In the present study, no determining effect of the applied LA methods on the course of the pre-apheresis Lp(a) levels was seen.

Considering all other parameters, we detected no difference between pre-apheresis levels over the time among the three groups, which is in contrast to the course of Lp(a) levels over the time. All lipid parameters were found to being acutely reduced by the extracorporeal therapy, as it has been shown in other studies [21].

Several studies demonstrated that LA is very effective in lowering cardiovascular events. There was a significant decrease of CVE induced by apheresis treatment in all our patients, in the mean by 83%. There was no difference considering the number of cardiovascular events per patient per year before nor during therapy between the three groups. The desirable level of pre-apheresis Lp(a) levels of <500 mg/L was not achieved in any of the patients. Considering the cardiovascular diseases in group 3 there was a significantly higher number of patients with either cardiac valve stenosis [22], peripheral arterial disease or carotid stenosis correlating with the higher mean Lp(a) levels (before the start of apheresis therapy and also pre-apheresis values) in this group.

5. Conclusions

LA is a very effective treatment for removing atherogenic lipoproteins which was shown by the fact that there is a more than 22% reduction of the pre-apheresis Lp(a) levels when compared to Lp(a) levels before the start of LA treatment. While the acute reduction of Lp(a) levels induced by LA treatment could be verified, this is not associated with the long term course of pre-apheresis Lp(a) levels. Unexpectedly, pre-apheresis Lp(a) levels behave differently in each patient over the time. Higher pre-apheresis Lp(a) levels are more likely to decrease over a long term period.

Patients with the very high Lp(a) levels should undergo a regular echo-cardiography and ultrasound investigations of their arterial vessels because they have an elevated risk for atherosclerotic changes as shown in this study.

It is well known that LA therapy decreases the body cholesterol pool of the patients which leads to the disappearance of xanthomas and xanthelasmata. For Lp(a) such a decrease of the pool could not be observed.

At this time no medication is available for decreasing Lp(a) levels. PCSK9 antagonists which reduce Lp(a) levels by about 30% are still scientifically explored, so nowadays the only way to effectively lower Lp(a) levels is the application of LA therapy.

Conflicts of interest

EG: none declared. BH: received honoraria, travel support and project funding from Miltenyi Biotec, B Braun Avitum, Fresenius Medical Care and Kaneka. UJ: was reimbursed travel expenses by Diamed, Fresenius Medical Care and Kaneka. He was paid honoraria for lectures by Kaneka, Diamed and Fresenius Medical Care as well as for lipidologic evaluations by Fresenius Medical Care.

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