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Increasing plasma lysophosphatidylcholine levels in patients with regular dextran sulfate lipoprotein apheresis

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Abstract

Objectives: Previously we found a highly significant increase of phosphatidylethanolamines (PE) in response to acute lipoprotein apheresis (LA) with whole blood dextran sulfate adsorption (DSA) in contrast to the overall tendency of reduction of lipid metabolites of all lipid classes in post-apheresis plasma. Therefore, the aim of the present study was to analyze long-term modifications of the plasma lipidomic profile in patients with repeated DSA apheresis.
Methods: Nine patients weekly treated with DSA were followed for 40 weeks. Pre- and post-apheresis levels of routine lipid parameters and lipidomic profiles of five apheresis sessions were assessed.
Results: The main finding of the present study was a progressive increase of pre- and post-apheresis plasma lysophosphatidylcholine (LPC) levels, which doubled in concentration at the end of the 40 week observation period. LPC metabolites which mainly contributed to this increase were LPC 20:4 > 18:0 > 18:1 > 16:0 > 20:3 > 18:2.
Conclusion: These data indicate that long-term application of DSA technology may be associated with a continuous increase in LPC levels. Possible pro- or anti-atherogenic consequences should be elucidated in further studies.

Keywords: Dextran sulfate adsorption; Lipoprotein apheresis; Lipidomics; Lysophosphatidylcholines

1. Introduction

Numerous studies have shown that lipoprotein apheresis (LA) is highly effective in the prevention of cardiovascular events in patients with severe derangements of lipid metabolism and rapidly progressing atherosclerosis [1–4]. Beside rigorous reduction of LDL-cholesterol (LDL-C) and Lipoprotein(a) (Lp(a)), the therapeutic effectiveness of LA has also been attributed to the reduction of fibrinogen, oxidized LDL and other markers of inflammation [5]. These findings indicate that the biological effects of LA cannot be sufficiently elucidated by traditional lipid parameters. Rapid progression of lipidomics technology and new insights into the role of selective lipid species in atherogenesis promote efforts to gain a deeper understanding of apheresis-induced modifications of lipid metabolism by analyzing selective lipid classes and discrete lipid molecules. In previous studies we were able to show that acute LA produced a very inhomogeneous picture of lipidomic changes [6] and that LA using dextran sulfate adsorption (DSA) was associated with a specific increase in

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phosphatidylethanolamines in comparison to lipid filtration [7]. These findings prompted the question of whether lipidomic effects observed in a single LA might have long-term effects on lipid metabolism in chronically applied specific LA technologies. The aim of the present study was, therefore, to investigate modifications of the plasma lipidomic profile in patients with repeated DSA LA in order to determine long-term changes in selective lipid classes and species.

2. Methods

2.1. Patients

Short- and long-term changes in plasma lipidome were studied in patients weekly undergoing LA by dextran sulfate adsorption (DSA; Liposorber® D, Kaneka). All patients gave written consent to the study, which was approved by the local ethics committee (EK199052011). Plasma samples of six men and three women (age: 37–75 years, body mass index: 23.4–34.0 kg/m^2;, treated blood volume: 7400 ± 450 ml) were obtained directly before, after and three days after the first and 40th apheresis sessions. All samples were shock frozen with liquid nitrogen and stored at −80 °C until analysis. The observation period covered 40 apheresis sessions realized in 40 weeks. Acute effects of apheresis were studied in five LA sessions (Fig. 1). Routine medication was maintained during the observation period.

2.2. Routine lipid parameters

Total cholesterol (TC), LDL-C, HDL-cholesterol (HDL-C), and Lp(a) were measured using the Roche automated clinical chemistry analyzer MODULAR (Roche Diagnostics GmbH, Mannheim, Germany).

2.3. Lipidomics

Shotgun lipidomics of blood plasma samples were performed as previously described [8–11]. Briefly, blood plasma samples were extracted with MTBE/methanol containing one internal standard for each quantified lipid class. The extracts were analyzed by dual polarity MS acquisitions. All measurements were performed on a QExactive mass spectrometer (Thermo Fisher Scientific, Bremen, Germany) equipped with a robotic nanoflow ion source TriVersa NanoMate (Advion BioSciences Ltd, Ithaca NY). FT MS spectra were analyzed by LipidXplorer software as described in the literature [10–13]. High resolution spectra of 190 lipid species in 12 major lipid classes were analyzed. Lipid classes analyzed were: cholesterol esters (CE), triacylglycerols (TAG), diacylglycerols (DAG); sphingomyelins (SM), ceramides (Cer), lysophosphatidylcholines (LPC), lysophosphatidylethanolamines (LPE); phosphatidyl-cholines (PC), ether phosphatidylcholines (PC-O), phosphatidylethanolamines (PE), ether phosphatidylethanolamines (PE-O), and phosphatidylinositol (PI).

2.4. Statistical analysis

Acute and long-term effects of DSA on routine lipid parameters and lipidomic profile were assessed by analysis of variance (ANOVA). All analyses were conducted using the SPSS Statistics 22 software.

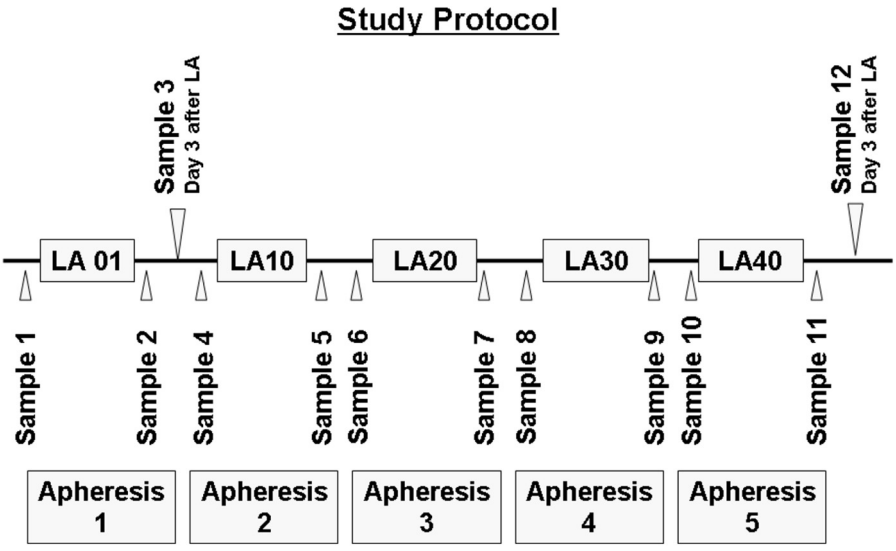

Fig. 1. Study protocol. LA: lipoprotein apheresis session; LA number represents consecutive numbering of performed apheresis sessions.