Short Communication

Lipoprotein Apheresis – Own Experience

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Abstract

Low density lipoprotein (LDL) apheresis is utilized in clinical practice with patients suffering from lipid disorders with a high and very high cardiovascular risk. One treatment allows to reduce the concentration of LDL by 55 – 80%. These treatments are recommended primarily for patients with a familial homozygous hypercholesterolemia, for whom treatments should be commenced as early as at the age of 5-8 years old. Therapy is also used for patients with a heterozygous form of hypercholesterolemia if, despite maximum doses of statins, further progress of clinically symptomatic atherosclerosis is observed. Apheresis is recommended when, despite a diet and maximum tolerable pharmacotherapy, the concentration of LDL is ≥ 300 mg/dl (7,7 mmol/l) or ≥ 200 mg/dl (5,2 mmol/l) throughout 6 months for patients with documented coronary heart disease. In recent years an indication to perform apheresis is also an isolated increase of lipoprotein (a), with values >60 mg/dl. The apheresis treatment lasts 2-3 hours and must be repeated every 1-2 weeks for the rest of the patient's life, it is safe and not associated with dangerous complications. Below we present the current state of knowledge regarding LA with a description of own experience.

Keywords: Cardiovascular risk; Hypercholesterolemia; Lipoprotein apheresis; Lipoprotein; Low density lipoprotein

Introduction

In accordance with the guidelines for treating hypercholesterolemia, it is recommended to use: statin, fibrates, ezetimibe, proprotein convertase subtilisin kexin type 9 - PCSK9, evolocumab or alirocumab, as well as apply treatment incorporating lipoprotein apheresis (LA). [1-3] LA procedures are publicly funded in Poland, carried out as part of hospital treatment (catalog of separate benefits, Hospitalization associated with LA). [4] LA is an invasive procedure, repeated every several days, which saves the lives of patients with no possibility of effective pharmacological treatment of lipid disorders. [3] This procedure makes it possible to reduce low density lipoprotein (LDL) and lipoprotein a (Lp (a)) to values assumed as a therapeutic goal in the treatment of lipid disorders in patients with cardiovascular disease. [3,5-7] In accordance with new guidelines for the management of dyslipidaemias, of the European Society of Cardiology, which appeared in September this year in a group of patients with low cardiovascular risk should achieve a target LDL concentration <115 mg/dl, in a group at moderate risk <100 mg/dl, in the case of high risk <70 mg/dl, and in patients with a very high risk of cardiovascular disease <55 mg/dl. [2] The therapy's inconvenience is the requirement of repeating it every several days until the end of the patient's life. It is limited by the fact that in order for the procedure to be financed by the National Health Fund (NHF), it must be carried out as part of hospitalization, which forces performance of procedures in intervals longer than is necessary to maintain a safe lipid concentration. [4]

In Poland apheresis treatment of patients with the most severe lipid disorders is practically non-existent (only 6 centers). All the while, in Germany the number of centers performing apheresis treatments is the highest in Europe, and clinical observations show that long-term application of LA contributes to regression and stabilization of atherosclerotic plaque and improves cardiovascular prognoses. [8] One treatment allows to reduce the concentration of LDL by 55–80%. In Poland these treatments are recommended primarily for patients with a familial homozygous hypercholesterolemia, for whom treatments should be commenced as early as at the age of 5-8 years old. Therapy is also used for patients with a heterozygous form of hypercholesterolemia if, despite maximum doses of statins, further progress of clinically symptomatic atherosclerosis is observed. Apheresis is recommended when, despite a diet and maximum tolerable pharmacotherapy, the concentration of LDL is ≥ 300 mg/dl or ≥ 200 mg/dl throughout 6 months for patients with documented coronary heart disease. In recent years an indication to perform apheresis is also an isolated increase of lipoprotein (a), with values >60 mg/dl. [7,8] The apheresis treatment lasts 2-3 hours and must be repeated every 1-2 weeks for the rest of the patient's life, it is safe and not associated with dangerous complications. [8-12]

Patients and Methods

The center from which the study originates has treated 5 patients (3 men and 2 women) using the cascade method. For all patients the relevant medical history recorded cardiovascular events, four patients have undergone coronary artery angioplasty procedures and two have undergone stent implantation. All have

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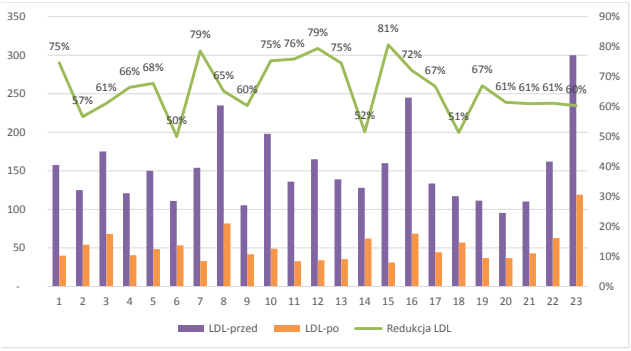
reported symptoms of low statin tolerance (myopathy) and have not reached the recommended LDL values when receiving their tolerated doses (according to the guidelines of the European Society of Cardiology and European Atherosclerosis Society. All were treated due to arterial hypertension; one patient had diagnosed type II diabetes. During apheresis treatment administering hypolipemic medication has not been stopped, maintaining doses tolerated by the patients.

Statistical Analysis

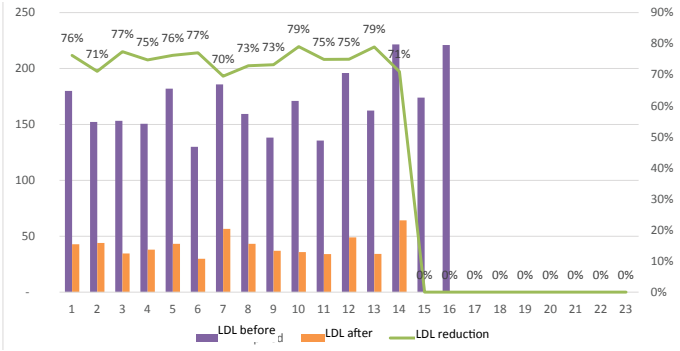
The obtained test results were subjected to statistical analysis using Microsoft Excel 2010. The results were presented as arithmetic means with standard deviation (SD).

Results and Discussion

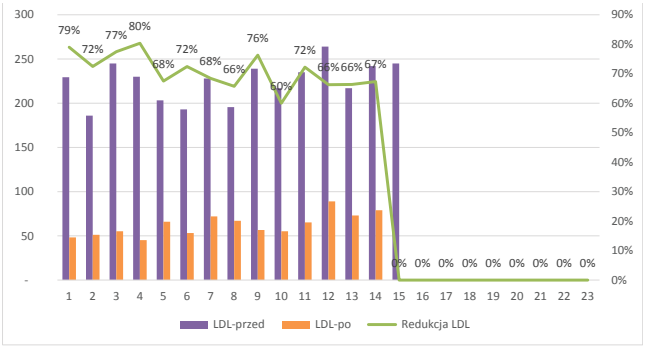
Apheresis treatments commenced in November 2016 for 2 patients, afterwards further patients were qualified and included in the therapy. The procedures were carried out using the ART Universal® device (Fresenius MC) using a MONET® therapeutic filtration system (Fresenius MC), with regional anticoagulation using a Anticoagulant Citrate Dextrose Solution, Solution A (ACD-A). It is assumed that during a single treatment approx. 30 - 50 ml of plasma/kg b. m. or a volume calculated according to the formula Estimated Plasma Volume - EPV= ((0.065 × mc (kg) × (1 - Ht)). The duration of each procedure is dependent on the achieved blood flow rates (QB) and set volumes of plasma to purify. Each procedure was commenced with QB 50 – 80 ml/min, then gradually, in time intervals (5 - 10 min.) and controlled by arterial tension and the patient's well-being, the flow was increased, achieving a maximum of 135 ml/min, the mean [SD] time of the procedure was 2:03 [0: 14] hours.



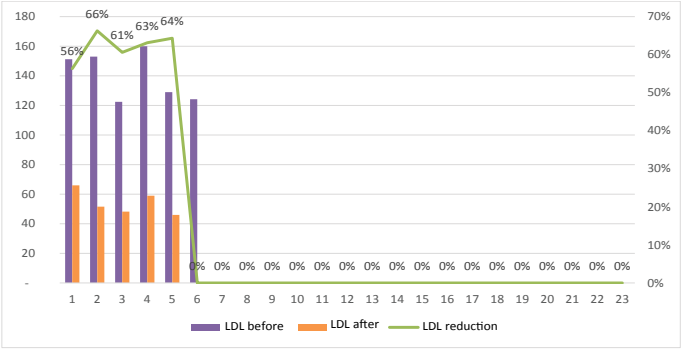
A. **Patient 1** – 23 procedures



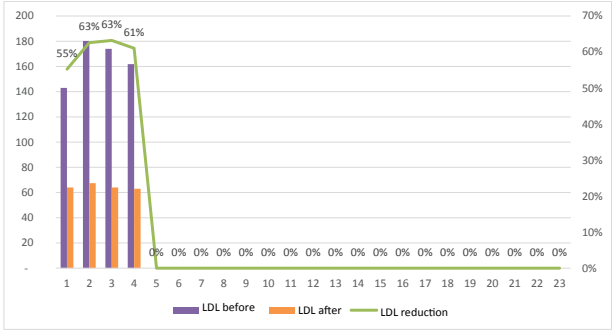
B. **Patient 2** – 16 procedures (in the final two procedures LDL has not been determined after the procedure)



C. **Patient 3** – 15 procedures (in the final procedure LDL has not been determined after the procedure)



D. **Patient 4** – 6 procedures (in the final procedure LDL has not been determined after the procedure)



E. **Patient 5** – 4 procedures.

Figure 1: Change in LDL (mg/dl) content during one procedure and % of reduction for all patients.

For all patients the procedures were carried out from peripheral access, with large venous vessels being punctured, usually in the elbow flexion. According to reimbursement of healthcare costs, apheresis was performed as part of hospitalization in the cardiology department at 14-day intervals. LA in the case of treating chronic lipid disorders should be performed in weekly or bi-weekly intervals, depending on whether or not the administered treatment achieves the intended therapeutic aim of decreasing LDL to a specific level. The frequency of treatments (7-14 days) is specified based on the recovery rate of the cholesterol/LDL concentration which should, respectively, be >50% for total cholesterol and >60% for LDL (from the starting value). So far, according to NHF recommendations, in Poland the treatments are performed in 14-day intervals. [4]

During the 64 performed procedures no dangerous complications have been observed, one patient during one of his treatments experienced hypotension which resulted in discontinuing the procedure. Hypokalemia was observed in one of the female patients after each treatment, potassium supplementation in nutrition on the day preceding the treatment and pharmacologically via oral administration prior to and during the procedure was used prophylactically. No complications have been observed in association with the anticoagulation used ACD-A, in the form of calcium management disorders. In the 10-20th minute of the procedure the value of ionized calcium (Ca++) behind the filter was monitored, which on average reached 0,30 mmol/l. Complications may arise during the apheresis treatment. The most important of those referenced in literature include: hypotension, bradycardia, stomach aches, nausea, vomiting, vertigo and headaches, paroxysmal redness, dyspnea, hypocalcemia, hypokalemia, anemia due to iron deficiency, allergic reactions, hemolysis and thrombocytopenia. Due to the risk of hypotonia in patients treated due to arterial hypertension, it is recommended to omit hypotensive medication on the day of the procedure. For patients requiring constant oral anticoagulation with warfarin or acenocumarol, prior to the procedure it is necessary to halt pharmacological treatment for at least 4 days and include low-molecular weight heparin. During treatment it is necessary to monitor morphology and iron levels and supplement if needed. It is not advisable to halt antiplatelet treatment. [12,15]

Each patient prior to and following the treatment was subject to control of lipid parameters: total cholesterol, LDL, HDL, TG. The greatest reduction was observed in the case of LDL, on mean [SD] reaching 63,3% [21], followed by total cholesterol (59% [2,3]), TG on mean [SD] by 58,8% [10], and HDL – 25,1% [5,8]. Due to the lack of possibility to determine Lp(a) values in the hospital laboratory, this parameter was not monitored.

An analysis was conducted of the mean LDL values achieved following the procedure from all apheresis treatments carried out for individual patients. The mean [SD] LDL concentration for the first patient was 51.04 [19.7] mg/dl, for the second 41.89 [9.1] mg/dl, for the third 63.14 [12.5] mg/dl, for the fourth 54.1 [7.4] mg/dl, and 64.60 [1.7] mg/dl for the fifth [Figure 1].

Conclusion

These data indicate achievement of recommended LDL values for people with cardiovascular disease, which in the analyzed group was not possible during pharmacological treatment. It should be emphasized that the described group of patients did not receive medications currently included in the treatment of hyperlipidemia, such as PCSK-9. Baum et al. in their work, emphasize that evolocumab treatment significantly reduced LA requirement in patients undergoing chronic LA. In addition, >50% of patients achieved LDL <70 mg/dl on evolocumab alone, demonstrating that in patients with pre-LA LDL ≤ 190 mg/dl, evolocumab may replace LA. In another study from Spain in a non-randomized open case series study of 10 adult patients diagnosed with FH already on long-term LA therapy, which used evolocumab. The authors observed reduces LDL and Lp (a) more effectively than LA and combination of evolocumab plus LA could be a therapeutic alternative to get lower LDL and Lp (a) levels in patients with very high cardiovascular risk. [15] There are no unequivocal reports of the possibility of completely replacing LA with currently available drugs. It seems necessary to develop new procedures for including and excluding patients from LA therapy.

Competing Interests

The authors declare that they have no competing interests.

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