

EFFECTS OF A NEWLY ESTABLISHED LIPID APHERESIS FOR A YOUNG HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA POPULATION AT THE DEPARTMENT OF PEDIATRICS AND ADOLESCENT MEDICINE IN VIENNA

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INTRODUCTION

Homozygous familial hypercholesterolemia (HoFH) is a rare but severe disorder of lipoprotein metabolism. HoFH prevalence is about 1 per 160 000 to 300 000. Children with HoFH present with highly elevated LDL-Cholesterol (LDL-C) plasma levels (> 500mg/dl / > 130 mmol), early xanthomas or xanthelasms and a high risk of premature cardiovascular events during childhood. Early diagnosis and treatment by strict fat reduced diet and medication of statins, ezetimibe and bile acid sequestrants are essential. Nevertheless therapy is mostly inefficient and therefore lipid apheresis has to be performed biweekly or weekly to reduce LDL-C.

AIM

Aim of this study was to describe the effect of lipid apheresis in pediatric HoFH patients aged < 6 years at the pediatric dialysis center of the Department of Pediatrics and Adolescent Medicine in Vienna.

OBJECTIVES AND METHODS

Lipid apheresis started biweekly in 4 children with hoFH aged 4-5 years (1 boy and 3 girls) in 2016. For this long-lasting central venous catheters were implanted. Data were analysed for the time period October 2016 until December 2017.

For lipid apheresis a Therasorb column by Miltenyi Biotec was used with a plasma Adasorb filled with 5% albumin and a volume of 100 ml. For the treatment volume the patients' plasma volume was taken twice times and filled up to 250 ml per cycle and 6 to 8 treatment cycles were performed. The patients did not need any additional fluid prior to apheresis and no cardiovascular instability was observed. Systemic anticoagulation consisted of bolus administration of citrate and heparin, followed by a continuous citrate/heparin infusion.

RESULTS

In total, the four children received regularly lipid apheresis (see Table 1). Total Cholesterol (T-C) decreased significantly by 65% ($p < 0.001$), LDL-C by 68% ($p < 0.001$), HDL Cholesterol by 37% ($p < 0.001$), and triglycerides by 30% ($p < 0.001$) post apheresis. Severe side effects of the long-lasting central venous catheters were catheter infections by staphylococcus and plesiomonas species.

DISCUSSION

Biweekly or 10/14 day intervals of lipid apheresis seem to be very successful in young aged children with HoFH by significant reduction of LDL-C of 68% and quick completion of the procedure.

Venous puncture is difficult in young aged children, because of small venous diameters and severe anxiety. Long-lasting central venous catheters seem to be acceptable alternatives.

The most frequent complications were catheter-associated infections by staphylococcus aureus. Two patients (2 girls) acquired a central venous catheter sepsis shortly after the implantation. One of the girls presented with repeated catheter-associated infections and need of intravenous administration of antibiotics, so finally the catheter had to be removed.

Another patient (boy) needed two times catheter replacement because of tunnel infection and finally received an arteriovenous shunt on his forearm. Another side effect of lipid apheresis in childhood was anaemia which occurred in all 4 children and was successfully treated by intravenous iron infusions weekly or biweekly.

CONCLUSION

Lipid apheresis is a very effective method to reduce T-C and LDL-C also in young children with HoFH. Long-lasting central venous catheters seem to operate acceptable, but severe infections are a major problem. Therefore other alternatives like arteriovenous shunts or venous punctures should be planned as early as possible.

	AGE*	GENDER	GENETIC MUTATION (HOMOZYGOUS)	CURRENT INTERVAL OF APHERESIS	CURRENT MEDICATION
PATIENT 1	5	f	LDLR c.2547+5 G>A	every 14 d	Atorvastatin 20 mg Ezetimib 10 mg Colesevelam 625 mg
PATIENT 2	4	f	LDLR c.1592 T>G	alternate 10-14 d	Atorvastatin 30 mg Ezetimib 10 mg Cholestyramine 4 g
PATIENT 3	4	m	LDLR c.1729 T>C	alternate 10-14 d	Simvastatin 30 mg Ezetimib 10 mg
PATIENT 4	5	f	c.1729 T>C	alternate 10-14 d	Simvastatin 40 mg Ezetimib 10 mg

Table 1 - Demographic data of treated patients. (* Age when starting with lipid apheresis)

PATIENT 1		
	BASELINE	AFTER 1 YEAR
TC (MG/DL)	320 (263-792)	106 (84-339)
LDL-C (MG/DL)	250 (183-733)	64 (40-299)
HDL-C (MG/DL)	43 (24-54)	27 (16-34)
TG (MG/DL)	110 (61-217)	71 (36-131)

Table 2 - Changes of baseline cholesterol and triglycerides levels pre and post lipid apheresis in Patient 1. P-value 0.000.

PATIENT 2		
	BASELINE	AFTER 1 YEAR
TC (MG/DL)	445 (310-741)	132 (89-325)
LDL-C (MG/DL)	395 (263-687)	107 (66-276)
HDL-C (MG/DL)	33 (25-43)	20 (16-35)
TG (MG/DL)	74 (38-105)	46 (16-112)

Table 3 - Changes of baseline cholesterol and triglycerides levels pre and post lipid apheresis in Patient 2. P-value 0.000.

PATIENT 3		
	BASELINE	AFTER 1 YEAR
TC (MG/DL)	564 (488-793)	204 (164-329)
LDL-C (MG/DL)	503 (431-742)	160 (124-294)
HDL-C (MG/DL)	47 (34-56)	29 (21-34)
TG (MG/DL)	61 (49-119)	57 (33-88)

Table 4 - Changes of baseline cholesterol and triglycerides levels pre and post lipid apheresis in Patient 3. P-value 0.000.

PATIENT 4		
	BASELINE	AFTER 1 YEAR
TC (MG/DL)	532 (422-632)	203 (141-230)
LDL-C (MG/DL)	480 (357-593)	169 (119-205)
HDL-C (MG/DL)	24 (17-27)	15 (10-17)
TG (MG/DL)	133 (60-309)	98 (50-202)

Table 5 - Changes of baseline cholesterol and triglycerides levels pre and post lipid apheresis in Patient 4. P-value 0.000.