



Letter to the Editor

Therapeutic apheresis in a pregnant woman with heterozygous familial hypercholesterolemia

Aféresis terapéutica en gestante con hipercolesterolemia familiar heterocigota

Dear Editor,

Pregnancy involves an atherogenic lipid profile driven by increased resistance to insulin, oestrogen, progesterone and placental lactogen.^{1,2} This increase may worsen the underlying hypercholesterolaemia in pregnant patients with heterozygous familial hypercholesterolaemia (HFH).³ Total cholesterol increases by 25–50% and LDL cholesterol (LDL-C) by 50%⁴ with a predisposition to endothelial damage in the foetus, which begins during intrauterine life, and postnatal susceptibility to arteriosclerosis.⁵

Therapeutic management and target achievement are complex, since lipid drug therapy is limited by the teratogenic risk and experience with therapeutic apheresis is limited.

We present the case of a 33-year-old woman with HFH diagnosed in 2019 (*LDLR* gene mutation), with corneal arcus and left Achilles xanthoma. Family history includes a father who died at age 50 from a myocardial infarction and a sister who had a cerebrovascular accident at age 29.

The patient continued with routine follow-up in Endocrinology, with ezetimibe and atorvastatin providing good lipid control. Due to her desire to have children, treatment was changed to colestyramine, with total cholesterol levels of 516 mg/dl and LDL-C of 402 mg/dl during the second trimester of pregnancy then, after a multidisciplinary we were consulted to start LDL apheresis, assessment. The patient had concomitant gestational diabetes.

After obtaining informed consent, under ultrasound and fluoroscopic control (with 1 second of time of fluoroscopy), a right jugular tunneled catheter was inserted in the 26th week of gestation and LDL apheresis was started, using the double filtration technique.

We used the Plasauto Σ^{TM} monitor indicating 1L as the target volume of plasma to be treated, 30% plasma/blood ratio, 10% drainage/plasma and 10% replacement/plasma, in order to avoid haemodynamic abnormalities and prioritise foetal well-being. After each session, a gestational ultrasound was performed, with no abnormalities observed in the foetus and the in the amount of amniotic fluid preserved.

The frequency of the sessions was based on the calculation of mean LDL-C or Cave (known as time-averaged LDL-C), with the target Cave being <250, with maximum LDL-C of 300 mg/dl. The blood flow used was 100 ml/min and an initial bolus of heparin sodium was administered as the anticoagulant treatment necessary for the technique. The catheter was sealed with 1% heparin.

A total of six sessions were carried out during pregnancy and six sessions during the lactation period; after all sessions a decrease in total cholesterol and LDL-C to target values was observed as agreed with the Endocrinology department (Table 1). The sessions were well tolerated clinically and haemodynamically.

In week 35 + 3 of pregnancy, the patient presented with premature rupture of membranes, with eutocic delivery of a male newborn, weighing 2,565 g, measuring 47 cm and Apgar scores of 9 and 10 at minutes 1 and 5, respectively.

In the sessions carried out during the lactation period, the volume of plasma treated was greater (2,500–2,800 cc per session), with all other parameters similar to the procedures described.

After completing the sessions, the tunneled catheter was removed without incident.

During pregnancy, a detailed assessment of lipid metabolism should be performed in patients with a previous diagnosis of HFH, not only due to the acute complications that may arise, but also because of future cardiovascular morbidity and mortality in the newborn.

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Table 1 – Pre- and post-session analytical parameters of LDL apheresis.

Session No.	TC	LDL-C	Cave	TG	IgG	Fibrinogen
1. Pre	516	402		407	894	572
1. Post	350	274.2	367.49	199	766	442
2. Pre	411	304.2		344	820	527
2. Post	331	252.8	290.32	221	727	416
3. Pre	424	323.6		282	864	567
3. Post	318	238.6	300.65	212	750	431
4. Pre	410	308		445	836	552
4. Post	305	222.4	286.48	228	732	412
5. Pre	417	298		421	892	508
5. Post	304	217.4	276.24	218	478	308
6. Pre	419	299.8		336	826	536
6. Post	263	193.4	271.07	158	590	362
7. Pre	492	401.06		219	996	677
7. Post	283	221.8	352.65	116	779	428
8. Pre	432	354.6		204	1,100	529
8. Post	229	176.9	306.62	114	832	296
9. Pre	375	315.2		116	1,040	446
9. Post	148	105.3	258.52	71	836	218
10. Pre	415	348		130	1,080	418
10. Post	151	110	283.74	63	783	212
11. Pre	408	348		107	1,160	396
11. Post	153	111.8	284.37	60	842	191
12. Pre	388	333.6		76	1,120	413
12. Post	118.7	84.1	266.23	42	837	191

IgG: immunoglobulin G (mg/dl); LDL-C: LDL cholesterol (mg/dl); TC: total cholesterol (mg/dl); TG: triglycerides (mg/dl).

Average LDL cholesterol calculation (Cave): $Cave = Cmin + K (Cmax - Cmin)$.

Cmin = LDL-C immediately after apheresis. Cmax = LDL-C immediately prior to apheresis. K or rebound coefficient = 0.73 (heterozygotes).

Despite the new lipid-lowering drugs that achieve optimal lipid control, their safety profile during pregnancy is inadequate owing to the risk of teratogenesis.^{6,7} Currently, in the different consensuses, LDL apheresis is considered to be part of the therapeutic arsenal of patients with HFH during pregnancy. The exact reference values for cholesterol during pregnancy are unknown, but the indications for starting therapeutic apheresis in the general population are: LDL-C >300 mg/dl without cardiovascular disease, and LDL-C >200 mg/dl with cardiovascular disease.^{8,9}

Double filtration is an extracorporeal procedure which, subsequent to plasma separation, processes the plasma through a second filter in order to eliminate components according to their molecular weight, such as circulating lipoproteins containing ApoB, mainly LDL-C and Lp(a). The American Society for Apheresis (ASFA) guidelines¹⁰ do not describe what the ideal regimen to use during pregnancy should be, and it is important to individualized for each patient and adapt the technique used.

Side effects are rare and mild, and include hypotension, headache, nausea and problems with vascular access, which the patient did not experience, perhaps due to the volumes used during pregnancy.

In conclusion, we report a case of a pregnant woman with HFH controlled with LDL apheresis, which involved a multidisciplinary approach and posed a therapeutic challenge given the lack of consensus documents on the use of this technique in pregnancy. The treatment regimen used is described, which was successful in our experience, with an adequate safety profile.

Key points

- Familial hypercholesterolaemia can pose a challenge in the therapeutic management of pregnant women.
- Double filtration is an extracorporeal procedure that selectively removes atherogenic components from plasma with an adequate safety profile.
- Therapeutic lipid apheresis can be considered part of the therapeutic arsenal in the management of familial hypercholesterolaemia in pregnant women.

Declaration of competing interest

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¹ Nephrologist specialising in “therapeutic apheresis” who advised us with regard to the apheresis guidelines.

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