Plasmapheresis as treatment for severe hypertriglyceridemia

Plasmaféresis como tratamiento de la hipertrigliceridemia grave

To the Editor:

Severe hypertriglyceridemia (HTG) is defined as plasma triglyceride levels higher than 1,000 mg/dL. Hypertriglyceridemia may be primary, such as familial HTG, or secondary to other causes such as chronic alcohol consumption. The most serious complication of HTG is acute pancreatitis[1]. While under normal conditions the mainstays of HTG treatment include diet, exercise, and lipid lowering drugs, severe HTG requires a treatment which is highly effective in the short term because of the risk of pancreatitis. Plasmapheresis is the treatment that meets these requirements. The case of a patient with severe HTG who required plasmapheresis is reported below.

This was a 28-year-old male patient who was admitted to the endocrinology department for hyperglycemic decompensation without ketosis. The patient had been diagnosed two years before with type 2 diabetes mellitus (DM) for which he was receiving treatment with metformin and vildagliptin with an irregular compliance. He had smoked a pack of cigarettes daily since the age of 16, but denied alcohol consumption. There was no other personal history of interest or family history of diabetes or other significant diseases. The patient had lost 30 kg in weight since DM was diagnosed, and in the previous 5 months had shown cardinal clinical signs of diabetes. He therefore consulted his primary care physician, who referred him to the endocrinology outpatient clinic after receiving the following laboratory test results: glucose 534 mg/dL, creatinine 0,6 mg/dL, sodium 134 mmol/L, total cholesterol 783 mg/dL, chylomicron cholesterol 617 mg/dL, HDL cholesterol 16 mg/dL, and triglycerides 16,792 mg/dL. On physical examination, the patient was found to have a weight of 75 kg, a height of 178 cm, and BP values of 117/78 mmHg. A capillary blood glucose test performed at the office found a value of 600 mg/dL, and the patient was therefore referred to the Emergency Department, where a continuous IV infusion of insulin was started. Confirmation laboratory tests showed the following values: WBC count 7,60 x 10^3 µL (normal differential), hemoglobin 26.4 g/dL (interference by triglyceride levels), hematocrit 43.2%, platelet count 178 x 10^3 µL, glucose 190 mg/dL, creatinine 0.5 mg/dL, ASAT 28 IU/L, ALAT 64 IU/L, total cholesterol 1,437 mg/dL, triglycerides 19,956 mg/dL, HDL 10 mg/dL, TSH 2.09 µIU/mL, and free T4 1.06 ng/dL.

Admission was decided upon, based on these results, and treatment was started with a fat-free diet and basal-bolus insulin therapy. Although the patient was asymptomatic, HTG was severe, and plasmapheresis was therefore decided upon. For this, a central venous catheter was placed in the right jugular vein. A total of 6,511 mL of blood (a little less than 1.5 times the patient's blood volume) was processed over 130 min, with albumin diluted in physiological saline used as replacement fluid. The patient remained hemodynamically stable during the procedure.

Forty-eight hours after plasmapheresis, the following laboratory tests results were obtained: WBC count 5.30 × 10^3 µL (normal differential), hemoglobin 12.5 g/dL, hematocrit 35.9%, total platelets 147,000, glucose 83 mg/dL, creatinine 0.5 mg/dL, ASAT 50 IU/L, ALAT 44 IU/L, total cholesterol 265 mg/dL, triglycerides 327 mg/dL, HDL 18 mg/dL, LDL 182 mg/dL, HbA_{1c} 21.3% (correct value, with no interference from triglyceride levels). Tyrosine phosphatase antibodies (anti IA-2) 1.14 U/mL (normal value < 1), anti-GAD/64K antibodies < 1.0 U/mL. The patient remained asymptomatic and stable during hospital admission, and experienced no complications due to the high triglyceride levels. An ophthalmological examination found no signs of diabetic retinopathy or changes due to triglyceride deposits.

The patient was discharged home with dietary instructions, a subcutaneous bolus-basal insulin regimen, fibrates, and statins. In a visit to the clinic 3 months after plasmapheresis, laboratory test results were as follows: total cholesterol 174 mg/dL, triglycerides 128 mg/dL, HDL 52 mg/dL, LDL 96 mg/dL, and HbA_{1c} 14%.

As noted above, HTG may have a primary or a secondary cause. Primary HTG is caused by genetic disorders such as lipoprotein lipase (LPL) and apolipoprotein lipase (Apo) C-II deficiency, familial HTG and others. There are multiple secondary causes, including DM, obesity, alcohol consumption, and drugs, and other less common causes such as amyloidosis and glycogenesis[2]. Intake of food with high saturated fat contents, hormone treatments (steroids, estrogens), pregnancy, and intercurrent diseases may act as factors triggering acute pancreatitis in these patients[2].

Drug treatment for severe HTG should be prescribed at diagnosis. Fibrates decrease triglyceride levels by 40%-60% and increase HDL levels, and are therefore considered the first choice drugs. Omega 3 acids and nicotinic acid decrease triglyceride levels by 45% and 30%-50% respectively[3,4]. Mean chain triglycerides have also been used in treatment because they decrease chylomicron production and stimulate fatty acid oxidation. Response to these treatments is slow, and they are therefore not helpful in patients with severe HTG. In these patients, the first measure should be absolute diet, which causes a rapid decrease in chylomicrons and triglyceride levels. Insulin and heparin may also be used in severe HTG. Insulin activates LPL and accelerates chylomicron degradation, while heparin stimulates LPL entry into the bloodstream. Clinical studies[1] have shown that both agents may decrease triglyceride levels alone or in combination. Many authors prefer insulin to heparin even in non-diabetic patients because the effect of heparin may be transient, as LPL levels increase in the bloodstream but LPL deposits decrease, with a resulting final LPL deficiency[1]. These treatments may achieve a decrease in triglyceride levels, but not as rapidly as with plasmapheresis.

Plasmapheresis is an extracorporeal clearance technique designed to remove from blood circulation harmful high molecular weight substances such as autoantibodies, immune complexes, cryoglobulins, endotoxins, and cholesterol-containing lipoproteins. To be removable by plasmapheresis, the substance should have a molecular weight greater than 15,000 kDa and not be filtered by more simple clearance procedures such as hemofiltration. It should also have a long half life, so that

extracorporeal elimination is much faster than endogenous elimination[5].

Plasmapheresis was first reported as treatment for severe HTG by Betteridge et al in 1978. Since then, several similar reports have been published[6,7]. Yeh et al[6] and Lennertz et al[7] showed that a single plasmapheresis session could decrease triglyceride levels by 70%.

Controversy exists about the technical details of apheresis (plasma exchange versus dual membrane apheresis), but there is a trend towards performing it using plasma exchange[6] and adequate fluid replacement (fresh frozen plasma or albumin), although no studies comparing these two approaches are available.

On the other hand, there are studies which show that mortality and morbidity due to complications of severe HTG decrease when plasmapheresis is performed without delay[8,9]. However, plasmapheresis is an expensive treatment and is not available at all hospitals. Current clinical guidelines for the use of therapeutic apheresis in clinical practice, issued in 2007, recommend the use of plasmapheresis in acute pancreatitis secondary to HTG at evidence category level C[10].

Conflict of interest

The authors state that they have no conflict of interest.

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Katty Manrique Franco,[a,*] Olga Sánchez-Vilar Burdiel,[a] Carmen Aragón Valera,[a] M. Soledad Sánchez Fernández,[b] Adela Rovira Loscos[a]

[a]*Servicio de Endocrinología y Nutrición, Fundación Jiménez Díaz-Capio, Madrid, Spain*
[b]*Servicio de Hematología-Hemoterapia, Fundación Jiménez Díaz-Capio, Madrid, Spain*

*Corresponding author. Katty Manrique Franco, Calle Salorino, 7, 4A, 28044 Madrid, Spain.
E-mail address: manriquekatty@hotmail.com (K. Manrique Franco).