Lipoprotein Apheresis

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KEYWORDS

• Lipoprotein apheresis • Familial hypercholesterolemia • LDL-C • CVD
• Atherosclerosis • Lp(a)

KEY POINTS

- Patients with familial hypercholesterolemia (FH) have early development of atherosclerosis and cardiovascular disease (CVD).
- Lipid level–lowering medications are not always successful in reducing increased low-density lipoprotein C (LDL-C) levels.
- Lipoprotein apheresis (LA) reduces LDL-C levels by more than 60% in patients with FH and reduces CVD events.
- LA also reduces lipoprotein (a) (Lp(a)) levels and CVD events.
- LA reduces inflammatory markers and blood viscosity.

INTRODUCTION

Apheresis, derived from the Greek word aphairein, meaning to take away, is applied to patients with familial hypercholesterolemia (FH) who are resistant to standard lipid level–lowering medications. Apheresis devices used for the reduction of plasma cholesterol levels can be separated into 3 general groups:

1. Nonselective plasma exchange, which simply removes all of the plasma volume through centrifugation, and was first introduced in 1967 by de Gennes and colleagues.[1]

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2. Semiselective ultrafiltration, developed by Agishi and colleagues[2] in 1980, which uses a double-membrane filtration and involves elimination of atherogenic lipoproteins based on particle size and geometric properties.
3. Selective lipoprotein apheresis (LA), which was developed in 1981 by Stoffel and colleagues[3] using a device containing 2 columns of sapharose gel coupled with polyclonal sheep apolipoprotein B (apoB)-100 antibodies. Newer selective LA devices have been developed involving not only antibodies to lipoproteins but negative charged environments to capture the positive charged apoB. The devices approved for use in the United States and Canada are based on the removal of charged lipoprotein particles.

CRITERIA FOR LIPOPROTEIN APHERESIS

The US Food and Drug Administration (FDA) set the criteria for LA in 1997, when the Kaneka Liposorber and B Braun HELP (heparin-induced extracorporeal low-density lipoprotein precipitation) systems were approved in the United States based on the following criteria.

Patients must show that, after 6 months of the maximum tolerated lipid level–lowering therapy and compliance with a low-saturated-fat, low-cholesterol diet, one of the following is still met:

1. Functional homozygous FH with low-density lipoprotein cholesterol (LDL-C) level greater than or equal to 500 mg/dL
2. Functional heterozygous FH with LDL-C level greater than or equal to 200 mg/dL in the presence of documented coronary artery disease (CAD)
3. Functional heterozygous FH with LDL-C level greater than or equal to 300 mg/dL in the absence of documented CAD

These requirements for therapy are much sterner than those of other countries that perform LA. In Germany, treatments are allowed for patients with CAD and LDL-C levels greater than 130 mg/dL, whereas Japan approves LA therapy for patients with CAD with a total cholesterol level greater than 250 mg/dL. To deal with this gap in treatment, some LA sites have negotiated with health care providers in allowing some high-risk patients with LDL-C levels greater than 160 mg/dL to receive LA.

Panels from the National Lipid Association (NLA) and the American Society for Apheresis (ASFA) recently recommended modifying the criterion for initiating LA therapy to include patients with any atherosclerotic cardiovascular disease (CVD), not just CAD, and lowering the LDL-C threshold in these patients to greater than or equal to 160 mg/dL.[4]

POTENTIAL PATIENT POPULATION WHO QUALIFY FOR LIPOPROTEIN APHERESIS

An estimate of the LA eligible population in the United States by the strict FDA criteria, assuming a prevalence of heterozygous FH of 1 in 500, is approximately 15,000 patients eligible for LA.[5] From the population of individuals intolerant of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins) (prevalence 10%–25%), another 10,000 patients could be added to the number who would qualify for LA.[6,7] Despite these estimates the current census in the United States of patients receiving LA is only 550. Potential explanations for the low number of patients receiving LA therapy include a lack of awareness; insufficient numbers of LA centers (fewer than 50 in the United States), resulting in patients traveling long distances for treatments; complexity of initiating an LA center; and the likelihood that patients with poor venous access will require a shunt/fistula or the belief by physicians that future lipid level–lowering drugs such as proprotein convertase subtilisin/kexin type 9 (PCSK9)