LIPOPROTEIN Apheresis: New Therapeutic Routes

Dr. Samir SAHEB
Endocrinology and Metabolism Department
Pitié-Salpêtrière Hospital
Assistance Publique Hôpitaux de Paris, France
Background

The introduction of new treatments for FH patients (PCSK9, Mipomersen, Lomitapide, anti-sense,…) will impact on LDL-apheresis treatments

1/ reducing LDL–apheresis frequency (H0FH)
2/ Stopping definitely (HeFH)

Therefore we need to explore new indications for LDL-apheresis regarding the pleotropic benefits:

1/ Lp(a) ? Currently recognized just in Germany
2/ Diabetic food ?
3/ Pre-eclampsia ?
4/ FGS ?
5/ ABMR ? This could potentially be of benefit for these patients with respect to progression of arteriosclerosis, in addition to lowering their LDL cholesterol.
There is a clear and independent association between C4d and microcirculation injury with poor outcomes in kidney transplant recipients with acute or chronic ABMR. Higher increments of C4d predict greater microvascular inflammation.

Prospective studies are required to determine whether the treatment of isolated C4d staining or microcirculation inflammation in patients with DSA improves outcomes and to guide preventive and therapeutic approaches, including plasmapheresis, IVIG and anti-complement and anti-B/plasma cell therapies.
There are a lot of similarities in the pathophysiology of events.

We have proposed an tandem with LDL-A and Immunoadsorption in seem double column.

This could potentially be of benefit for these patients with respect to progression of arteriosclerosis, in addition to lowering their LDL cholesterol & DSA.
Several studies demonstrate an apparent benefit regarding these factors during LDL apheresis. LDL apheresis affects many of these factors including the complement cascade, the cytokine network and several other inflammatory mediators.
Several studies demonstrate an apparent benefit regarding these factors during LDL apheresis

- **Significant reduction in E-selectin, VCAM-1 and ICAM-1**
  


- **Reduction in the proinflammatory HDL-bound apolipoprotein-E (ApoE) and also inhibits the reverse cholesterol pathway.**


- **LDL apheresis columns seem to adsorb many proinflammatory:**


Apheresis techniques

- **LIPOSORBER Liposorber®** (Kaneka Corporation, Osaka, Japon)
- **DALI** (Direct Adsorption of Lipoproteins, Fresenius Medical Care Technology, Allemagne)
- **Immunoadsorption** (TheraSorbTM-MLDL et TheraSorbTM-LDL 100 adsorbers, Miltenyi Biotec, Allemagne)
- **HELP system** (Heparin-induced Extracorporeal LDL Precipitation, B Braun, Allemagne),
- **DFPP:**
  - Asahi Kasei Medical, Japon (moniteur PlasautoΣ, Cascadefl o™ EC50),
  - Fresenius Medical Care Technology, Allemagne (moniteur Artuniversal, systeme MonetR)
  - Infomed SA, Suisse ( systeme HF-440 ou CF100).

- All 4 methods have proved to be similarly efficient when used weekly or biweekly to lower LDL cholesterol and Lp(a)
- The introduction of new drugs may alter the position of lipoprotein apheresis within the therapeutic spectrum.
New indications needed

clinician side:

• To explore these new indications, we need serious studies

• Considering the fact that each center performing LDL apheresis has a relatively limited number of patients, multicenter trials would be required

• Because we need large cohorts, we must combine our data and share our findings & Development of a register to document our data

Industrial side:

• develop new columns
• review the prices CONSUMABLES
• financing studies
Purpose:
- Therapeutic membrane plasmapheresis in medical practice;
- Hemosorption.

The “HEMOFENIX” device is:
- completely automatic plasmapheresis procedure;
- portability;
- convenient usage;
- system of control, self-diagnostics and signaling;
- guaranteed safety of the plasmapheresis procedure;
- compliance with the Safety Standards;
- during the procedure simultaneously:
  - form elements are returned to the patient’s blood system;
  - plasma is collected into the special receiving bag;
  - patient’s plasma is substituted.

Technical characteristics:
- blood output - up to 100 ml/min;
- quantity of plasmas received - not less than 0.8 l/hour;
- dosed anticoagulant feeding;
- time of continuous work - up to 10 hours;
- weight - 15 kg;
- size 450x320x120 mm;
- power consumption - under 70 W;
- automatic mode of work and electronic self diagnostics.