

# Dialysis Strategies for AKI in Paroxysmal Nocturnal Hemoglobinuria

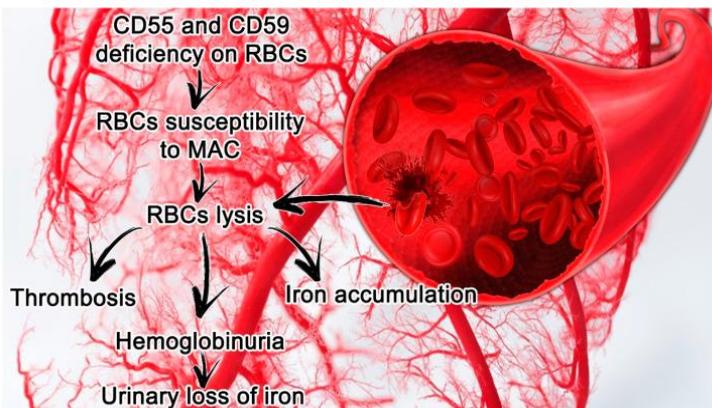
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Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disease that presents an estimated incidence of 1.3 cases per million per year. It is characterized by hemolysis, bone marrow dysfunction with peripheral blood cytopenia, hypercoagulability, thrombosis, renal impairment and arterial and pulmonary hypertension. (Figure 1).



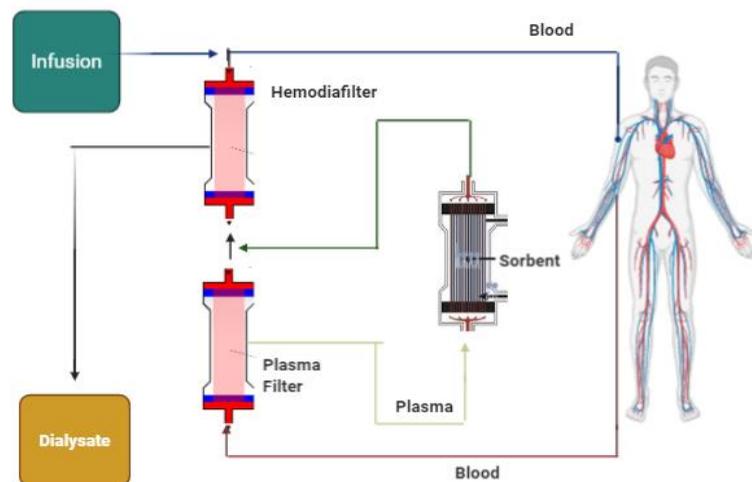
PNH-related AKI is due to the interaction and aggregation of hemolysis products, Tamm–Horsfall protein and the production of tubular casts causing intratubular obstruction and damage, inducing an inflammatory response, interstitial nephritis and fibrosis. In order to remove large molecular weight solutes and protein-bound uremic toxins, high- and medium-cutoff membranes, convective therapy and protein adsorptive membranes can be useful tools in PNH-related AKI. Convective technique is directly linked to plasma ultrafiltration and dependent on the specific solute sieving coefficient and on membrane permeability. The backfiltration mechanism represents a crucial mechanism in the removal of medium-high solutes during ultrafiltration. During HD treatment with a high-flux dialyzer, there is a large drop in blood compartment axial pressure that leads to a blood compartment pressure lower than the dialysate compartment pressure.

These mechanisms, in addition to the oncotic properties of plasma proteins in blood compartment, induces a passage of the ultrafiltrate from the dialysate to the blood, in the opposite direction with respect to the blood–dialysate direction.

This concept leads to the process of “internal hemodiafiltration”, a mechanism that happens during HD with high-flux prescription.

The use of membranes with major permeability, larger pore size and decreased hollow-fiber inner diameter amplifies the internal filtration during the HD session, improving the clearance of large-solute compounds. In the proximal section of the dialyzer, this mechanism promotes convection effect; at the same time, backfiltration will compensate in the distal part. An ideal dialytic prescription to reach these results, should guarantee a blood flow of at least 300 mL/min with a dialysate flow of 500 mL/min or higher.

A promising alternative for current dialysis strategies in the course of AKI in PNH is represented by Coupled Plasma Filtration Adsorption (CPFA), a detoxification technique combining a plasma adsorption circuit with a CRRT. The circuit is made of a plasma filter, a resin-adsorbent cartridge and a hemofilter (Figure 2).



The goal of this treatment is to restore normal immune function by non-selectively adsorbing both pro- and anti-inflammatory mediators, and the greatest result is achieved with substances with high-medium molecular weights.

CPFA includes 5 steps:

1° Step: Blood predilution with a replacement fluid to prevent clotting in the circuit.

2° Step: A fraction of plasma is separated from blood with a plasma filter and then runs through the adsorbing cartridge,

3° Step: the cartridge will non-selectively remove almost all of the pro and anti-inflammatory mediators and endotoxins.

4° Step: Plasma rejoins the rest of blood passing through a standard hemofilter.

5° Postdilution replacement fluid is eventually added to the purified blood, which is re-infused into the patient.

CPFA can play a major role for PNH patients by the adsorption of hemolysis products, removal of inflammatory mediators and treatment of AKI, with the concomitant action of CVVH.

**Conclusions:** PNH is characterized by a plethora of insidious symptoms and damage mechanisms such as hemolysis, peripheral cytopenia, bone marrow dysfunction, thrombosis, arterial and pulmonary hypertension.

Kidney involvement is a common feature of PNH patients but despite the increased knowledge of this syndrome, the most appropriate strategy and choice of therapies are still up for debate. The nephrologist has the task of choosing the most suitable treatment to modulate complement activation and plays a leading role in managing the dangerous case of AKI. Valid options are represented by immunoadsorption, hemodialysis filters that use convective techniques, and backfiltration, or CPFA.

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