Hemodialysis Membranes

Ronco C and Clark WR. Hemodialysis membranes. *Nat Rev Nephrol*. 2018; 14:394-410.
doi: 10.1038/s41581-018-0002-x.

BACKGROUND

Hemodialysis is an extracorporeal process in which the blood is cleansed via removal of uremic retention products by a semipermeable membrane. Traditionally, dialysis membranes have been broadly classified based on their composition (cellulosic or non-cellulosic) and water permeability (low flux or high flux). Incorporation of innovative manufacturing processes have led to consideration of other parameters for classification including new permeability indices, hydrophilic vs hydrophobic balance, adsorption capacity, and electrical potential.

AIM

To provide clinicians with an updated analysis of dialysis membranes and dialyzers, highlighting online hemodiafiltration and new therapies such as expanded hemodialysis, and considerations governing the clinical acceptable balance between large-solute clearance and albumin loss for extracorporeal therapies.

OVERVIEW

History of Dialyzers

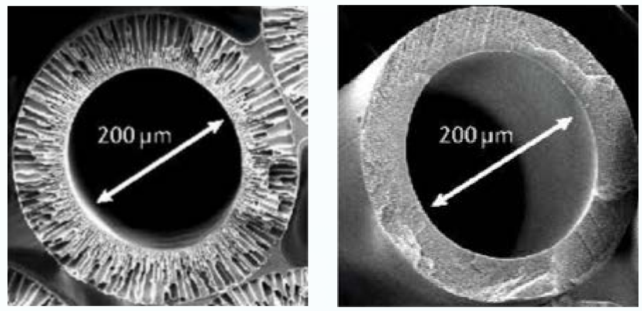
The availability of devices like the rotating drum kidney, coil dialyzer, and Kiil dialyzer allowed the use of dialysis to grow but it had many limitations. Of note were the high blood compartment volumes required and the inefficient mass transfer characteristics. In the late 1960s the hollow-fiber artificial kidney revolutionized dialysis by providing improved geometry in terms of blood rheology and solute mass transfer. Specific advantages included an improved surface-area:volume ratio in the blood compartment and decreased boundary layer effects with acceptable end-to-end pressure drops. These made the hollow-fiber configuration the main choice in dialysis. At present (2018) approximately 300 million hollow-fiber hemodialyzers are utilized worldwide.

History of Hollow-fiber Membranes

Categorization of dialysis membranes have traditionally been based on their material composition, either cellulosic or synthetic membrane groups. The use of unmodified cellulosic membranes has dropped precipitously over the past decades, to the point of effective absence from the market (i.e. no longer manufactured). Dialyzers with synthetic high-flux membranes now dominate clinical practice.

Synthetic membranes were originally developed for a dialysis application more than 40 years ago to address the relative bio-incompatibility and limited permeability of unmodified cellulosic membranes. The first highly permeable membrane, sulfonated polyacrylonitrile (AN69), was introduced in the late 1960s. Subsequent development included polysulfone membranes, which had very thick walls (75-100 μm), and despite higher permeability, were not conducive to diffusion-based therapies. Their use was originally limited to convection-based hemofiltration. Modern synthetic membranes (e.g. polyethersulfone (PES)) have thinner walls (20-50 μm) and higher permeability, permitting diffusion and convection to be employed simultaneously. Please see Figure 1.

Polysulfone Wall thickness 75-100 μm | **Polyethersulfone Wall thickness 30 μm**



Polysulfone:
- Synthetic polymer-asymmetric
- Hydrophobic structure
- High hydraulic permeability
- HIgh sieving properties
- Exclusively used for convective therapy (hemofiltration)

Polyethersulfone:
- Synthetic polymer-microporous
- Hydrophobic-hydrophilic
- High hydraulic permeability
- HIgh sieving properties
- Combination diffusive-convective therapy (high-flux hemodialysis and hemodiafiltration)

Figure 1. Physical Characteristics of Synthetic Membranes. Adapted from Ronco and Clark.

The majority of synthetic membranes (e.g. PES) used for contemporary dialysis have an asymmetric structure. In contrast, synthetic membranes similar to cellulosic membranes (e.g. AN69 and poly (methyl methacrylate) (PMMA)) are structurally symmetric.

New Membrane Classification

Focus on Solute Permeability Properties

Conventional membranes that are used in hemodialysis generally provide high clearance for small solutes such as urea (60.055 Da)[1] and creatinine (113.12 Da)[2]. However, membranes in current use provide limited clearance of compounds >10 kDa. Although these membranes have relatively large mean pore sizes (compared to unmodified cellulosic membranes), they still offer mass transfer resistance to the diffusive removal of large solutes. Furthermore, (membrane) fouling has a considerable effect on convective solute clearance, especially for molecules >10 kDa.

In typical hemodialysis operating conditions, the water permeability characteristics for a standard high-flux dialyzer result in a fairly large drop in the blood compartment axial pressure during treatment. The pressure drop is sufficiently large that the blood compartment pressure is less than the dialysate compartment pressure in normal operating conditions.

There is a point at which the ultrafiltrate begins to be driven from the dialysate to the blood as opposed to the 'standard' (blood-dialysate) direction. This combination of filtration and backfiltration, termed internal filtration, is considered to be the predominant mechanism by which larger compounds are removed during standard high-flux dialysis. Maximizing the