High-Efficiency and High-Flux Hemodialysis

Sivasankaran Ambalavanan
Gary Rabetoy
Alfred K. Cheung

Hemodialysis remains the major modality of renal replacement therapy in the United States. Since the 1970s the drive for shorter dialysis time with high urea clearance rates has led to the development of high-efficiency hemodialysis. In the 1990s, certain biocompatible features and the desire to remove amyloidogenic β2-microglobulin has led to the popularity of high-flux dialysis. During the 1990s, the use of high-efficiency and high-flux membranes has steadily increased and use of conventional membrane has declined [1]. In 1994, a survey by the Centers for Disease Control showed that high-flux dialysis was used in 45% and high-efficiency dialysis in 51% of dialysis centers (Fig. 3-1) [1].

Despite the increasing use of these new hemodialysis modalities the clinical risks and benefits of high-performance therapies are not well-defined. In the literature published over the past 10 years the definitions of high-efficiency and high-flux dialysis have been confusing. Currently, treatment quantity is not only defined by time but also by dialyzer characteristics, i.e., blood and dialysate flow rates. In the past, when the efficiency of dialysis and blood flow rates tended to be low, treatment quantity was satisfactorily defined by time. Today, however, treatment time is not a useful expression of treatment quantity because efficiency per unit time is highly variable.
3.2 Dialysis as Treatment of End-Stage Renal Disease

Dialyzers

**FIGURE 3-1**
Centers using high-flux dialyzers have increased threefold from 1986 to 1996 because of their ability to remove middle molecules. (From Tokars and coworkers [1]; with permission.)

**DEFINITIONS OF FLUX, PERMEABILITY, AND EFFICIENCY**

<table>
<thead>
<tr>
<th>Flux</th>
<th>Measure of ultrafiltration capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low and high flux</td>
<td>based on the ultrafiltration coefficient (Kuf)</td>
</tr>
<tr>
<td>High flux: Kuf &gt;20 mL/h/mm Hg</td>
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<table>
<thead>
<tr>
<th>Permeability</th>
<th>Measure of the clearance of the middle molecular weight molecule (e.g., β₂-microglobulin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low permeability: β₂-microglobulin clearance &lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>High permeability: β₂-microglobulin clearance &gt;20 mL/min</td>
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<table>
<thead>
<tr>
<th>Efficiency</th>
<th>Measure of urea clearance</th>
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<tbody>
<tr>
<td>Low efficiency: KₐA &lt;500 mL/min</td>
<td></td>
</tr>
<tr>
<td>High efficiency: KₐA &gt;600 mL/min</td>
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</tbody>
</table>

K₀ — mass transfer coefficient; A — surface area.

**FIGURE 3-2**
The four high-performance extracorporeal therapies for end-stage renal disease are listed [2].

**FIGURE 3-3**
Definitions of flux, permeability, and efficiency. The urea value KₐA, as conventionally defined in hemodialysis, is an estimate of the clearance of urea (a surrogate marker of low molecular weight uremic toxins) under conditions of infinite blood and dialysate flow rates. The following equation is used to calculate this value:

\[
KₐA = \frac{QbQd}{Qb-Qd} \ln \left[\frac{1-Kd/Qb}{1-Kd/Qd}\right]
\]

where K₀ = mass transfer coefficient
A = surface area
Qb = blood flow rate
Qd = dialysate flow rate
ln = natural log
Kd = mean of blood and dialysate side urea clearance

As conventionally defined in hemodialysis, flux is the rate of water transfer across the hemodialysis membrane. Dissolved solutes are removed by convection (solvent drag effect).

Permeability is a measure of the clearance rate of molecules of middle molecular weight, sometimes defined using β₂-microglobulin (molecular weight, 11,800 D) as the surrogate [3,4]. Dialyzers that permit β₂-microglobulin clearance of over 20 mL/min under usual clinical flow and ultrafiltration conditions have been defined as high-permeability membrane dialyzers. Because of the general correlation between water flux and the clearance rate of molecules of middle molecular weight, the term high-flux membrane has been used commonly to denote high-permeability membrane.
High-Efficiency and High-Flux Hemodialysis

**FIGURE 3-4**
Theoretic $K_o A$ profile of high- and low-flux dialyzers and high- and low-efficiency dialyzers. Note that here the definition of $K_o A$ applies to the product of the mass transfer coefficient and surface area for solutes having a wide range of molecular weights, and is not limited to urea. Note also the logarithmic scales on both axes [3]. $K_o$—mass transfer coefficient; $A$—surface area. (From Cheung and Leypoldt [3]; with permission.)

**CLASSIFICATION OF HIGH-PERFORMANCE DIALYSIS**

<table>
<thead>
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<th>Type</th>
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<tr>
<td>High-efficiency low-flux hemodialysis</td>
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<tr>
<td>High-efficiency high-flux hemodialysis</td>
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<tr>
<td>Low-efficiency high-flux hemodialysis</td>
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</tbody>
</table>

**FIGURE 3-5**
Classification of high-performance dialysis. Some authors have defined high-efficiency hemodialysis as treatment in which the urea clearance rate exceeds 210 mL/min. High-flux dialysis, arbitrarily defined as a $\beta_2$-microglobulin clearance of over 20 mL/min, is achieved using high-flux membranes [3,4].

**FIGURE 3-6**
Comparison of urea clearance rates between low- and high-efficiency hemodialyzers (urea $K_o A = 500$ and 1000 mL/min, respectively). The urea clearance rate increases with the blood flow rate and gradually reaches a plateau for both types of dialyzers. The plateau value of $K_o A$ is higher for the high-efficiency dialyzer. At low blood flow rates (<200 mL/min), however, the capacity of the high-efficiency dialyzer cannot be exploited and the clearance rate is similar to that of the low-flux dialyzer [3,6]. $K_o$—mass transfer coefficient; $A$—surface area. (From Collins [6]; with permission.)

**CHARACTERISTICS OF HIGH-EFFICIENCY DIALYSIS**

- Urea clearance rate is usually >210 mL/min
- Urea $K_o A$ of the dialyzer is usually >600 mL/min
- Ultrafiltration coefficient of the dialyzer ($K_{uf}$) may be high or low
- Clearance of middle molecular weight molecules may be high or low
- Dialysis can be performed using either cellulosic or synthetic membrane dialyzers

$K_o$—mass transfer coefficient; $A$—surface area.

**FIGURE 3-7**
Characteristics of high-efficiency dialysis. High-efficiency dialysis is arbitrarily defined by a high clearance rate of urea (>210 mL/min). High-efficiency membranes can be made from either cellulosic or synthetic materials. Depending on the membrane material and surface area, the removal of water (as measured by the ultrafiltration coefficient or $K_{uf})$ and molecules of middle molecular weight (as measured by $\beta_2$-microglobulin clearance) may be high or low [3,4,6,7].