Effects of novel manufacturing technology on blood and dialysate flow distribution in a new low flux “α Polysulfone” hemodialyzer

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ABSTRACT: The main target for low flux hemodialyzers is an efficient low molecular weight solutes clearance. Such efficiency is largely dependent on the optimization of diffusion between blood and dialysis solution. The diffusion process can be impaired if there is a mismatch between blood and dialysate flow distribution in the dialyzer. Thus optimized flow distribution both in the blood and dialysate compartment becomes quintessential for the maximal efficiency of the diffusion process within the hemodialyzer. The present paper describes the distribution of the blood and dialysate flows in a new low flux polysulfone hollow fiber hemodialyzer characterized by a specific undulation of the fibers and a new cutting technology of the fibers for an improved micro-flow condition in the blood compartment headers. Twelve Diacap α Polysulfone LO PS 15 (1.5 sqm) (B.Braun Medizintechnologie, Melsungen Germany) were employed for the study. Six were analyzed in vitro and six were studied in vivo. Blood flow distribution was studied in vitro by dye injection in the blood compartment during experimental extracorporeal circulation utilizing human blood with hematocrit adjusted at 33%. Sequential images were obtained with a helical scanner in a fixed longitudinal section of the dialyzer 1 cm thick. Average and regional blood flow velocities were measured utilizing the reconstructed imaging sequence. The method allowed the calculation of single fiber blood flow (SF Qb) and the mass transfer zone (MTR) definition in digitally subtracted images. The patterns 20-10 and 40-30 were utilized. The same technology was used to evaluate flow distribution in the dialysate compartment after dye injection in the Hansen’s connector. Regional dialysate flow was calculated in central and peripheral sample areas of 1 cm². Six in vivo hemodialysis treatments on patients with end stage renal disease were performed at three different blood flow rates (250-350 and 450 ml/min) in order to measure urea, creatinine and phosphate clearance. Macroscopic and densitometrical analysis revealed that flow distribution was homogeneous in the blood compartment while in the dialysate compartment a slight difference between the peripheral and central regions in terms of flow velocity was observed. This however was not generating channeling phenomena. Urea creatinine and phosphate clearances were remarkably high and so were the Kt/V observed in all sessions, especially in relation to the studied blood flows.

In conclusion, a significant blood to dialysate flow match with optimized countercurrent flow condition was observed in the studied hollow fiber hemodialyzers. Such optimization might be due both to the improved dialyzer design at the level of the blood header and to the specific fiber undulation that prevents dialysate channeling. (Int J Artif Organs 2003; 26: 105-12)

KEY WORDS: Blood flow, Dialysate flow, Hemodialysis efficiency, Clearance
INTRODUCTION

The utilization of countercurrent flow allowed the development of remarkably efficient hemodialyzers already in the early seventies. However, performances of hemodialyzers have been frequently inconsistent due to lack of standard in production and manufacturing processes and consequent variable degree of blood to dialysate flow mismatch. The efficiency of a hemodialyzer is largely dependent on its ability to facilitate diffusion between blood and the dialysis solution. The diffusion process can be impaired if there is a mismatch between blood and dialysate flow distribution in the dialyzer (1-5). Nevertheless, for many years dialyzers have been produced with standard methods and only few innovations have been proposed in this field with flow distributions in several cases less than optimal. Only recently, new methods of analysis, newer manufacturing processes and new requirements of efficiency and performance, have spurred a renewed interest in improving the design of each component of the hemodialyzer (6-9). While these innovations have been focusing on the sieving characteristics and hydraulic properties in high flux hemodialyzers, the most important aspect considered in low flux hemodialyzers is the optimization of the diffusion process (10-15).

In the present paper we studied the distribution of the blood and dialysate flows in a new low flux hollow fiber hemodialyzer equipped with a recently developed Polysulfone membrane “α Polysulfone”. Such hemodialyzers are characterized by a specific undulation of the fibers designed to prevent dialysate channeling. Furthermore, the blood compartment headers are created with an innovative cutting technology of the fibers generating a so-called “mirror-surface” for an improved micro-flow condition at the blood inlet.

METHODS

Twelve Diacap α Polysulfone LO PS 15 (1.5 m²) (B.Braun Medizintechologie, Melsungen Germany) were analyzed in the study. Technical data of the hemodialyzer are reported in Table I.

In vitro study

Blood flow distribution was studied in three dialyzers by dye injection in the blood compartment during experimental extracorporeal circulation utilizing human blood with hematocrit adjusted at 33%. Sequential images were obtained with a helical scanner in a fixed longitudinal section of the dialyzer. Layer analysis was 1 cm thick. Average and regional blood flow velocity and wall shear rates were measured utilizing the reconstructed imaging sequence. The method was previously published elsewhere (15) and it allows the calculation of single fiber blood flow (SF Qb) and single fiber wall shear rate (SF wSh) in different regions of the hemodialyzer. The same technology was used in three different dialyzers to evaluate flow distribution in the dialysate compartment after dye injection in the Hansen’s connector. Regional dialysate flow was calculated in central and peripheral sample areas of 1 cm² according to a previously published method (16). An additional image analysis was carried out utilizing a technique of image subtraction and isodensity maps with pixel color enhancement. The analysis allows for the identification of the dye mass transfer zone from the point of maximal dye saturation of the blood compartment to the point of absolute absence of dye, in a specific image derived by the digital subtraction of two selected images. For this analysis the images 10, 20, 30 and 40 were utilized. Since every image corresponds to 0.5 seconds, the analysis conducted on the patterns 20-10 and 40-30 correspond to the progression of the flow in five seconds in two different points of the dialyzer. The mass transfer zone, normally utilized for the sorbent cartridges to analyze the adequacy of the unit design and the adsorption kinetics, is in this case utilized to describe the homogeneity of the flow distribution in the blood compartment.

**TABLE I - TECHNICAL DATA OF THE HEMODIALYZER STUDIED**

<table>
<thead>
<tr>
<th>Membrane</th>
<th>α Polysulfone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area</td>
<td>1.5 m²</td>
</tr>
<tr>
<td>Number of fibers</td>
<td>10240</td>
</tr>
<tr>
<td>Length of the fibers</td>
<td>26 cm</td>
</tr>
<tr>
<td>Fiber internal diameter</td>
<td>200 micron</td>
</tr>
<tr>
<td>Membrane thickness</td>
<td>40 micron</td>
</tr>
<tr>
<td>Blood compartment volume</td>
<td>90 ml</td>
</tr>
<tr>
<td>Sterilization</td>
<td>Gamma irradiation</td>
</tr>
<tr>
<td>Filter case</td>
<td>Polycarbonate</td>
</tr>
<tr>
<td>Sealing</td>
<td>Polyurethane</td>
</tr>
<tr>
<td>Membrane ultrafiltration coefficient</td>
<td>6.5 ml / h / mmHg x m²</td>
</tr>
<tr>
<td>Dialyzer ultrafiltration coefficient</td>
<td>9.8 ml / h / mmHg</td>
</tr>
</tbody>
</table>
The same flow distribution analysis was carried out on the dialysate compartment after dye injection in the lower Hansen connector.

**In vivo study**

Six in vivo hemodialysis treatments on six chronic hemodialysis patients with mature functioning A-V fistula were performed at three different blood flow rates (2=250; 2=350 and 2=450 ml/min). In each treatment urea, creatinine and phosphate clearance were measured. In each patient, hematocrit was determined at the beginning of the hemodialysis session. Standard midweek hemodialysis sessions were studied. The dialysate contained (mmol/l): sodium 139, potassium 1, chloride 108, calcium 1.75, magnesium 0.5, bicarbonate 36 and acetate 3. Dialysate flow rate was always 500 ml/min. Clearance was calculated both from the blood side and the dialysate side utilizing the following formulas:

\[
K_b = \frac{(Q_{bi} \times C_{bi} - Q_{bo} \times C_{bo})}{C_{bi}}
\]

\[
K_d = \frac{(Q_{do} \times C_{do})}{C_{bi}}
\]

Where K is clearance in ml/min, \(K_b\) is the clearance from the blood side and \(K_d\) is the clearance from the dialysate side, \(Q_{bi}\) is blood flow at filter inlet in ml/min, \(Q_{bo}\) is blood flow at filter outlet in ml/min, \(C_{bi}\) is arterial and \(C_{bo}\) is the venous concentration of the solute, \(Q_{do}\) is dialysate flow at filter outlet in ml/min, and \(C_{do}\) is solute concentration in the spent dialysate. The average values of blood and dialysate side clearance were taken as a reference for each patient. When mass balance error was greater than 5% the test was discarded and repeated. Urea clearance calculation was performed using whole blood flow, while creatinine and phosphate clearance calculation was performed using plasma flow (11). Clearances were measured at 15 (\(T_{15}\)) and 225 (\(T_{225}\)) minutes after the start of the dialysis session. All sessions lasted 240 minutes. Blood flow rate, dialysate flow rate (\(Q_D\)) and ultrafiltration rate were kept constant at 0 ml/min. Arterial and venous blood samples were drawn simultaneously. A constant time period was maintained between blood drawing and centrifugation to ensure the same degree of equilibration between intracellular and plasma compartments in vitro. Samples were analyzed for urea and creatinine using the standard enzymatic assays. Dialysate collection time for the dialysate side clearance calculation was 10 minutes.

**RESULTS**

**In vitro study**

A remarkable homogeneity of the density profiles describing the flow distribution in the blood compartment was observed in the studied dialyzers. The visual effect is capable alone of demonstrating the optimal utilization of the whole cross sectional area available for the flow (Fig. 1). From the subsequent images, a slightly parabolic profile of the dye can be seen, but the differential velocity between the periphery and the central region of the bundle is negligible (Fig. 3). In particular, the analysis of the mass transfer zones carried out on the digitally subtracted images (Images 20-10 and 40-30) displays a very compact and short length. Such observation demonstrates that the progression of the flow is remarkably
Flow distribution in α Polysulfone hemodialyzers

**Fig. 2** - Values of average, maximal and minimal velocity in the blood and dialysate compartments.

**Fig. 3** - Computer enhanced imaging technique utilized to display flow distribution in the blood compartment (see explanation in the text) (A, B, C represent three different hemodialyzers).
homogeneous and the discrepancy between peripheral and central fibers is virtually absent. This further demonstrates the good design of the blood port that distributes the blood homogeneously in the cross sectional area of the fiber bundle. With a maximal MTR of 4.8 cm, we can speculate that a maximum of 3 seconds occurs before all the fibers are fully utilized. In a unit 25 cm long, this approaches a condition of plug flow. The average calculated blood flow per fiber was 0.0292 ml/min and the average calculated flow velocity per fiber was 1.388 cm/sec (Fig. 2). Minimal variations from these values are present in peripheral and central fibers of the bundle.

The same pattern of homogeneity of flow distribution is observed in the dialysate compartment (Fig. 4) where however a longer mass transfer zone is detected by the computer enhanced imaging technique (Fig. 5). This results from an average flow velocity of 1.31 cm/sec but a greater dispersion of local velocities in comparison to the blood compartment. Since the mass transfer zone is by far below the length of the dialyzer, we can still describe the dialysate flow distribution as advantageous. This effect is definitely due to the special undulation of the fibers that provide a homogeneous resistance to dialysate in the inter-fiber compartment.

In vivo study

The clearances of urea, creatinine and phosphate, recorded in the studied sessions are reported in Figure 6. There is a progressive increase in efficiency passing from 250 to 350 and 450 ml/min of blood flow. However, the relative increase from 250 to 350 is greater than from 350 to 450 ml/min, showing that with the highest flow, a limitation due to the surface area starts to be displayed.
Nevertheless, at each blood flow, the small solute clearances are remarkably high and this can be explained by an optimized countercurrent configuration.

DISCUSSION

Small solute removal in low flux dialyzers is obtained primarily by diffusion. Diffusion is affected by blood and dialysate flow rates, temperature, surface area of the dialyzer and thickness of the membrane. Assuming all other factors are constant, the diffusion process is basically dependent on the concentration gradient between blood and dialysate (10, 11). This is strongly affected by the blood and dialysate flow rates and by the distribution of the countercurrent flows in their relative compartments. It is evident that any possible mismatch between blood and dialysate flow distributions can create a significant reduction in the efficiency of the filter (10). In some cases blood flow distribution may be less than optimal due to blood viscosity properties or to a poor distribution of the flow at the blood inlet port (11, 12). In such conditions, the external fibers of the bundle may be penalized by a lower flow velocity compared to the fibers located in the central region of the bundle. On the other hand, fiber packing density may be higher in the central region of the bundle and dialysate flow may be limited in that region by an increased resistance. Under these circumstances, dialysate tends to flow at higher speed in those regions of the filter where blood flow velocity is minimal and vice-versa (13). This effect may be the cause of inconsistent performances of the hemodialyzer and clearance values may result lower than those expected from theoretical calculations (14).

To prevent such inconvenience, technical improvements have been recently proposed in the blood and in the dialysate compartment of hollow fiber hemodialyzers. These include an optimized design of the blood ports, an adequate fiber density in the bundle and a carefully designed dialysate compartment pathway, also improved by special undulation of the hollow fibers.

In this paper we have utilized a technique previously described to analyze countercurrent flow distributions in the blood and dialysate compartment (15-25). Further to our previously utilized helical scanning technique, we have employed in this case a new computer enhanced imaging technique that allows the construction of a color density curve. The S shaped density curve describes the transition from a region along the length of the dialyzer in which all the fibers are perfused by blood, and the region in which no one fiber is yet perfused. Similarly to what occurs in the evaluation of sorbent cartridges, we have defined the length of the segment of the dialyzer in which the curve is inscribed “the mass transfer zone”. A mass transfer zone longer than the unit would imply that some fibers have completely perfused the unit until the venous end, before some other fibers have still to be perfused at the arterial entrance. This would describe a condition of extremely uneven distribution. On the contrary, a short mass transfer zone generally describes a well distributed flow with simultaneous perfusion of the all the fibers in the bundle.

In our study, this new analytical method allowed us to demonstrate an excellent distribution of the flow both in the blood and in the dialysate compartment. This condition, confirmed by excellent small solute clearances, can be justified by some technical improvements implemented in the new $\alpha$ Polysulfone dialyzers.

Potting technology: Most synthetic hollow fibre membranes have to be closed at both ends before casting of the bundle into the dialyzer housing by polyurethane. This sealed part of fibres is cut away afterwards and does not remain within the dialyzer. This procedure ensures that the inner side of hollow fibres will not be closed with polyurethane in order to ensure blood flow through all membranes. Several technologies for this sealing step are exploited by dialyzer manufacturers, e.g. glue sealing, hot wire melting and two step potting. With Diacap® $\alpha$ Polysulfone, a novel sealing technology is applied. Fibre ends are closed in such way that easy penetration of
spaces between fibres with polyurethane is possible. This allows for smaller amounts of polyurethane within the dialyser. Furthermore, a greater portion of the fibre length contributes to solute transport and consequently to clearance. Consequently, ratio of effective membrane area to surface area in blood contact is enhanced resulting in lower foreign surface contact of blood at the same effective surface area. Additionally, reduced polyurethane mass reduces the amount of leachable substances from this dialyzer component.

Cutting: Besides membrane characteristics, the highest quality of cutting surface of polyurethane block with embedded hollow fibres is essential for hemocompatibility of dialyzers, because this surface is in direct contact with blood. Even after intensive rinsing, abraded particles may adhere to cutting surface. Rough surface structure increases foreign surface area in blood contact and deteriorates flow conditions in the inlet zone. Sophisticated cutter blade geometry, computer controlled cutting process for each individual dialyzer and 100% visual inspection of each cutting surface ensures the high quality of dialyzers. An example of such a concept is evident in Figure 7 where a scanning electron micrograph (SEM) of cutting surface of Diacap® α Polysulfone dialyzer is reported at two different magnifications.

Membrane undulation: It has been shown that dialyzer clearance for small and middle molecules can be improved significantly by a so called Moire structure of hollow fibre (21). Homogenous distribution of fibres in the bundle and improved homogeneous dialysate flow conditions are achieved by a wavy structure of the fibres. This structure results in uniform spacing between fibres and avoids formation of flow channels of dialysate. Characterization of the Moire structure can be given by several parameters like wavelength, amplitude, phase and spacial orientation of individual fibres. Recent studies show that high packing densities are also favourable for good solute transport on the dialysate side (22). An optimum combination of wave structure parameters was chosen with Diacap® α Polysulfone dialyzer for the best balance of fibre spacing and packing density. As an additional effect, priming of the dialysate side and removing of air bubbles that may block solute transport is improved by this undulated bundle makeup.

CONCLUSION

The present study has permitted the evaluation of the possible impact of new solutions oriented to the improvement of the blood and dialysate pathway configuration. In particular, the use of a special sealing and cutting technology seems to contribute to an improved flow distribution in the blood compartment. Furthermore, a defined undulation of hollow fibers may help in reducing the negative effects due to dialysate channeling. A more homogeneous distribution of the blood and dialysate compartments was demonstrated by our radiological technique, utilizing the helical scanning procedure. Further insights seem to be obtained by the computer enhanced flow imaging technique (CEFI).

The optimization of blood and dialysate distribution in
the hemodialyzers studied is also confirmed by an improved performance in terms of small solute clearances. This suggests a definite improvement of the diffusion processes inside the dialyzer due to an optimization of the countercurrent effect on blood to dialysate solute gradients (23-25).

The radiological technique described in this paper seems to be extremely useful in evaluating the flow distribution either in the blood or in the dialysate compartments. It offers a detailed analysis of the regional flow velocity and opens the possibility of detailed controls of further future modifications in hemodialyzer design.

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