Stages of future technological developments in haemodialysis

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Abstract. Understanding the needs of the patients, dialysis staff, and nephrologists is the first logical step in the technological development of better haemodialysis devices. This includes the understanding of large and small uraemic toxins and their removal by dialysis membranes, pathophysiology of intradialytic symptoms, and problems associated with vascular access. Each of these areas can benefit from profiling techniques. Profiling of urea (urea kinetics), solute clearance profiles of dialysis membranes, and volume profiling are areas that are undergoing active investigations and incorporation into clinical practice. Volume profiling currently entails the monitoring of intravascular and total body fluids as well as the measurement of vascular access flow. Development of sophisticated software is necessary to integrate data from various profiling techniques into dialysis equipment in a meaningful manner in order to optimize the dialysis treatment. The ultimate benefits of these devices should take into account the medical, psychosocial, and financial aspects of various parties involved.

Introduction

With continuous research and development in the past half century, haemodialysis has evolved into a routine and safe treatment modality for the excretory function in patients with renal failure. An implantable 'bionic' artificial kidney is obviously desirable. Although exciting work is being performed in several laboratories in this area, the complexity of such an organ makes it unlikely that it will be fully developed and employed clinically in the near future. Another interesting strategy for renal replacement is xenotransplantation. There are, however, major immunological and public health issues that need to be resolved before clinical trials can be undertaken on this modality. Transplantation using allografts is well established. One limitation of this modality is the relative lack of available organs. Another relates to the efficacy and side-effects of the immunosuppressive agents.

Recent data suggest that residual renal function is better preserved during peritoneal dialysis compared to haemodialysis. This would imply that peritoneal dialysis may be advantageous in patients who are just starting ESRD therapy and still have considerable amounts of residual renal function, in addition to patients who are poor candidates for haemodialysis for a variety of reasons, such as a lack of potential vascular access sites and unstable haemodynamics. Technical failure and the relative inadequacy of small-solute clearance, however, necessitate the switching of peritoneal dialysis to haemodialysis for many patients.

Since extracorporeal therapy is likely to remain the primary modality for ESRD patients in the next decade, it would seem prudent to devise equipment that can improve the efficiency and quality of the treatments. Removal of fluid and solutes during haemodialysis or haemofiltration almost inevitably leads to alterations in volume and/or chemistry in various body compartments. In addition, other interventions during the extracorporeal therapy, such as anticoagulation and nutrition supplementation, frequently alter the blood milieu. Monitoring and adjusting the profile of these variables in relationship to time are essential in improving the quality of haemodialysis treatments.

This communication will outline the phases of development of techniques that involve profiling during haemodialysis and haemofiltration from a clinician’s and clinical investigator’s viewpoint.

Replacing renal functions

The kidneys are primarily involved in excretory, metabolic, and endocrine functions in the maintenance of homeostasis of the body. Excretion entails both small solutes and middle molecules. Although haemodialysis is usually considered as a substitute (albeit marginal) for the excretory function, the correction of acid-base and alterations in serum sodium or calcium concentrations are essentially replacement of part of the kidney's metabolic functions. The administration of recombinant erythropoietin and calcitriol assumes some of the endocrine functions. Since the nephrolog-
According to this analysis, 48% of EDTA abstracts and dialysis personnel are called upon to replace various renal functions, a sophisticated haemodialysis system should assist them in achieving some of the goals in all these areas.

Steps to improve current haemodialysis equipment

A number of steps should be undertaken for the improvement of haemodialysis equipment, similar to the development of most biomedical and non-biomedical products. Some of these major steps are outlined in Table 1. For each of these steps, fluid volume will be used as an example. Wherever appropriate, other areas and techniques will also be discussed to further illustrate the point.

Recognizing the needs

In global terms, the needs of the patients and the dialysis personnel are simple. We need the most expeditious dialysis treatment with the least side-effects, inconvenience, and costs. Most patients would like to have shortened and symptom-free dialysis sessions, which would also decrease the work load and hassle for the dialysis staff.

Clinical research often influences the attitude, and consequently the demands of the practicing nephrologists and dialysis staff. In this respect it would be of interest to survey the current investigations in the field of dialysis. The abstracts in the sections related to haemodialysis and haemofiltration that were submitted to the 1995 European Dialysis and Transplant Association (EDTA) annual meeting and the 1995 American Society of Nephrology (ASN) annual meeting were arbitrarily categorized and partially presented in Table 2. Each abstract was placed into only one category, depending on the relative emphasis as perceived by the author of the present paper. The total number of abstracts included in the analysis was also somewhat arbitrary. For example, in the ASN, abstracts on calcium and phosphorus were placed into a section separate from those for dialysis. Exclusion of these as well as other abstracts obviously decreases the total number of abstracts and therefore increases the fraction that each included category represents. According to this analysis, 48% of EDTA abstracts and 48% of the ASN abstracts belong to the first nine categories, which are primarily technology-related. When the EDTA and ASN abstracts were combined, the top four categories were vascular access (11%), blood pressure/volume/symptoms (9%), urea kinetics (9%), and membranes (7%).

Vascular access is intimately associated with the other technology-related topics. For example, the luminal diameter of the access is an important determinant of the maximal extracorporeal blood flow; conversely, the blood flow characteristics may produce long-term effects on the structure of the vessel wall. Besides biocompatibility, interest in dialysis membranes is focused primarily upon their transport properties of middle molecules. This interest in middle-molecule transport and urea kinetics indicates that nephrologists continue to be concerned about the efficacy of removal of uraemic toxins. Removal of fluids by the dialysis membrane by itself is seldom an issue. Rather, the concern is how well the patient tolerates the removal within a relative short period of time.

Understanding the mechanisms

Uraemic toxins and solute clearance profiles

Understanding the uraemic toxins and the pathophysiology of intradialytic symptoms is important in the improvement of dialysis equipment. This is, unfortunately, a difficult task. Optimizing solute removal requires a knowledge of which solutes are toxic. Although there is a great deal of controversy surrounding this area, there is no doubt that uraemic toxins span a large range of molecular weights. Urea (60 daltons) is deleterious [1,2], so are some proteins with molecular weights greater than 10,000 daltons, such as β2-microglobulin [3], granulocyte inhibitory protein [4], and others.

Table 1. Steps to improve haemodialysis equipment

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>(1)</td>
<td>Recognizing the medical or technical needs of patients, dialysis personnel,</td>
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<tr>
<td>(2)</td>
<td>Understanding the mechanisms underlying those needs</td>
</tr>
<tr>
<td>(3)</td>
<td>Designing a device, method, or algorithm that would address those needs</td>
</tr>
<tr>
<td>(4)</td>
<td>In vitro, animal, and/or clinical studies to establish the usefulness of the</td>
</tr>
<tr>
<td></td>
<td>device, method, or algorithm</td>
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<td>(5)</td>
<td>Integration into the machine</td>
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<td>(6)</td>
<td>Large-scale clinical trial, more definitive outcome, and cost analysis</td>
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</table>

Table 2. Abstracts on haemodialysis/haemofiltration

<table>
<thead>
<tr>
<th>Category</th>
<th>EDTA 1995</th>
<th>ASN 1995</th>
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<tbody>
<tr>
<td>BP/volume/symptoms</td>
<td>15 (15%)</td>
<td>27 (6%)</td>
</tr>
<tr>
<td>Vascular access</td>
<td>7 (7%)</td>
<td>58 (13%)</td>
</tr>
<tr>
<td>Membranes</td>
<td>8 (8%)</td>
<td>25 (6%)</td>
</tr>
<tr>
<td>Urea kinetics</td>
<td>5 (5%)</td>
<td>44 (10%)</td>
</tr>
<tr>
<td>Other kinetics</td>
<td>2 (2%)</td>
<td>19 (4%)</td>
</tr>
<tr>
<td>CRRT</td>
<td>4 (4%)</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>2 (2%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Other technology</td>
<td>2 (2%)</td>
<td>16 (4%)</td>
</tr>
<tr>
<td>Reuse</td>
<td>1 (1%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Iron/erythropoietin</td>
<td>34 (34%)</td>
<td>27 (6%)</td>
</tr>
<tr>
<td>Nutrition</td>
<td>1 (1%)</td>
<td>30 (7%)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>0 (0%)</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1 (1%)</td>
<td>14 (3%)</td>
</tr>
<tr>
<td>Outcome</td>
<td>5 (5%)</td>
<td>53 (12%)</td>
</tr>
<tr>
<td>Calcium/phosphorus</td>
<td>4 (4%)</td>
<td>NI</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>9 (9%)</td>
<td>91 (21%)</td>
</tr>
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BP, blood pressure; CRRT, continuous renal replacement therapy; NI, not included in analysis.
The next question is how much of these solutes should be removed during dialysis? Unfortunately, the answer is largely unknown at present. A great deal of effort has been devoted to the study of urea kinetics during haemodialysis in the past decade, because urea is toxic and it is easy to measure. The relationship between mortality and Kt/V of urea over a broad range (e.g. Kt/V of 1.0–2.0 and beyond) has, however, not been firmly established [5–7]. Even less is known about the effect of middle-molecule removal on clinical outcome [8]. Several retrospective studies have suggested that the types of dialysis membrane employed affect patient survival rates [9, 10]. The prospective, randomized, multicentre HEMO Study sponsored by the US National Institute of Health that is currently in progress will address the effect of middle-molecule removal on patient survival and mortality. In that study, β₂-microglobulin is used as the middle-molecule marker and the kinetics of this marker will also be carefully examined [11].

**Intradialytic symptoms**

Although many other factors contribute to changes in blood pressure and acute intradialytic symptoms, volume changes undoubtedly play an important role. Changes in volume are not limited to the plasma compartment, they also occur in the extravascular and intracellular compartments. A concern of high-efficiency dialysis, especially when coupled with very high predialysis plasma urea concentration and low sodium dialysate, is the development of dysequilibrium syndrome. In this scenario, shifting of fluid into the intracranial compartment appears to be causative [12]. This is an example in which osmolality profiles have a profound impact on compartmental volumes, which in turn are important in the pathogenesis of intradialytic symptoms. The intricate and precise relationship among osmolality, compartmental volumes, and the many other factors which control these two variables and symptoms, unfortunately, are not well understood.

Among several other factors [13,14], intravascular volume depletion has been well established as a cause of symptomatic hypotension during haemodialysis. Intradialytic muscle cramps associated with intravascular volume depletion sometimes occur in the absence of hypotension [15]. Presumably, compensatory cardiovascular responses, including vasconstriction, are sufficient to maintain the blood pressure under these circumstances, but are incapable of preventing other manifestations of volume depletion. In a manner somewhat analogous to urea transport, the intercompartment transfer of fluid (i.e. refilling of the intravascular compartment) is an important determinant of the ability to remove fluid during haemodialysis. Conceivably, patients with rapid spontaneous refilling rates are less prone to intradialytic hypotension.

**Problems associated with vascular access**

An arteriovenous fistula with high blood flow rate can cause high output heart failure or steal syndrome and ischaemia in the distal portion of the extremity. The latter is observed frequently in diabetic patients who have underlying diffuse microvascular disease. The inability of the native arteriovenous fistula to mature is another frequent problem in this population. Finally, stenosis and occlusion of a previously functional fistula are all too familiar to many patients and dialysis personnel. Gradual stenosis creates the problem of dialysate blood flow recirculation and decreases the overall efficiency of the dialysis treatment [16]; furthermore, it is often a harbinger of total occlusion of the fistula. Therefore, developing convenient methods to measure fistula blood flow rates and detect recirculation would be very useful.

**Designing a device, method, or algorithm**

**Monitoring urea removal**

Within certain limits and constraints, the Kt/V value of urea has been shown to inversely correlate with patient mortality rate [5–7,17,18]. Routine determination of urea Kt/V or urea reduction ratio is commonly performed. With the postdialysis rebound of plasma urea concentration, especially after high-efficiency dialysis and in patients with low intercompartmental transfer coefficients (Kₐ) of urea, however, Kt/V can overestimate the true removal of urea by as much as 20%. Development of double-pool models improves the accuracy of the Kt/V value [19].

Another method of measuring urea removal by haemodialysis involves the direct measurement of the removed urea in the spent dialysate. Collection of the dialysate from an entire session is cumbersome [20]. Automated equipment that intermittently samples the spent dialysate is available, but the result of the urea determinations on these samples are usually not known until some time after the dialysis session. Intradialytic continuous on-line urea monitoring of the dialysate overcomes these problems and permits the accurate determination of the total amount of urea removed [21]. In order to calculate the clearance, K, however, the blood urea concentration would still need to be established. In addition, a separate method of determining the volume of distribution of urea, V, is required for the calculation of Kt/V. Instead of normalizing against the urea distribution volume, the Kt term can theoretically be normalized using another variable, such as the body weight or body surface area. The usefulness of these latter approaches to predict clinical outcome needs to be validated in future clinical studies.

**Middle-molecule removal**

The glomerular filtration barrier is, in general, permeable to solutes that are 60 000 daltons or smaller. It therefore appears prudent to aim at removal of solutes with molecular weight up to 60 000 daltons by haemodialysis, until more is known about the larger uraemic toxins. The pore sizes of the membrane must be relatively uniform, however, in order to minimize the...
loss of albumin. The surface charges of the solute are also important determinants of its permeability across the glomerular barrier [22]. To the extent that the solute clearance profile across the dialysis membrane should be similar to that of the glomerulus, it may be reasonable to construct dialysis membranes that are anionic on their surfaces. A problem with an anionic artificial surface, however, is its potential ability to activate kininogen and generate vasoactive kinins, as in the case of the AN69 membrane [23].

What markers should be used to define the solute clearance profile of dialysis membranes? At present, the use of a variety of solutes with a broad range of molecular weights seems reasonable. Urea, creatinine, phosphate, uric acid, and β2-microglobulin are convenient markers for clinical studies. For *in vitro* studies, glucose oligomers (with MW up to 1 000 daltons) can also be used to profile the smaller solutes [24]. β2-Microglobulin is impractical for *in vitro* studies using simulated dialysis circuits because of the expense or efforts required to obtain large quantities of the protein. In contrast, several other proteins with somewhat similar molecular weights, such as myoglobin, ribonuclease, and cytochrome C are available commercially at reasonable costs. Limited results suggest that the clearance profiles of polydisperse dextran by dialysis membranes are comparable to those of several proteins with equivalent sizes [25]. Whether these proteins are better markers than dextran for uraemic toxins in the middle-molecule range are at present unclear, since neither have been qualified in clinical outcome trials and the most relevant uraemic toxins in the 10 000–60 000 dalton range have not been identified.

Let us assume that the more dialysis, the better the clinical outcome. One must then consider the factors that limit the removal of small solutes and middle molecules. Two major factors that govern urea removal are the surface area of the dialyser membrane and the dialysate flow rate. With the modern high-efficiency dialysers (especially those with surface areas greater than 2.0 m²), and machines that deliver high dialysate flow rates (greater than 800 ml/min), the major limiting factors appear to be the fistula blood-flow rate and the transfer of urea between different compartments inside the body [19,26]. For middle molecules, such as β2-microglobulin, the limiting factor is still the permeability of the dialysis membrane, although the Ks for β2-microglobulin also plays a role [27,28].

Convection is a more effective method of removing β2-microglobulin and other proteins through high-flux membranes [29]. The employment of haemodialysis should therefore facilitate the removal of both small solutes and middle molecules.

### Monitoring volumes

The wide availability in the last few years of continuous plasma volume monitoring has made it possible for investigators to examine more precisely the relationship between plasma volume and intradialytic symptoms [15,30]. The use of continuous monitoring of haematocrit in this setting is based on the assumption that if red cell mass remains constant, plasma volume is inversely proportional to the haematocrit. Therefore the relative change in plasma volume can be readily deduced from the change in haematocrit, but the absolute plasma volume cannot be established by this technique. Hypothetically, hypotension and/or symptoms would develop when the plasma volume decreases to a certain critical value. Previous studies by others [31] and us [15,32] have suggested that this is a valid concept, and implied that by maintaining the plasma volume above a certain absolute critical level, hypotension and volume-related symptoms can be reduced. Other proposed predictors of intradialytic events using this technique include the absolute or percent change in haematocrit from the predialysis value [30,33] and the rate of change in haematocrit. Confirmation of these concepts will allow development of algorithms to prevent volume-related symptoms.

In addition to isotonic saline, depleted central plasma volume can be restored by the administration of hypertonic glucose or mannitol or colloids, reverse Trendelenberg position, or an increase in the dialysate sodium concentration. Techniques that continuously monitor plasma volume would provide a convenient means to examine the efficacy of these agents to refill the plasma compartment and the factors that govern the variability among individual patients in response to these agents. Since high plasma osmolality favours plasma refilling from the intracellular space, monitoring plasma osmolality would provide some indirect information on the kinetics of compartmental volume shifts as well.

In patient with acute renal failure undergoing acute haemodialysis, underperfusion and further ischaemic insult to the native kidneys may result from the intravascular volume depletion that occurs during haemodialysis. The intradialytic urine output may provide an additional guide for the dialysis ultrafiltration rate. Diameter of the inferior vena cava as determined by ultrasound as an indicator of intravascular volume in haemodialysis patients have recently been described [34,35]. This technique, however, provides only static values and cannot be used for continuous monitoring during dialysis.

Volume monitoring can potentially assist in the establishment of dry weight in dialysis patients. However, both haematocrit determination and ultrasound of vena caval diameter, estimate only intravascular volume but not interstitial or intracellular volume. Intravascular volume is not necessarily an accurate indicator of dry weight because of the slow plasma refilling relative to the rate of intravascular fluid removal under certain circumstances. This is clearly exemplified by the patient who has large interdialytic fluid gain but develops shock during haemodialysis when substantial peripheral oedema is still present. Determination of extravascular fluid volumes is therefore important. Deuterium distribution space has been a gold standard for total body water, but it is impractical for routine use and cannot be used for
continuous monitoring. Single-frequency bioelectric impedance measurement is convenient but it only assesses total body water [36]. Multiple-frequency bioelectric impedance spectroscopy appears to be a more promising tool in assessing total body water and intracellular water [37]. It is also simpler to perform and softwares are being developed that allow frequent determinations during haemodialysis. Since the intracellular compartment is a major reservoir for fluids, determination of intracellular water can also provide information on the potential plasma refilling capacity during intravascular volume depletion.

Monitoring vascular access

Both haematocrit monitoring [38] and ultrasonic devices [39] can provide information about fistula recirculation rates following bolus injection of a dilution indicator such as saline, although the former tends to give higher values than the latter. Total blood flow through the arteriovenous fistula can also be assessed by these techniques but requires the reversal of the dialyser afferent (arterial) and dialyser efferent (venous) tubings prior to the saline injection [40]. The inconvenience of this procedure can be circumvented by the incorporation into dialysis machines of hardware that would allow temporary reversal of blood flow in these tubings. Automated injection of saline would also standardize the flow rate of the saline injection and potentially diminish the variability in results. Besides the dilution technique, access blood flow can also be estimated from haemocoagulation techniques [41]. Haemoconcentration, in turn, can become readily accomplished by a temporary increase in ultrafiltration in the dialyser.

Establishing usefulness of the device, method, or algorithm

Similar to the development of new drugs and other new devices, the safety and usefulness of the invention should be tested in several phases. The earlier phases are usually performed in vitro or in animals. For example, we [41] and others [42] have examined in an in vitro model the utility of continuous haematocrit (volume) monitoring for the measurement of access blood flow, and others have used ultrasonic equipment to measure access blood flow in animals [43].

We have also examined the utility of haematocrit monitoring in the prediction of acute intradialytic symptoms in six chronic haemodialysis patients [15]. An absolute haematocrit threshold at which dizziness, muscle cramps and/or nausea occurred was experimentally derived individually for each patient. An algorithm was devised to manipulate ultrafiltration in order to avoid the haematocrit threshold at which plasma volume became depleted, and at the same time achieved the desired total fluid removal. We found that by using this technique and algorithm, intradialytic symptoms could be reduced by approximately 50%.

Inasmuch as the dependence of blood pressure and symptoms on blood volume varies greatly from patient to patient, it is conceivable that certain patients would benefit from one algorithm, other patients would benefit from a different algorithm, while some patients would not benefit from volume monitoring at all. Presumably, patients who are very sensitive to changes in intravascular volume status would benefit. Hence it appears appropriate to identify these patients by either studying the suspected individuals repeatedly using this technique or by identifying the clinical and laboratory characteristics that separate them from the others. The usefulness of the technique at this stage can be established by a large number of observations in a small number of patients instead of small number of observations in a large number of patients.

Integration into the machine

Closed-loop feedback control

A number of profile monitoring devices have been clinically employed during haemodialysis with various degrees of integration into the dialysis machine. Air-bubble detector (which can be considered as a profile monitor), dialysate conductivity, total blood volume processed, dialysate sodium concentration adjustment, and dialyser arterial and venous pressure monitors have long been part of dialysis machines. Continuous dialysate urea monitoring has been used in a number of clinical centres. Conceivably, when the urea removal has reached the predesignated level, an alarm can be triggered to signal for the termination of the treatment.

Continuous haematocrit (volume) monitoring has recently been incorporated into commercial dialysis machines. The plasma volume profile is continuously recorded and displayed on a screen. The optimal algorithm to utilize the profile to prevent hypovolaemic symptoms, however, has yet to be developed. One approach is to devise a fixed algorithm in which a fixed criterion (such as absolute haematocrit) would signal the dialysis personnel to intervene. The signalling can result simply from frequent browsing of the monitor display by the dialysis personnel or from an alarm that can be preprogrammed at different haematocrit values for individual patients. The intervention can be predetermined by a fixed protocol or arbitrarily decided by the dialysis personnel. In such an open-loop control system, responses are usually slow and the interventions often lead to underachieving or overshooting of the target. In addition, it is labour intensive.

Another approach is closed-loop feedback control in which a predetermined criterion automatically triggers some interventions by the machine. The interventions alter the haematocrit, which then signals the control to either continue the interventions, discontinue the interventions, or change to other interventions, according to predefined algorithms. The optimal interventions under a given set of conditions may be difficult to ascertain.
Yet another approach is an extension of the closed-loop feedback system. Instead of a fixed formula or complex mathematical model, however, fuzzy logic is used to guide the response. An example is depicted in Figure 1 in which blood volume is altered not only by the ultrafiltration rate, but also by the serum osmolality, which governs intercompartmental fluid shifts in addition to other factors. The options for interventions, in turn, are numerous, including the reverse Trendelenberg position, alteration in ultrafiltration rates, saline infusion, and mannitol infusion, all of which can be administered with various intensities. In such a complex and dynamic system involving multiple components interrelated in a largely non-linear manner, interventions may be best determined by fuzzy logic, which is in essence decision making based on artificial intelligence continuously enhanced by previous experiences derived from the individual patient. Theoretically this approach would allow integration and meaningful communications among multiple monitoring and control systems in the dialysis machine and produce the most optimal results.

Closed-loop systems can also be applied to other areas such as heparinization, where anticoagulation activity would serve as the monitored signal and the dose of heparin serves as the intervention. Likewise, for diabetic patients and those who receive intradialytic parenteral nutrition, a closed-loop utilizing a glucose sensor and an automated insulin delivery system would allow for tight and convenient control of plasma glucose.

Other features

Clinical data such as blood pressure, haematocrit, serum calcium and phosphorus, predialysis and post-dialysis weights, and previous treatment details can be stored in computers in the dialysis machine and the current intradialytic or historical longitudinal profiles can be readily displayed on screens. Other features incorporated into the haemodialysis machines may also be helpful; for example, an automatic blood sampler with or without filtration of the plasma using a minidialyser, computerized algorithm for the determination of calcitriol and erythropoietin dosage based on the individual patient’s stored data, and software and hardware that interact with other treatment modalities commonly used in the intensive care unit (urine output volume, vasoconstrictors, supplemental oxygen, respirator which also regulates plasma pH). Finally, input, analysis, and output of data for quality assurance programmes and billing are desirable.

Multipurpose dialysis machines

Both haemodiafiltration and peritoneal dialysis offer certain advantages. Some patients may benefit from employing these modalities in conjunction with haemodialysis. For example, a patient on peritoneal dialysis who enjoys its smooth and large fluid removal capability may wish to supplement the clearance of small solutes with intermittent haemodialysis. A dialysis machine that is equipped to generate sterile pyrogen-free fluids (for example, by using membranes with filtration and adsorptive capacity) can provide the fluids as haemodialysate, substituting fluid for haemofiltration, as well as peritoneal dialysate. Preferably the haemodialysis machine will also possess features that function as a dialysate cycler for automated peritoneal dialysis. A paired double pump for haemofiltration can also be used for plasmapheresis purposes. Patients who perform nightly haemodialysis at home should have the dialysis data transmitted on-line to the surveillance dialysis unit via a telephone modem.

Large-scale clinical trial, definitive outcome, and cost analysis

A large-scale clinical trial with more definitive long-term outcome goals may further establish the usefulness of a particular device. For example, such a trial may identify the subpopulation of patients who can benefit from the routine employment of continuous volume monitoring devices to decrease intradialytic symptoms or to achieve the proper dry weight. A more definitive outcome would be the reduction of cardiovascular events and hospitalizations resulting from better fluid removal and the chronic reduction of burden on the heart.

Finally, cost analysis should be performed for the patient, dialysis unit, and third-party payer. Can the employment of the device translate into less morbidity and hospitalization? Does the mere perception by the patients that they are utilizing sophisticated equipment offer them psychological benefits? Is the reduction in required dialysis personnel as a result of automation of dialysis equipment desirable or do the patients need more personal interactions? In this regard, the requirements for in-centre patients may be different from those for patients on home haemodialysis. Do the dialysis units benefit or suffer from the financial standpoint? These are some of many questions that warrant consideration.