

The Current Status and Future Directions of Hemodialysis Machine Technology

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Patients with renal disease undergo a progressive loss in renal function that eventually necessitates treatment by dialysis to sustain life. Dialysis is a blood purification process that removes waste products arising from metabolism and dietary intake. The process can also correct electrolyte abnormalities and acid-base balance. Fluid gained in between treatments—which is generally undertaken three times weekly and lasts between 3-1/2 to 4 hours—is also removed during dialysis. Dialysis utilizes an artificial kidney linked to a machine that produces the dialysis fluid, which facilitates the diffusion process. The machine monitors treatment and ensures that the equipment reverts to a “fail safe condition” in the event of malfunction, thereby protecting the patient. The purpose of this paper is to review the current status of dialysis machine technology and discuss emerging trends.

Dialysis Machine Technology

Simply, the dialysis machine consists of:

- 1) A blood pump-driven extracorporeal circuit that incorporates pressure monitoring pre and post blood pump, and which is disposed of after each use;
- 2) A hydraulic circuit, linked to proportioning, heating, and degassing elements to produce dialysis fluid at the correct ionic concentration and temperature by blending treated water with a concentrated elec-

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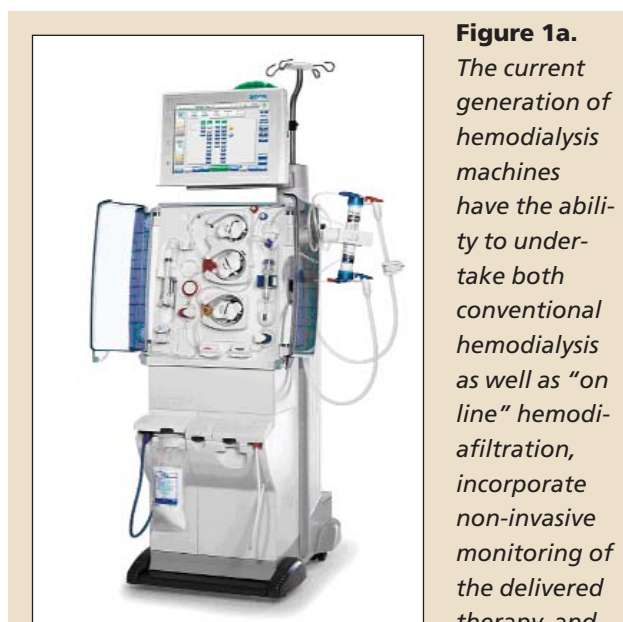


Figure 1a. The current generation of hemodialysis machines have the ability to undertake both conventional hemodialysis as well as “on line” hemodiafiltration, incorporate non-invasive monitoring of the delivered therapy, and utilize a

touch-screen monitor with self-explanatory menus to speed the setting-up and nursing management of the patient. The most recent of these systems is the Fresenius Medical Care 5008 hemodialysis system introduced into clinical practice in the summer of 2005. Illustration Courtesy of Prof. Dr. Jörg Vienken, Fresenius Medical Care, BioScience Department.

trolyte solution; and

- 3) An electronic module for monitoring and control.

The hydraulic circuit of the machine is non-disposable, and the circuit is cleaned and disinfected by chemicals or heat after each use.

Early dialysis treatments placed the patient at considerable risk, and to minimize such risk in the event of equipment malfunction, establishment of international



Figure 1b. *The Gambro Phoenix hemodialysis system incorporates real-time evaluation of hemodialysis efficiency. The machine may also be linked to proprietary software for tracking, analysis, and optimization of therapy. Illustration Courtesy of Gambro Dasco, Medolla, Italy.*

and national standards dealing with electromechanical safety led to the introduction of monitoring for a number of technical parameters. Parameters monitored included pressure in the venous and arterial segments of the extracorporeal circuit to warn of accidental disconnection, kink, or obstruction in the bloodlines or dialyzer; an air bubble detector to detect any air bubbles present in the blood circuit; the dialysis fluid composition (ionic concentration or conductivity, temperature); and pressure. A separate system monitored for the presence of blood in the dialysis fluid, which would signify a leak in the dialyzer membrane. Other alarms indicated electrical power or water supply failure. The monitoring of the patient during treatment was conducted by nursing or medical staff supervising the procedure.

The above parameters continue to be monitored in the current generation of hemodialysis machines. However, current machines also have the added ability to monitor patient response to the treatment and measure the dose of therapy delivered by using repeated non-invasive measurements. (1-3) (Figures 1a and 1b)

The process of hemodialysis requires large volumes of treated water (~150 liters/treatment). The methods of water treatment used, as well as the clinical significance of failure to achieve optimal chemical and microbiological contaminant removal, are discussed elsewhere in this publication. Under certain circumstances, the availabili-

ty of large volumes of water may be a problem, and in such instances different approaches to delivery of treatment are needed. Dialysis fluid regeneration offers the potential to use reduced volumes of treated water. The original dialysate regeneration system was the REcirculating DYalysis (REDY), which used only ~6 liters of dialysis fluid that was continuously recirculated through a sorbent cartridge during treatment. The cartridge removed all waste products present in the dialysis fluid via active immobilized enzymes and chemicals contained in the cartridge, and released sodium bicarbonate and acetate. Prescribed amounts of calcium, potassium, and magnesium were infused into the cleaned dialysate to form fresh dialysate. Although the classical REDY system is no longer in production, two equivalent systems are available for clinical use: the Allient Sorbent dialysis technology system (Renal Solutions, Warrendale, PA) and the RDS 3001 system (Dialysis Parts & Supplies Inglewood, CA).

An alternate approach that does not rely on sorbent technology is the Fresenius Genius System (Fresenius Medical Care, Bad Homburg, Germany) (Figure 2), which uses dialysis fluid prepared in batches by mixing sterile ingredients (electrolytes and glucose) with pre-heated ultra pure water. The prepared fluid is contained in a thermally insulated glass tank (~90 L). During treatment, the dialysis fluid drawn from the top of the system passes through the dialyzer and is returned at the bottom. Due to differences in temperature and specific gravity between used and clean dialysis fluid, a sharp interface exists within the container and there is no mixing of used and clean dialysis fluid. This concept is similar to that used in the Aksys system for home hemodialysis.

As the dialysis fluid circuit is totally sealed during operation, fluid removal or ultrafiltration from the patient is conducted by the use of a peristaltic pump that removes from the reservoir a volume equivalent to that required to be removed from the patient. This causes an imbalance in pressure between the blood and dialysate pressures, and re-equilibration occurs due to the transfer of fluid from the patient into the reservoir. (4) In contrast to conventional hemodialysis systems, the system operates from a single 24 volt power source or battery, making it convenient for use in emergency situations.

During the dialysis process, fluid gained between treatments from cellular metabolism and dietary intake is removed. In early dialysis systems, the removal of such fluid was accomplished by the generation of a pressure

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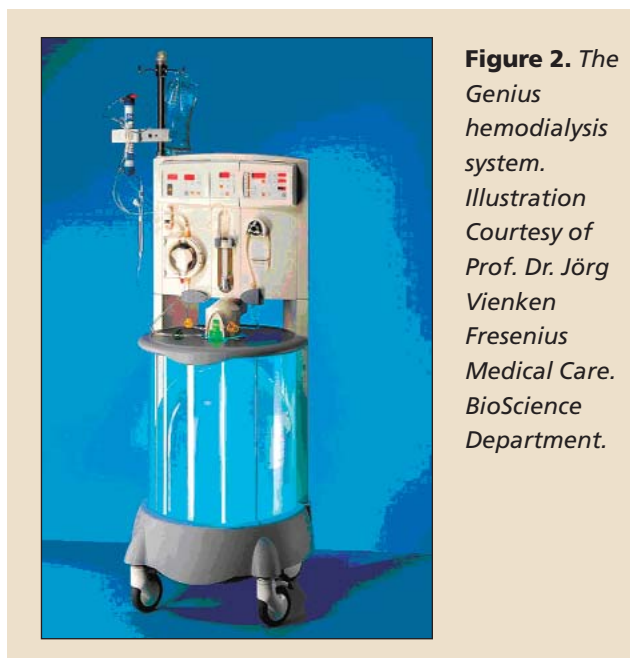


Figure 2. *The Genius hemodialysis system. Illustration Courtesy of Prof. Dr. Jörg Vienken Fresenius Medical Care. BioScience Department.*

gradient across the dialyzer membrane and the continuous monitoring of the patient weight using bed scales. This approach was crude and difficult to replicate on a sessional basis because of the variability in the dialyzer membrane hydraulic permeability. Current machines use microprocessor-linked volumetric fluid removal systems to provide accurate monitoring and control of the fluid removal from the patient during treatment. Despite this, dialysis patients continue to experience a fall in blood pressure during treatment, requiring nursing intervention and the infusion of saline to provide volume expansion. While this corrects the fall in blood pressure, it has the potential to increase patient sodium load, leading to thirst and necessitating a higher rate of fluid removal to be applied.

The problem of vascular stability in the dialysis patient has resulted in a number of different approaches to be used in preventing this problem. The simplest of these is the measurement of the patient's blood pressure during treatment, accomplished by using an automated blood pressure module. This approach fails to provide a continuous measurement, it cannot warn the patient and nursing staff of an impending fall in blood pressure, and the presence of a blood pressure cuff on the arm throughout treatment is poorly tolerated by some patients. Newer approaches to blood pressure measurement are currently the subject of research. Such methods are able to provide a beat-by-beat analysis of the patient's

cardiac function and, if linked to control systems, can automatically modulate the fluid removal to minimize impact on the patient. (5)

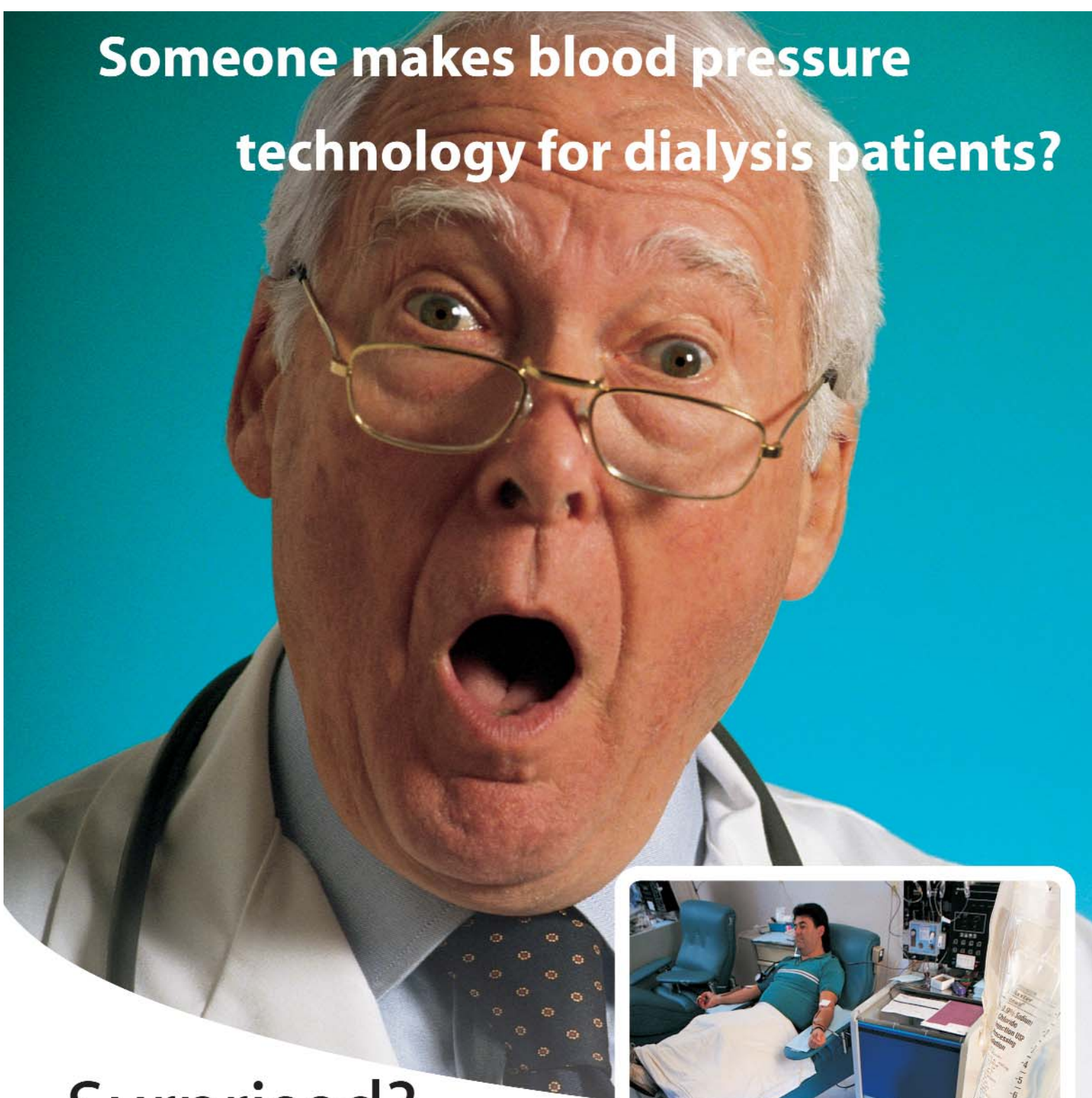
In addition to the simple method of blood pressure monitoring, alternate approaches are available. Their clinical utilization as well as their availability on machines used in the U.S. varies. Such methods include blood volume monitoring, profiling of fluid removal with or without dialysis fluid, sodium profiling, or the use of isothermic dialysis.

As the dialysis process removes fluid directly from the patient's intravascular space, which is refilled with fluid from the extracellular space (the tissue), characterization of the refill rate during dialysis provides an early warning of the patient's tolerance to the rate of fluid removal. Such characterization comes from the use of a surrogate parameter, such as the patient's red blood cell or hematocrit level. Because red blood cells are too large to pass through the dialyzer, the red blood cell mass remains constant during dialysis. Changes in hematocrit represent changes in blood volume due to an inverse relationship between hematocrit and blood volume. (Figure 3) The temporal profile slope indicates the patient's response to the fluid removed during treatment. Whereas this approach is useful in guiding fluid removal during treatment, it is not an adequate guide to target post-dialysis weight for the patient. (6)

Profiled dialysis is a conceptual approach based on the continuous modulation of dialysate sodium and ultrafiltration rate, either singly or in combination, according to pre-established profiles. (7) Patient response to such profiles can vary from treatment to treatment, making it difficult to establish a standard profile for the patient, and when the dialysis fluid sodium is profiled, there may be an undesirable sodium gain during dialysis. (8)

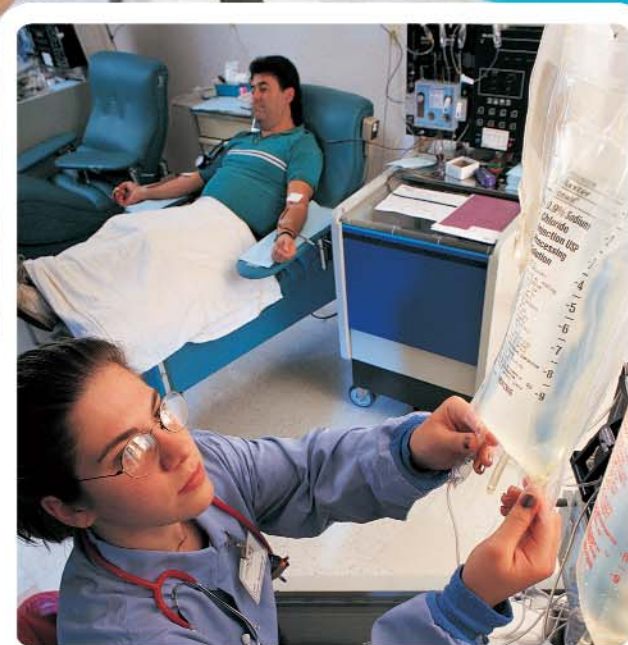
The dialyzer is an efficient heat exchanger, and blood returning to the patient takes on the temperature of dialysate, resulting in heat gain by the patient. This, in turn, results in a small increase in core temperature which stimulates the hypothalamus leading to vasodilatation and a fall in blood pressure. In the mid 1980s, Fresenius Medical Care began the technical development of the BTM (Blood Temperature Monitor), which measures arterial and venous blood temperatures in the extracorporeal circuit by a non-invasive procedure and calculates thermal parameters and body temperature, permitting isothermic dialysis to be performed. The benefits of

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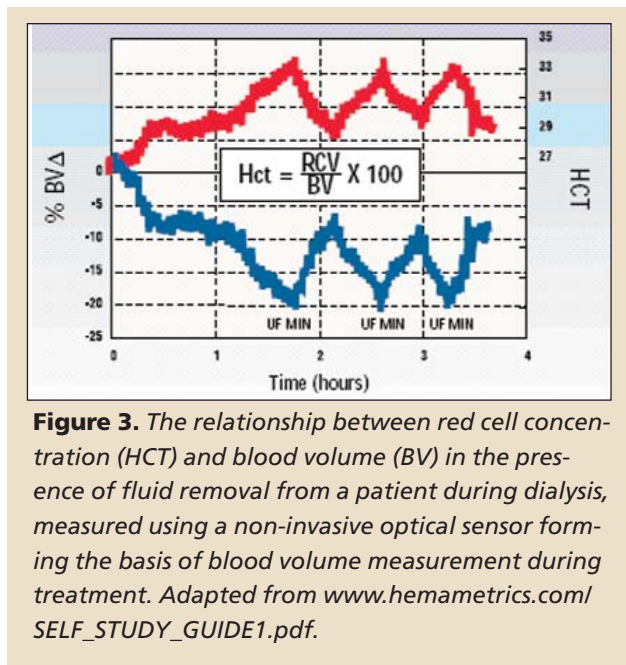


Figure 3. The relationship between red cell concentration (HCT) and blood volume (BV) in the presence of fluid removal from a patient during dialysis, measured using a non-invasive optical sensor forming the basis of blood volume measurement during treatment. Adapted from www.hemametrics.com/SELF_STUDY_GUIDE1.pdf.

such an approach in improving vascular stability during dialysis have been demonstrated in a large multi-center European study. (9) A very useful byproduct of the technology used to measure temperature is the ability to perform automatic vascular access recirculation tests during dialysis using a thermodilution procedure.

The aim of fluid removal during dialysis is to return the patient to his or her “dry weight.” Dry weight may be defined as the post-dialysis weight of the patient at which there is a normal hydration state and symptoms indicative of over- or underhydration are absent. Clinically, this weight is established through subjective assessment of the patient and consideration of patient blood pressure during and between treatments. This approach is imprecise and hampered by the fact that some liters of fluid may accumulate in the patient before clinical symptoms appear, and interdialytic weight gain may not simply be a question of fluid gain—changes in lean body mass, fat mass, or nutritional status also contribute.

Objective methods such as bioelectric impedance technology are being developed to assess the patient’s dry body weight. Three variants of this concept are available: the normovolemic-hypervolemic slope method (10), the resistance-reactance or bioimpedance vector approach (11), and the measurement of the segmental bioimpedance of the calf. (12) Further refinement and larger scale clinical studies are needed before such approaches are introduced into routine clinical practice.

Dialysis Machine Technology: Trends and Future Developments

Hemodiafiltration

Currently, the adequacy of dialysis treatment is assessed by the measurement of urea removal. Increasingly, it is recognized that removal of other compounds—many of which may have molecular weights in excess to that of urea—is required to ensure patient well being and minimize longer term complications associated with dialytic treatment. (13) One example of such a molecule is β_2 -microglobulin, a small (11kD) polypeptide that forms the invariant subunit of the class I HLA-antigens (Human Lymphocyte Antigen) on the cell membrane and which is shed on cellular turnover. Normally, the compound would be cleared by the human kidney, and in dialysis patients amyloid deposits composed of β_2 -microglobulin as the major constituent protein are localized in joints and periarticular bone and lead to destructive arthropathy. Because of the compound’s molecular size, conventional dialysis procedures offer negligible removal, so alternate approaches such as hemodiafiltration are required to effectively remove this compound. Hemodiafiltration is a process that combines diffusive solute removal across a high permeability membrane with convective solute removal. To facilitate the convective solute transport across the membrane, blood entering the dialyzer is mixed with a sterile electrolyte solution that is removed during the passage of the mixture through the dialyzer. Early approaches used pre-prepared fluid, which was expensive and limited the volume of replacement fluid that could be used during a single treatment. Current approaches use online production of sterile and non-pyrogenic substitution fluids based on the dialysis fluid. The microbiological purity of such fluid is 10^{-6} colony-forming units/mL of bacteria and <0.03 IU/mL of endotoxin. (14)

Sorbents

An alternate approach to enhancing the removal of uremic toxins is the use of sorbents. There are several sorbent-based devices either on the market or under study, but in general their use does not necessitate special equipment unless used for the treatment of liver failure or combined renal and liver failure. (15,16)

Increased Frequency of Treatment

Most hemodialysis patients in the United States undergo dialysis three times a week for 3½ to 4 hours per session.

This regimen has been the modal type of hemodialysis since end stage renal disease was added to the Medicare program. Payment policy, also known as the composite rate, is based on such a treatment regimen. A number of small scale U.S. and European studies have been assessing the potential clinical benefits of more frequent (between five and seven times per week) treatments using either long nocturnal dialysis, typically provided at home, or short daytime dialysis, generally performed in a dialysis center. Preliminary information from such experiences has generally been very positive, but randomized prospective trials have to date been lacking. This issue is being addressed by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, which are funding a prospective clinical trial comparing short daily hemodialysis with conventional dialysis and long nocturnal dialysis with conventional dialysis. Patient recruitment for the study has begun and it is envisaged that studies will be completed by fall 2008. The issue of reimbursement for more frequent HD (daily or nocturnal) performed at home or in a facility and for patient training for more frequent hemodialysis is concurrently being addressed by the Kidney Patient More Frequent Dialysis Quality Act of 2005 (HR 3096) which is in its “infant stages” of passage.

The interest in undertaking more frequent treatments has reawakened interest in home hemodialysis. Historically, this type of treatment was popular, but its use in recent years has declined. (17) To meet this renewed interest in home treatments, easy to use dialysis systems have been developed. Two such systems are the Aksys personal dialysis system (PHD) (Aksys, Ltd. Lincolnshire, IL), combining water treatment, dialysis delivery, and reprocessing into a single machine that uses a low volume of dialysis fluid (~50 L) of “injectable quality” and hot water ($85\text{ }^{\circ}\text{C} \pm 5\text{ }^{\circ}\text{C}$) disinfection for both the blood and dialysate pathways. As in the Fresenius Genius system, the dialysis fluid is recirculated and separated by the previously described concept. The NxStage Systems One (NxStage Medical Inc, Lawrence, MA) is the smallest commercially available hemodialysis systems, its dimensions being 15×15×18 inches and its weight 70 pounds. The system consists of the NxStage Cyclor and a disposable blood and dialysis fluid circuit cartridge that mounts integrally within the cyclor. The system is designed to deliver hemofiltration, hemodialysis, and/or ultrafiltration to

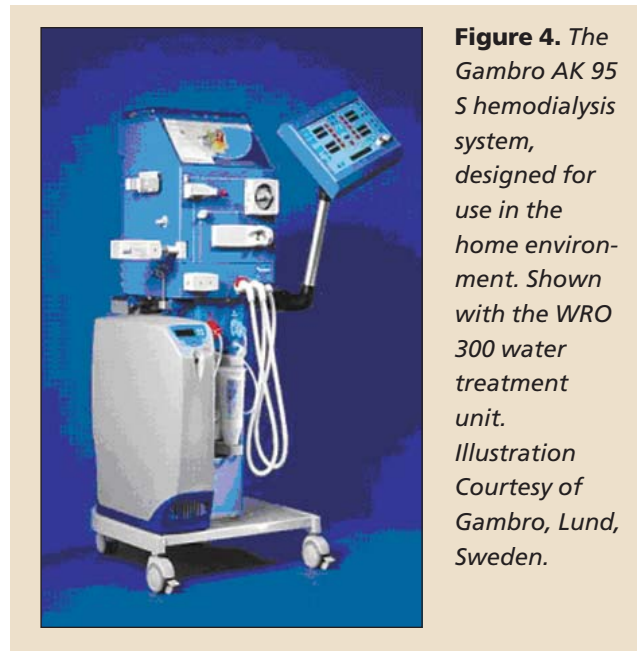


Figure 4. The Gambro AK 95 S hemodialysis system, designed for use in the home environment. Shown with the WRO 300 water treatment unit. Illustration Courtesy of Gambro, Lund, Sweden.

patients for up to 2 ½ hours. (18,19)

In addition to these specially designed systems, variants of commonly used hospital systems are also available for home applications (Figure 4).

As the patient is away from a hospital environment, an important element of such systems is the incorporation of user-friendly interfaces via display screens that offer task-oriented prompts, step-by-step setup instructions, and problem solving during alarm situations.

When used in the home for conventional treatments, the blood flow rates are similar to those in the hospital; long overnight treatments, on the other hand, use lower blood flow rates. Associated with such flow rates is a rare, but as-yet unresolved, technical issue: the risk of accidental disconnection of the vascular access during sleep, leading to hemorrhagic complications.

Monitoring and Biofeedback

As discussed, during dialysis a number of technical and patient-related parameters are monitored. The control of such parameters is generally by means of an open-loop system in which the value of the parameter of interest is set at the beginning of the treatment session and is not modified unless there are events during treatment which call for operator-performed adjustments to be made.

In contrast, a closed-loop control approach involves the continuous measurement of the variable of interest. The system itself monitors the variable and, via

controllers, linkages, and actuators, is able to adjust settings throughout the treatment. This approach has seen only a limited application for a small number of parameters, notably blood pressure and blood volume, in hemodialysis, and further developments are likely to ensure that the treatment is more efficient and physiological. (20-23)

Currently, hemodialysis machines operate independently from the information infrastructure within institutions. Integration will facilitate improvements in technical support and patient care.

Concluding Comments

Hemodialysis relies upon the application of technology to facilitate and monitor both the patient and the machine during treatment. The technology in use today has evolved from that used in the early treatments and permits treatments to be performed safely both in the hospital and in the home, and has played an important part in reducing associated nursing and technical workloads. In the future, technology has the potential to offer further advances and improvements, but new developments are costly and their clinical utilization will be determined by the demonstration of evidence of benefit. In the current financial climate this may be a limiting factor for major technological advances. ■

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