CHANGING THE PARADIGM OF MODALITY SELECTION
By Stephen Fadem, MD, FASN
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EDITORIAL:
CHANGING THE PARADIGM OF MODALITY SELECTION
By Stephen Fadem, MD, FASN
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BRIDGE OF LIFE HELPS BRING ECUADORIAN DOCTORS TO U.S.

By Kelsey Rood

Drs. Martha Barreno and Ivannia Delgado came to Los Angeles through the Bridge of Life – DaVita Medical Missions™ program to train with local nephrologists at UCLA and Cedars-Sinai Medical Center. Their training has included patient care, reuse techniques, machine maintenance, and nutrition and anemia workshops. After their stay is complete, they will have received more than two months of arduous training with some of the nation’s top dialysis care providers.

Barreno and Delgado are both currently pediatricians in their hometown of Guayaquil, Ecuador. They work at Ecuador’s Dr. Roberto Gilbert Elizalde Children’s Hospital, where this past December the Bridge of Life – DaVita Medical Missions program helped establish the country’s first dialysis clinic. The hospital is currently dialyzing six patients ages 12 to 16. Four of these patients are receiving hemodialysis and the other two are receiving peritoneal dialysis. The partnership with Bridge of Life has already brought many changes to the children’s hospital, and both doctors believe their training in the U.S. will help provide additional care for the region.

“DaVita arrived just in time for many of our patients,” says Delgado. “We usually receive patients when they are in terminal condition. Before our partnership with Bridge of Life– DaVita Medical Missions, we did not have the resources or necessary tools to help care for these children. Now, we are able to care for both our current patients and the many children in Ecuador who are in need of dialysis.”

The first five weeks of the doctors’ training was done at Cedars-Sinai Medical Center. Here they trained with Dr. Hector Rodriguez and learned the different types of treatment strategies available to dialysis patients, how to care for nephrology patients, and the process of reuse. The following three and a half weeks were spent at the University of California, Los Angeles (UCLA), training with Dr. Isidro Saluski and several of UCLA’s local technicians. They spent time reviewing medical strategies and care management for patients on hemodialysis and...
peritoneal dialysis. The final two weeks of their training were spent at local Lifeline Vascular AccessSM centers, where they attended workshops on anemia and nutrition.

Both Barreno and Delgado had some background in nephrology, but neither had learned about managing patients’ nutrition and the importance of monitoring their mineral counts such as iron. They described the reuse process as one of the most important things for them to take home to their hospital. Currently, Ecuador does not have a process for reuse, and the implementation of this process is considered a main component to sustaining the availability of hemodialysis in the country.

Barreno and Delgado attended La Universidad Catolica, Santiago de Guayaquil. They did their medical training in various hospitals throughout Ecuador and finished their pediatrics residency in 2003 at the Elizalde Children’s Hospital. Prior to entering the hemodialysis field, they worked in different areas of the children’s hospital. Dr. Barreno worked in the intensive care unit, while Dr. Delgado cared for patients coming into the emergency room.

Ecuador is one of many countries that do not have treatment options available for patients suffering from kidney disease or kidney failure. The Bridge of Life – DaVita Medical Missions program is dedicated to bringing life-sustaining dialysis treatment to less developed countries through technical support, rigorous training, equipment and supplies, and thousands of teammate hours dedicated to building dialysis facilities from the ground up.

Although there are no statistics on kidney disease in Ecuador, both Barreno and Delgado believe there are many cases of kidney disease and kidney failure that go undocumented in their country. They strongly believe the DaVita partnership will help foster awareness in the country so that these undocumented patients may be able to prevent or delay kidney disease and kidney failure. Because of the lack of documented cases, it is hard to know the number of people who have died from kidney failure; however, one thing is clear: The number continues to climb.

“We have several patients back in Ecuador who suffer from kidney disease and kidney failure. It has been our privilege to work with such intelligent and dedicated professionals during this two-month period. We are excited to get home and make this training come to life for our patients,” said Delgado.

Barreno and Delgado have expressed appreciation for the support and attention they have received since being in the United States. Although most of their time was spent training with local dialysis care providers, they also had an opportunity to visit some of the local attractions, including the L.A. Zoo, Disneyland and even Las Vegas.
“This has been the most enriching experience of my career, both personally and professionally,” said Barreno. “The people we have met are incredibly intelligent, hard-working and kind-hearted individuals. They have shared a wealth of knowledge with us, and we cannot wait to bring this training back to Ecuador to teach our colleagues new techniques and, most importantly, to treat our patients with the best care.”

The Guayaquil dialysis clinic is one of three DaVita has opened outside the United States in underserved communities to help care for those suffering from kidney disease and kidney failure. DaVita has provided technical support, equipment, supplies, training and thousands of employee (teammate) hours to build dialysis facilities in Cameroon and Ecuador. Partnership opportunities are continuing to grow throughout Central and South America, India, Pakistan, the Philippines and Sri Lanka.

“Bridge of Life – DaVita Medical Missions brings lasting change by opening access to dialysis care and chronic kidney disease (CKD) education to countries where it’s needed most,” said Kent Thiry, DaVita chairman and CEO. “This program gives us an opportunity to make a difference in the lives of those we’re privileged to touch.”

DaVita Nephrologist, Dr. Mehendru, gave a generous $25,000 donation to the Bridge of Life program during the DaVita Physician Leadership Meeting in Las Vegas this past September.

To learn more or to donate to the Bridge of Life, please visit: www.bridgeoflifemm.com
The idea of World Kidney Day was conceived in the fall of 2002. The concept of World Kidney Day emerged from a consideration of the following observations:

1. Chronic kidney disease (CKD) is very common, and appears to affect roughly 10 percent of the adult population, not only in the United States but worldwide.
2. CKD substantially increases the risk of cardiovascular and cerebrovascular disease, which, even without this increased risk, is the most common cause of death worldwide.
3. Moreover, CKD, once established, may progress to end-stage renal disease (ESRD) if the patient lives sufficiently long.
4. There are now treatments for CKD that are proven to slow, and sometimes even stop, the progression of CKD to ESRD.
5. Based on available evidence from the general population, it seemed reasonable, although not proved in the CKD population, to conclude that reduction of risk factors for cardiovascular and cerebrovascular disease, which are commonly present in CKD patients, will reduce morbidity and mortality from these conditions.
6. Evidence strongly indicates that large proportions of individuals with CKD are not diagnosed. When they are diagnosed with CKD, they frequently are not managed with proven, state-of-the-art treatments.
7. This problem is particularly unfortunate because state-of-the-art medical care for slowing progression of CKD and treating most of the cardiovascular and cerebrovascular risk factors is not expensive.
8. In summary, CKD has recently been identified worldwide as a common and very serious medical illness and public health threat. Moreover, a critical gap had emerged between the availability of effective therapies for this condition and the healthcare that most people with this malady were actually receiving.

The International Federation of Kidney Foundations (IFKF) and the International Society of Nephrology (ISN) co-sponsor World Kidney Day. World Kidney Day, which is the second Thursday of each March, is intended to increase public awareness of the facts stated above. World Kidney Day was celebrated for the first time on March 9, 2006. In a tribute to the energy and commitment of the worldwide kidney community, celebratory events were held in 45 countries. On March 8, 2007, World Kidney Day was observed in 66 countries. In many countries, World Kidney Day was observed in a number of cities with kidney disease detection programs; scientific, educational or public relation events for health care professionals, government officials and the public at large; or the institution of more effective kidney disease management programs.

What can DaVita® physicians and other healthcare workers do for World Kidney Day? The answer is: many things. These include supporting your kidney foundation or society of nephrology, participating in kidney disease detection programs, educating your patients, their families and the public concerning the need for periodic check-ups for kidney disease, and advocating for universal kidney disease detection and treatment programs. Comprehensive kidney disease detection and management programs are springing up across America in government and for-profit healthcare management programs as well as in private-practice settings. Can you establish such a program in your community?

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Alternatives to standard, thrice weekly, in-center hemodialysis are now available that use various increases of treatment duration and/or frequency, in center and at home. The most common is daily (5-6 days per week), short (2-3 hour) dialysis usually done at home. Frequent (5-6 days per week) nocturnal (6-8 hours while asleep) home hemodialysis is the most studied and perhaps has the best outcomes. In-center nocturnal (6-8 hours while asleep) hemodialysis offered 3-5 days per week is also an increasingly popular alternative.

This article’s goals are to review:
• Reasons for these alternatives;
• History of their development;
• Technologies used to implement them;
• Their strengths and limitations versus standard hemodialysis.

REASONS ALTERNATIVES WERE DEVELOPED

Although significant improvements have occurred in standard, thrice-weekly hemodialysis including bicarbonate dialysate, volumetric control, large biocompatible dialyzers and erythropoietin, a number serious problems still remain including:
• Hypertension coupled with large intradialytic weight gains, intradialytic cramps and hypotension;
• Low quality of life and physical function;
• An intractably high mortality rate.
Kjellstrand summarized the reasons to consider alternative regimens:

- **Severe underlying medical problems:** “particularly cardiovascular disease, and intolerance to the ‘unphysiology’ and rapid ultrafiltration of regular hemodialysis treatments three times per week.”
- **Social indications:** “Apparently shorter sessions do not interrupt a whole day as much as longer dialysis sessions. Second the well—known post dialysis ‘hangover’ and fatigue are not present with daily dialysis.”

Kjellstrand himself had developed the “unphysiology hypothesis” to describe cycling of molecules and fluids independent of total clearance as important causes of uremic symptoms. Pieriatonin, Lockridgeand Ting have emphasized selection of complex, intolerant patients in their pioneering programs. An interesting report by Lindsay confirmed that “time to recovery” is much shorter, very important to patients, and correlates with more complex quality of life instruments in both short, daily and frequent, nocturnal compared to standard regimens.

Potentially most important of all are the observational data of improved survival from frequent nocturnal and short daily dialysis compared to the failure of increased doses of standard thrice-weekly hemodialysis to reduce mortality in the HEMO study.

Home regimens also help address the presently non reimbursed costs associated with more frequent treatments, and growing critical shortage of nursing staff in general.

**HISTORY**

Soon after Scribner developed chronic hemodialysis in 1960 the shortage of resources and the cost of in-center treatment led Kirby in 1961 and Sheldon in 1963 to propose home hemodialysis. The first patients went home in Boston, Seattle, and London in 1963-64 and the first nocturnal at home dialysis occurred in 1965. By 1973, 40% of patients in the U.S. did home hemodialysis but, after the creation of many outpatient facilities caused by the ESRD legislation of 1972 and the development of home peritoneal dialysis, this fell to less than 0.1% doing home hemodialysis by 2004.

The modern era in North America began in 1994 when Drs. Uldall and Pierratos in Toronto began a frequent, nocturnal home hemodialysis program followed by a similar program by Lockridge in Virginia in 1997, and Ting’s start of an in center, short daily program in California in 1996.

Industry has responded to this new interest first with the now defunct Aksys PHD system designed specifically for short, daily home dialysis, Fresenius’ adaptation of it’s 2008 series as the 2008K for home use, the Renal Alliance modernization of the sorbent technology popular in the 70’s, and the increasingly popular NxStage System One. Patient advocacy has also increased as, for example, the Home Dialysis Central website sponsored by the Medical Education Institute. Finally, DaVita has made a major commitment to the development of more the 130 home hemodialysis training centers throughout the U.S.

**DESCRIPTIONS OF THE ALTERNATIVE REGIMENS AND TECHNOLOGIES**

**Frequent, short:**

In center, short daily programs typically switch patients from standard, thrice weekly treatments to six times weekly but keep total treatment time, dialyzer, blood and dialysate flows unchanged. Short, daily home dialysis can use standard dialysis machines but more commonly employ machines such as the NxStage System One.
The NxStage System One employs a drop-in cartridge for easy set-up and take-down of a 70lb portable machine that can be used with either bags of dialysate or with a proprietary deionizing system called the Pureflow. These features, along with partnering arrangements with DaVita have made this system by far the most popular. As of this date it is used by over 2000 patients at more than 300 centers in the U.S.

Similar to peritoneal dialysis, the NxStage system is dialysate-limited with the typical patient using ~ 21 L per treatment. Although limited published outcome data and clinical experience appears similar as such it may not be directly comparable to short, daily in center regimens (Table 1).

Frequent, nocturnal:

Typically Fresenius 2008 machines are used. The 2008 K has a smaller profile and user interface designed for patient use. Either reverse osmosis or deionizing systems with dedicated plumbing installations are required. The NxStage system has been used by some for frequent, long, nocturnal dialysis but the dialysate limitations make this use quantitatively different the typical frequent nocturnal regimens.

Table 1 shows typical treatment parameters for these alternative regimens.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Treatments/wk</th>
<th>Treatment time (hrs)</th>
<th>Blood Flow Rate (ml/min)</th>
<th>Dialysate Flow Rate (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional HD</td>
<td>3</td>
<td>2</td>
<td>400</td>
<td>500</td>
</tr>
<tr>
<td>Short Daily HD</td>
<td>6</td>
<td>4</td>
<td>400</td>
<td>800</td>
</tr>
<tr>
<td>Nocturnal HD</td>
<td>6</td>
<td>7-8</td>
<td>200</td>
<td>300</td>
</tr>
<tr>
<td>NxStage HD</td>
<td>6</td>
<td>2.5-3.5</td>
<td>400</td>
<td>130</td>
</tr>
</tbody>
</table>

Comparative quantification of these regimens is typically done using Gotch’s standardized Kt/V model (Table 2). The usefulness of this theoretical model, is not, however, established.

Table 2 shows standardized Kt/V for each modality.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weekly spKt/V</th>
<th>Weekly stdKt/V</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>-</td>
<td>1.7</td>
</tr>
<tr>
<td>HD (HEMO Std)</td>
<td>4.0</td>
<td>2.1</td>
</tr>
<tr>
<td>HD</td>
<td>4.0-4.8</td>
<td>2.6-2.9</td>
</tr>
<tr>
<td>Short Daily HD</td>
<td>4.0-5.0</td>
<td>2.7-3.2</td>
</tr>
<tr>
<td>Nocturnal HD</td>
<td>7.0-9.0</td>
<td>4.6-5.0</td>
</tr>
<tr>
<td>NxStage HD</td>
<td>2.7-3.0</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Access and monitoring:

The need for frequent cannulization and the risk of needle dislodgement have been addressed by the use of the “buttonhole” technique and local wetness monitors. Central monitoring while available is not generally felt to be required even for nocturnal dialysis. Tunnelled catheters are also less problematic in home compared to in center patients.

COMPARISONS WITH STANDARD HEMODIALYSIS

The majority of reports compare changes in patients after switching from standard, thrice weekly treatments to short, daily or frequent, nocturnal. Comprehensive reviews by Suri for short, daily and Walsh for frequent nocturnal have found:

- Systolic or mean arterial pressures or blood pressure medications decreased in nearly all studies;
- Health Related Quality of Life improved in most studies;
- Anemia or erythropoietin usage, and serum albumin improved in most studies;
- Phosphorus control is typically much better with frequent nocturnal.

Improvements in sleep disorders, cognitive function, vitamin D levels, exercise capacity, vascular functions and other have also been
reported predominantly with frequent, nocturnal regimens.

Mortality has not been evaluated in randomized trials. An observational study by Blagg19 of 117 short, daily patients on the Aksys machine reported a standardized mortality ratio of 0.39 while Lockridge reported mortality rate of 2.4% per patient-year for 35 frequent nocturnal patients.

The only published randomized, controlled trial of any type is one by Culleton et al which compared frequent nocturnal with standard thrice-weekly found significant reductions in blood pressure medications, phosphate binders, and left ventricular mass by MRI.20

Two NIH randomized, controlled trials are underway, one of in-center short, daily versus standard three-weekly; the other of home, frequent, nocturnal versus home, thrice-weekly nocturnal.6 Neither study is powered to assess mortality but rather use combined health-related quality of life and left ventricular mass by MRI as their primary outcomes.

CONCLUSIONS

Alternative hemodialysis regimens such as short daily and frequent nocturnal usually performed at home clearly appear to improve blood pressure control, and health-related quality of life compared to standard hemodialysis. Important surrogates for survival such as left ventricular mass also seem to improve and observational data suggests improved mortality. Renewed clinical and patient interest, technological advances such as the NxStage System One, and the commitment of large providers such as DaVita have resulted in recent significant increases in the number of centers offering and patients using these modalities.

The number of patients who can ultimately use these modalities may reach between 10-20% of the population. This will depend in large part on changes in reimbursement for number of treatments per week, provider interest, and patient selection criteria. The later include suitable environment, water, electricity, and space as well patient/partner characteristics such as visual acuity and reading comprehension, manual dexterity, and adherence to procedures.
I am what you may describe as a seasoned dialysis consumer. I visited dialysis units to do my therapy thrice weekly for over fifteen years and did Continuous Ambulatory Peritoneal Dialysis (CAPD) at home for more than twelve years. After a misadventure with a transplant (that appears to be a pattern with me), I returned to the world of hemodialysis. After much research, I decided that nocturnal home hemodialysis was the therapy of choice for me. My unit wouldn’t set up a home training program. I found one that would. My doctor wrote a letter of justification to cover the fourth treatment per week and my new dialysis center agreed to absorb the costs of additional weekly treatments (there’s no overhead or staff expenses at home and the dialyzers cost twenty-something dollars a pop). One year later, I was in business.

Everyone has his individual strengths and challenges. For me, I had to factor in my hearing loss. Without my hearing aid, I hear very little. Add the fact that I’m a very sound sleeper to the equation and the result is a potential earthquake with the machine shutting down and me not having a clue. Though some have reported doing dialysis alone at home, it was fairly easy to determine that I required another set of ears in the room.

Next, I had to factor in my somewhat rickety joints. Not too many folks with lots of amyloid build-up in their system (from decades of dialysis) switch to home hemodialysis. But that was my plan. With compromised hand function, there were certain tasks that were difficult: lifting the heavy jugs, connecting the Hanson lines,
spiking the saline bags, closing certain clamps. It was clear that I would also need an extra set of hands.

There was one thing I did have. It was the passion and determination to see this through. I found two wonderful people willing to help me, and the adventure began. Initially there were a few mishaps that were tremendous learning opportunities. The will to do this sustained me through the biggest hurdles.

For months I had trouble sleeping. My shoulder would get inflamed. I had difficulty finding a comfortable position. I woke up about every hour and stared at the machine’s computer screen, checking all the levels and looking at the amount of treatment time that remained. Then I’d fall asleep just before the treatment ended and wake up exhausted. I suffered from sleep deprivation and was not a happy camper. I consulted with my nurse and doctor. We decided I would start playing around with the times to try to find the balance that would provide both excellent dialysis and restful sleep. I tried dialyzing from the evening into the night, ending in the middle of the night and returning to sleep. I hated that. I tried dialyzing three nights alternated with two mornings. That worked for a while but it began to feel that all I was doing was dialyzing.

One night, after a particularly exhausting day, I asked my helper to turn the machine away from me. I closed my eyes and almost immediately fell asleep. The next morning I awoke, shocked to realize that I had slept through the night. This radical shift, I believe, was the shift from deep within my subconscious. I was not a sleeper during all my years of in-center hemodialysis. The machine faced me and I tended to it during my run. It gave me peace of mind to know how to adjust all the controls and handle any alarms. I prevented many a mishap that way. I was doing the same thing at home. But then I realized something. We were so meticulous in the set-up that MO, my machine, almost never alarmed during the run. That night, I had developed faith in the process and in myself. After a year of struggle, I stopped resisting and turned a major corner.

There is a Zen-like aspect to the initial set up. Everything drops away as my helper and I move through the process. We approach each treatment as if we are doing it for the first time. We are mindful of our actions and focused on the job at hand.

Especially the sticking of the needles. I have an A-V fistula that was created in 1975. One year later, I learned how to insert the needles. After more than a decade of doing CAPD, I wasn’t sure if I remembered how to do it when I returned to hemodialysis. I did. But by this time, I had lost a significant amount of fine motor ability in my hand and it was tougher to grasp the needle. I researched the buttonhole technique. I was trained in the school of site rotation and the concept of a buttonhole went against my principles. Yet the idea of creating a tunnel that would result in painless sticks and an overall decrease in scar tissue was very appealing, considering the type of therapy I was now doing.

I thought about this as I inserted the needles for each treatment. Where do I place the buttonholes? How do I choose the optimal spots? My fistula is precious to me and I did not want to do anything to cause it harm. One day I placed the needle in a spot where I felt no pain and thought the angle was just right and I simply knew. For the next several treatments I returned to that particular spot and by the fourth time, it slid in.

The scabs – that’s a whole other story. The buttonhole technique requires that you remove the scab from your previous visit to the site- kind of like lifting up the door. It is a practice that takes focus- sometimes easy and quick and other times challenging. I use the side of the tip of an 18-gauge needle and with the help of a mini flashlight the my helper shines directly on the site, I go for it.
I’ve heard that one secret of life is to learn to like what you do and do it completely with all of your attention. In a way the needle insertion is like a meditation practice. I am in the moment, engaged in the task at hand and all other thoughts fall away. As with any dialysis practice, there is no place for short cuts. I prep the sites meticulously with alcohol wipes. Excellent technique is a powerful prevention tool. Establishing the buttonholes and doing routine scab removal has been challenging at times but mostly straightforward once I developed the knack. Overall, buttonholes are an excellent investment in my well-being and peace of mind.

It’s now over two years that I do nocturnal home hemodialysis. After lots of experimentation and with the full support of my doctor and nurse, I have discovered a schedule that works best for me given my logistics (the machine not being in my home and needing a helper). I dialyze an average of nine hours for four nights a week at my sister’s home. I don’t skip more than one night and don’t dialyze more than two nights in a row.

My chemistries are excellent. My blood pressure is great. I have not needed phosphate binders in over two years. My joint function has not worsened and may have even improved. I have significantly more stamina. I no longer have to endure feeling sick from the therapy that sustains me either during or after the treatment. This is an awesome thing. It is said that everything we need is already here, just waiting to be discovered. I feel extraordinarily grateful to have discovered the type of dialysis therapy that gives me back the potential to thrive once again.

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OVERVIEW OF IN-CENTER & HOME NOCTURNAL DIALYSIS

By Linda Francisco, MD

It is well known that the mortality rate of patients undergoing maintenance hemodialysis remains unacceptably high. An extremely high morbidity and relatively low quality of life have also been observed in the chronic hemodialysis patient. It has been suggested that the institution of more intensive dialysis regimens may improve morbidity and possibly mortality among this patient population, although more controlled, randomized studies are still needed for the evaluation of intensive dialysis.

The impact of higher-dose dialysis on patient mortality and morbidity has been studied in several randomized clinical trials in the past, including the National Cooperative Dialysis Trial and the HEMO study.

The latter trial, conducted from 1995 to 2002, and the largest conducted to date on long-term hemodialysis patients, was designed to determine if a higher dose of dialysis – as provided by a three-times-per-week schedule – or the use of high-flux dialyzers decreased mortality and morbidity in long-term hemodialysis patients. Those patients randomized to the high-dose arm (mean equilibrated Kt/V of 1.53) had a mortality rate that was no different than patients randomized to the standard-dose arm (mean equilibrated Kt/V of 1.16). Post hoc analysis revealed that in the high-flux group, significant reductions were seen in the risk of death from cardiac causes and in the combined outcome of first hospitalization for cardiac causes or death from cardiac causes.
Several explanations are possible for the negative results of primary and secondary outcomes of the HEMO study. First, the increase in the weekly clearance of small molecules such as urea in the high-dose arm of the trial was relatively small. The standard or weekly Kt/V urea for the two groups was approximately 2.4 and 2.0 respectively, indicating a weekly Kt/V urea value that was only about 20 percent higher in the high-dose group. Similarly, the clearance of middle molecules is much more dependent on the total time on dialysis. Patients in the high-dose group were on dialysis an average of 90 minutes more per week (or only 15 percent more) than patients in the standard arm. When the HEMO study results are viewed in this light, the failure of these modest changes in small and middle molecule clearance to result in improved patient outcomes is not quite as surprising. This further enforces the need for studies that create a greater difference in the small and middle molecule clearance to determine if indeed there is an improvement in mortality and morbidity in higher-dose dialysis.

Controlled studies are needed to compare these conventional regimens to hemodialysis associated with longer duration and higher frequency, with evaluation of the outcomes as defined by improved laboratory and decreased usage of erythropoietin stimulating agents (ESAs), improved Kt/V values, decreased morbidity and mortality, and improved quality of life. With this in mind, nocturnal hemodialysis was introduced as a more desirable alternative to conventional dialysis, with greater time on dialysis and greater clearances of small and middle molecules. It was thought that nocturnal dialysis could provide superior dialysis based on dose, duration and frequency. It would also take advantage of the rather unproductive time during the nightly sleep.

Nocturnal hemodialysis can be done either at home or in-center. Nocturnal hemodialysis at home is generally performed five to seven nights per week during sleep for a variable amount of time, based upon the length of sleep usually desired. This can be from six to 12 hours.

In-center nocturnal hemodialysis is generally performed three nights per week for eight to 10 hours, depending on the center availability. In either home or in-center nocturnal hemodialysis, the dialysate composition is a sodium bath of 140 mEq/L, a potassium bath of 2 mEq/L, a bicarbonate bath of 28-35 mEq/L, and a calcium concentration of 2.5-4 mEq/L. A higher-dialysate calcium is prescribed for patients with high ultrafiltration volumes. The blood flow rate is generally between 200 and 300 cc/min, depending on clearances, and the dialysate flow rate is anywhere from 100 to 800 cc/min. The in-center nocturnal hemodialysis would tend to favor the higher end of blood flow and dialysate flows since the actual time per week on dialysis is less than for home nocturnal hemodialysis; i.e. three days per week versus five days per week. The typical ultrafiltration volume is one to two liters, with a range of one to seven liters per dialysis treatment. Any dialyzer membrane can be used, including small-surface-area dialyzers, but most centers use high-flux dialyzers. In addition, nocturnal hemodialysis can be performed with any hemodialysis machine, and existing machines can be modified for the requirements of the longer dialysis treatment. Dialyzer reuse can be employed, and the usual reuse technique is applied. Anticoagulation is also used, and it accounts for approximately 1,000 U of Heparin per hour of dialysis.

Vascular access for nocturnal dialysis is the same as it is for hemodialysis. Central venous catheters are used, although these are considered less popular, especially with the fistula-first initiative. Preferably, arteriovenous fistulas are used. Arteriovenous grafts have also been successful in nocturnal dialysis.

As mentioned above, nocturnal hemodialysis can be performed in the home or in the dialysis facility. If home hemodialysis is done at night, remote monitoring can be done via regular telephone lines or the Internet. Live monitoring provides the following benefits:
1. It helps prevent blood from clotting in an idle extracorporeal system.
2. It provides reassurance to the patient.
3. It ensures compliance.
4. It aids in data collection.

If hemodialysis is performed in the dialysis facility, nursing personnel provide the same benefits.

In addition to the monitoring performed above, there are other safety measures that can be employed with in-center or home nocturnal hemodialysis, such as inexpensive moisture sensors that are placed strategically on the floor to detect dialysate and/or blood leaks.

Patient groups that can be preferentially targeted for recruitment for home nocturnal hemodialysis include patients who are followed in a chronic kidney disease clinic prior to the development of end-stage kidney disease. This prevents the state of dependence frequently encountered in an in-center unit. Training can be instituted very early and patients can recognize the benefits of self-care settings. Another group that can be targeted includes patients who are ineligible for a kidney transplant, in that nocturnal dialysis can be viewed as the modality of independence closest to kidney transplantation. Patients with significant morbidities such as cardiac disease, diabetes mellitus, severe hypertension, dialysis-related symptoms, and/or large interdialytic weight gain can also be good candidates for home or in-center nocturnal dialysis. Patients who fail continuous ambulatory peritoneal dialysis yet want to maintain some degree of independence should be considered for home nocturnal hemodialysis. The final group that is very frequently benefited by nocturnal hemodialysis, whether in-center or home, includes large-sized patients and patients not adequately dialyzed because of poor blood flow in their access.

Nocturnal hemodialysis is usually associated with marked benefits including improved solute clearance and quality of life. Patients will declare their improvement of quality of life almost uniformly. There is noted to be much better blood pressure control and a reduction of medication requirements for control of hypertension. A recent randomized study from the University of Calgary demonstrated improved left ventricular mass, reduced blood pressure medications to achieve control, and improved mineral metabolism, as well as improved measures of quality of life.

Reports have shown that urea and phosphorus clearances can been increased with nocturnal hemodialysis, and hemoglobin values can be managed with less erythropoietin usage. Some reports have suggested an enhanced survival rate; however, this requires further analysis. At present, there are no published randomized trials of nocturnal hemodialysis. As a result, some investigators think that studies comparing nocturnal hemodialysis to conventional hemodialysis should be performed to better understand the benefits of nocturnal hemodialysis.

Presently, the National Institutes of Health is sponsoring two clinical trials via the Frequent Hemodialysis Network to determine the impact of “short dialysis hemodialysis,” defined as six-times-per-week hemodialysis for 1.5 to three hours per session, and “long nocturnal daily hemodialysis,” defined as six-times-per-week hemodialysis for six to eight hours per session. Hopefully, these studies will give us better insight into the improvement in morbidity, mortality, quality of life, blood pressure control and improved response to erythropoietin.

In summary, nocturnal hemodialysis done at home or in-center offers another modality of care for patients with end-stage renal disease, and it should be available to patients. Further studies are required to evaluate the benefits and indications for its usage.

REFERENCES


As we advance in our ability to provide services to patients with advanced kidney disease, we can enjoy a refreshment in techniques that allow patients to extend a normal lifestyle. Using alternate modalities instead of staff-assisted in-center hemodialysis shows great promise to improve quality of life and patient outcomes. Furthermore, it may help redistribute and control healthcare costs, expanding the value of service for patients.

Current modality choices for End Stage Renal Disease

While the incidence of new dialysis patients in the U.S. increased from 104,853 to 106,912 persons between 2004 and 2005, the rate of increase slowed when compared to years past. This is against upward trends for diabetes and obesity, and against an increased population reaching the age group most likely to reach End Stage Renal Disease (ESRD). It suggests that better management efforts in the early stages of kidney disease are paying off. Patients undergoing dialysis are also faring better; the adjusted mortality rate of ESRD patients has fallen over the past 10 years, from 217 per 1,000 patient-years to 163.6 per 1,000 patient-years.1 As CKD care improves across the entire spectrum of the disease, patients should be offered modality alternatives to in-center hemodialysis.2,3 This has been the focus in DaVita dialysis centers.

In 2005, there were 340,057 prevalent dialysis patients in the U.S. Of these, 311,919 received hemodialysis in a center. In 2005 there were only 138 self-care hemodialysis patients, while in 2007 there were 600 active self-care patients in 58 DaVita centers alone. Home hemodialysis patients numbered 2,105 in 2005, while in 2007 DaVita alone had 1,000 patients on home dialysis and a growth rate of 120 percent. At DaVita, 60 facilities now care for more than 300 in-center nocturnal patients.

The most common home dialysis option is peritoneal dialysis (PD). In 2005, the U.S. continuous ambulatory peritoneal dialysis (CAPD) population was 10,732 and the continuous cycler peritoneal dialysis (CCPD) population was 15,163.1 This modality has a tremendous potential for patients who desire to dialyze at home but are unable to meet home-hemodialysis training requirements or lack a suitable partner.

To date there has not been solid data that favors the mortality rate of hemodialysis over peritoneal dialysis, and there is not adequate data to make a definitive analysis of the mortality rates in home hemodialysis, but there are opportunities for cost savings and quality of life that arise when selected patients choose alternative modalities.
Cost comparisons between modalities

Although the costs for dialysis services continue to rise, one must take into consideration that the mean age of incident patients in 1980 was 52.8, and it is now 62.8. Costs for patients between 50 and 59 are $3.55 billion vs. $2.39 billion for patients 10 years younger. Of the $19.3 billion spent on ESRD cost, $8.72 billion is spent on diabetics. Physician capitation fees account for $624 million, a relatively small fraction of dialysis costs. These fees are roughly equal to Evaluation and Management (E&M) non-nephrology inpatient and outpatient services, and one-third the cost of erythropoietin stimulating agents (ESAs) – $1.86 billion. Per patient, nephrology services average $2,606 per year, and ambulance service provider costs average $1,861 per year.

In analyzing healthcare costs in the dialysis population, the most significant opportunity for savings is in-home dialysis. The average dialysis patient costs Medicare $68,808 per year – hemodialysis averaging $69,758 and peritoneal dialysis $50,847 per year. Kumar, et al.,4 reported their experience with 12 home hemodialysis patients studied over three years. In the entire study period there were 11 hospital admissions – 0.56 admissions per patient per year, with a mean length of stay of 3.7 days. The mean serum albumin increased from a baseline of 3.9±0.3 to 4.3±1.1 (P= 0.015). Adjusted hospital days have fallen in the past 10 years, from 16.7 in 1995 to 13.9 in 2005, but the total inpatient bill is $6.96 billion. Although this study is small, it indicates that as home hemodialysis becomes more popular, hospital utilization and dialysis costs may fall further.

A Canadian study of 19 in-center and 24 nocturnal hemodialysis patients showed a cost difference of around $10,000. Nocturnal home hemodialysis costs were $55,139±7,651 versus 66,367±17,502 (P=0.03). This study also calculated a utility score using the standard gamble method, and demonstrated that home nocturnal dialysis was associated with a higher utility score than in-center hemodialysis, 0.77±0.23 versus 0.53±0.35 (P = 0.03). When costs were adjusted for quality and represented in quality-adjusted life-years, in-center hemodialysis was $125,845 contrasted with $71,443 for patients dialyzing at home.5

Opportunities to improve quality of life

Home hemodialysis preceded hemodialysis by more than 10 years,6 and was well underway when peritoneal dialysis was first introduced. In centers that historically offered both, peritoneal dialysis allowed an increase of 42.5 to 67.5 percent in the population of home patients.7 A 1998 quality-of-life survey from Australia showed that transplantation and home hemodialysis patients had the highest quality-of-life scores, followed by CAPD patients. Although demographics were adjusted, in-center hemodialysis lagged behind the peritoneal group.8

In the London (Ontario) Daily/Nocturnal Hemodialysis Study, 23 quotidian and 22 conventional thrice-weekly patients were compared using three sets of quality-of-life assessment tools. Quotidian patients had better fluid management, less cramping, headaches, dizziness, hypotension and other blood pressure problems. They were able to reduce fluid restrictions, and all opted to remain on the quotidian therapy.9
Other studies have also demonstrated a high quality of life in home hemodialysis patients. In two recent studies there were no differences, the more recent noting better sexual function in the nocturnal home group and more social support in the peritoneal dialysis group.

**Opportunities to improve mortality rates**

Hyperphosphatemia, sleep apnea, residual renal function and hypertension are among the well-recognized risk factors for cardiovascular disease in dialysis patients. When reviewing mortality rates and reasons for hospitalization, cardiovascular disease was the major cause of both. Thus, a modality that will help to alleviate any and all of these risks should help improve outcomes in dialysis. Nocturnal hemodialysis and peritoneal dialysis may each have specific advantages in reducing dialysis mortality rates.

**Hyperphosphatemia**

The elimination kinetics of phosphorus has been studied in thrice-weekly and daily dialysis. Nocturnal hemodialysis is associated with the removal of 4,985±1827 mg/week of phosphorus versus 2,347±697 mg/week with conventional dialysis with a lower serum phosphorus (4 mg/dL versus 6.5 mg/dL). This has eliminated the need for binders in nocturnal hemodialysis patients. Short daily hemodialysis binder requirements decrease, but depend upon the treatment time.

**Sleep apnea**

Sleep apnea has been shown to be an independent risk factor for patients on dialysis. Both nocturnal hemodialysis and nocturnal peritoneal dialysis have been effective in correcting sleep apnea in renal-failure patients. Thus far, there are no studies confirming a beneficial effect of short daily dialysis on sleep apnea.

**Residual renal function**

In peritoneal dialysis, residual renal function is preserved. Residual renal function has been shown to be an important predictor of mortality in this population. In Hong Kong, peritoneal dialysis is the predominant form of therapy. At the University of Hong Kong a prospective observational study of 231 peritoneal dialysis patients compared left ventricular mass index, residual glomerular filtration rate and C reactive protein as well as hemoglobin, serum albumin and blood pressure. Longitudinal follow-up and Kaplan-Meier analysis demonstrated an increase in all cause and cardiovascular mortality related to C reactive protein, residual renal function and the left ventricular mass index (P < 0.0001), with death rates highest for patients with all three risk factors. The authors emphasize the importance of therapy that will preserve residual renal function for as long as possible in the ESRD patient.

**Hypertension and other markers**

It has been postulated that, because nightly hemodialysis over a longer dialysis time best approaches the ideal Kt/V, it has been demonstrated to reduce hypertension, left ventricular hypertrophy LVH, heart rate variability, arterial stiffness and endothelial dysfunction. It has also been shown to reduce the need for ESAs as well as inflammatory markers.
Short daily dialysis has also been shown to be advantageous over conventional hemodialysis, particularly with respect to left ventricular mass index, Kt/V, blood pressure control and lower AGE levels.\textsuperscript{34}

**Summary**

There are many opportunities to reduce the costs of dialysis therapy and redistribute compensation toward modalities leading to better patient outcomes. As we strive to improve these outcomes, reduce mortality and improve quality of life, we revisit modes of therapy that now show great promise. Many of the studies that show the benefits of more frequent dialysis are small and poorly powered. To help provide accurate and reliable data, two randomized controlled trials in Canada and the U.S., the Frequent Hemodialysis Network (FHN) Daily Trial and the FHN Nocturnal Trial, have been funded by the National Institutes of Health.

The FHN Daily Trial is a randomized controlled trial that will follow a projected 250 subjects for one year. They will be randomized to either conventional hemodialysis three days per week, or to more frequent hemodialysis delivered for 1.5 – 2.75 hours, six days per week. The two primary outcomes are a composite of mortality with the change over 12 months in left ventricular mass by magnetic resonance imaging, and a composite of mortality with the change over 12 months in the SF-36 RAND physical health composite (PHC) quality-of-life scale.

The nocturnal study, with a projected enrollment of 250, will randomize patients to a conventional thrice-weekly or six-hours-six-times-a-week treatments at home with a standardized Kt/V of 4.0. The primary health outcomes are a composite of 12-month mortality and the change over 12 months in left ventricular mass by cine-MRI, and a composite of 12-month mortality and the change over 12 months in the SF-36 RAND physical health composite.

![Figure 1. A paradigm that allows the patient to choose between various dialysis modalities.](image-url)
As nephrologists become involved in the management of chronic kidney disease patients at earlier stages, they play the key role in developing a future patient plan for alternative modalities that will preserve the quality of life, provide cost-effective care and reduce dialysis morbidities. Figure 1 shows a proposed schema that might be useful. The ideal therapeutic modality will help reduce costs, facilitate patients continuing gainful employment, and reduce dialysis morbidities. As home dialysis becomes more practical, and as more and more scientific publications demonstrate its advantage over conventional dialysis, the paradigm should shift to offering more home dialysis versus in-center dialysis, for selected patients. Patients choosing home therapy have the options of peritoneal dialysis or home hemodialysis. Those who select in-center therapy should have the options of staff-assisted, self-care or nocturnal in-center dialysis.

REFERENCES

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07E-130-U991-1
June 2007
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