



CLINICAL UPDATE: THE RENAISSANCE OF HOME HEMODIALYSIS

Charles H. Rodenberger, M.D.

Hypertension and Kidney Specialists of Lancaster

When I previously reported on the renaissance of frequent home hemodialysis in 2008, there were already strong observational data that indicated multiple benefits from this long available but little used modality.¹ Still, the lack of randomized studies left room for considerable skepticism among providers and payers. Interestingly, I have not found evidence of skepticism among patients in the literature or even in anecdotes, and despite the skeptics, use of home hemodialysis in the U.S. continues to increase exponentially, reflecting patient and physician satisfaction with the modality.

NEW CLINICAL STUDIES

Since my 2008 report, a seminal randomized, controlled study of frequent in-center hemodialysis has been published, and preliminary data from a randomized, controlled study of frequent nocturnal *home* hemodialysis have been reported. Those studies, coupled with ongoing data from an observational study of home hemodialysis with the newest and most frequently used home dialysis equipment, have all advanced our understanding of this renal replacement modality.

Most importantly, two long awaited, NIH-sponsored studies from the Frequent Hemodialysis Network Trial Group have been completed. In the first, 125 patients were randomly assigned to in-center hemodialysis 6X per week, and 120 patients to in-center dialysis 3X per week. Both groups were followed for an initial period of 12 months. Co-primary endpoints were a composite of death or 12 month change in left ventricular mass as assessed by MRI, and a composite of death or 12 month change in the physical-health composite score from the Rand 36-item health survey. These are well established markers of survival, cardiovascular risk, and physical well being. Pre-specified parameters for secondary end points incorporated the Beck Depression Inventory, assessment of cognitive function using the Trail Making Test, serum albumin and phosphate concentration, erythropoietin requirement, systolic BP, antihypertensive drug number, and death and hospitalization. (The short duration of the

trial and the small number of patients precluded use of death or hospitalization as primary outcomes.)

The conventional dialysis group was ultimately dialyzed an average of 2.88x/week, while the frequent dialysis group, though prescribed 6x/week, was dialyzed 5.17x/week. Results were remarkably positive. The hazard ratio for death or *increase in LV mass* for the frequent dialysis cohort was 0.61 (95% CI 0.46-0.82); the hazard ratio for death or *decrease in physical health score* for the frequent dialysis group was 0.70 (CI 0.53-0.92). Secondary endpoints that were statistically significant included marked reduction in systolic BP and use of antihypertensive medication, and a reduction in serum phosphorous concentration. Moreover, all other pre-specified secondary outcomes trended towards favoring more frequent dialysis. The death rates were not significantly different - 9 in the conventional group and 5 in the frequent dialysis group.

Unfortunately, but consistent with general experience to date, the frequent dialysis group experienced a significant increase in difficulties with vascular access. The hazard ratio of time to first access-related intervention was 1.71 (95% significance 1.08-2.73). Nonetheless, there was no statistical difference in access failure, and the trend actually favored the frequent dialysis cohort.

The second Frequent Hemodialysis Network Trial Group Study, the Nocturnal Trial (NCT00271999), compares nocturnal *home* dialysis 6X per week versus conventional hemodialysis 3X per week, also at *home*. Prespecified primary and secondary endpoints are the same as the previous trial, and the 12 month study duration was the same. This trial had a more 'active' treatment arm, at least 6 hours, 6x/week, versus the first study's 2.5-4 hours 6x/week. Also, in the first study both arms were carried out in a dialysis center, while in the second study both were at home. The second study has not been published, but preliminary results were reported at the American Society of Nephrology meeting in November 2010, with further updates at the National Kidney Foundation meeting in late April 2011.

Enrollment in the Nocturnal Study was even more challenging than in the Daily Study and reached only 87

patients. In the report to date, statistical differences were not identified, though the trend in the primary endpoint was toward a benefit of more intensive treatment. A similar non-significant trend toward increased access problems was also reported. Details of the study await publication.

A third study, the FREEDOM (Following Rehabilitation, Economics, and Everyday Dialysis Outcomes Measurements) Study (NCT00288613) is a nonrandomized observational study sponsored by the manufacturer of the most widely used home hemodialysis machine in the United States, the NxStage One. This ongoing study aims to enroll 500 patients and reports data on an ongoing basis. It enrolls patients who are covered by Medicare and have not previously used the NxStage One dialysis system; the comparator is a matched conventional in-center cohort. Various economic and clinical parameters are being followed for at least one year. The stated primary outcome is hospitalization days/patient-year. Secondary outcomes are similar to those of the FHN Study, including non-treatment related medical costs, and multiple intermediate outcomes.

Preliminary data presented at the Annual Dialysis conference in February show a marked improvement in both mental and physical health by the Rand-36 Health Survey and significant improvement in symptoms of restless legs syndrome and overall sleep quality. Other 12 month interim data include a standardized mortality ration of 0.53, a significant improvement in the Beck Depression Inventory, and a reduction in post-dialysis recovery time (time till recovery of usual sense of well being and energy) from 8.9 to 1.2 hours. Impressive to me is an overall drop in total “treatment time”—which includes not only actual dialysis time, but also two-way travel time, preparation and wrap-up time, and recovery time—from an average of 46 hours to 30 hours per week, despite a 50 % increase in actual time dialyzing. Publication of the 12 month data is forthcoming in the *Clinical Journal of the American Society of Nephrology*.

EXPERIENCE IN LANCASTER

Our experience in Lancaster County now includes about 25 patients currently self treating with frequent hemodialysis at home. I have been personally astounded by the positive results, considering the generally dreary wellness status with conventional hemodialysis. Our observations have generally paralleled the findings of the

above studies. Post dialysis fatigue has been minimized or eliminated. Energy, appetite, and even libido have improved. Dietary potassium, salt, and fluid restrictions have been dramatically reduced. Antihypertensive use has dropped markedly, with most patients off all anti-hypertensive medications. Positive patient impressions of self care and malleable treatment times and schedules with home dialysis are nearly universal.

Challenges remain. Access issues continue to challenge patients, physicians, and payers, though it's unclear whether this worsens with frequent dialysis. Excellent ‘stick teachers,’ diligent access surveillance, and patient acceptance of precise access care will help. Ongoing formal study of stick techniques, devices, and pharmacologic agents may reduce access complications. Patient anxiety can be substantial when complications arise; well-trained, available, and compassionate nurses and physicians are vital. Others challenges loom larger. The logistics of supply delivery, storage, and movement frustrate many patients. Lack of support, and sometimes frank resistance, from home health suppliers, pharmacists, and even physicians undermine acceptance. Growth of this modality is still impeded by the resistance of both government and commercial payers to change, despite apparent overall reduced costs.

Questions remain. Who are suitable candidates? What is an optimal amount of dialysis? How will we pay for the supplies and training? Who will pay for the water and electricity needed at home? Though patients who choose home dialysis are classically younger and healthier, the physiologic benefits of frequent dialysis would imply even greater benefit in more chronically ill ESRD patients. Wide experience in Canada, and even limited experience here, support this approach. How will we provide this kind of dialysis, especially when CMS disallows frequent in-center dialysis? Can regulatory, logistical, and financial barriers be overcome to allow “home dialysis” in nursing homes? Sparing transportation alone would be cost saving and beneficial to patients.

As with most clinical decisions, we are necessarily practicing with incomplete and imperfect data. But the health promise of frequent home dialysis has now moved from “possible” to “probable” and, I would argue, “beyond reasonable doubt.” The challenge now lies in gaining acceptance and support by payers, providers, and the public to disseminate this advance in patient care.

REFERENCES

1. Rodenberger, CH. The renaissance of home hemodialysis. *J Lanc Gen Hosp*. 2008; 3:129-135
2. The FHN Trial Group. In-Center Hemodialysis Six Times per Week versus Three Times per Week. *N Engl J Med* 2010; 363:2287-2300