Home Dialysis

By Ankur Shah

A top area to watch in 2020 is the new emphasis on home dialysis. On July 10, 2019, President Donald Trump signed an executive order launching Advancing American Kidney Health. Based on this executive order, the US Department of Health and Human Services (HHS) released three major goals to improve kidney health. The first goal is that 80% of incident kidney failure patients in 2025 receive a home modality of dialysis or a transplant. To facilitate this goal, mandatory and voluntary reimbursement models are being released. The mandatory model, ESRD Treatment Choices, will incentivize the provision of dialysis in the home.

In addition to the focus on home dialysis, HHS has also set goals of reducing the number of Americans reaching end stage kidney disease by 25% and doubling the number of kidneys available for transplantation by 2030, and calls for a public awareness initiative to increase awareness of kidney disease for both patients and providers as well as for funding to support the development of an artificial kidney.

There is a large anticipated educational need to meet the lofty goals of 80% of patients receiving dialysis in the home setting or a kidney transplant. A recent survey of graduating nephrology fellows in the United States found that 46% of trainees would like to receive additional instruction during fellowship in peritoneal dialysis, and a 2010 survey of 133 early career nephrologists showed 45% did not feel competent in the management of peritoneal dialysis patients. A remarkable finding of a 2010 survey of nephrologists was that 93% would choose a home modality as their initial renal replacement therapy modality. Furthermore, many myths exist regarding selection of patients suitable for peritoneal dialysis despite literature disputing the myths, including that obesity, diabetes, and autosomal dominant polycystic kidney disease are contraindications.

In 2020, *Kidney News* will launch a new series, Peritoneal Dialysis 101, which is meant to serve as an introduction to peritoneal dialysis, the most prevalent form of home dialysis, for physicians. The series will include articles on the history of peritoneal dialysis, outcomes, debunking myths, and basics of prescribing, and will conclude with options for further education in home dialysis. ■

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Suggested Reading

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Shared-Care Dialysis Improves Patient Outcomes: Building the Evidence

By Martin Wilkie and Steve Ariss on behalf of the SHAREHD team, University of Sheffield, UK

All across medicine, there is strong evidence that people who understand and are engaged in their own healthcare have better outcomes. There are several reasons for this, including being able to make quality healthcare choices, knowing when to seek help, and knowing how to reduce the risk for the development of complications (1). The body of literature in this area is large; diabetes mellitus care is a strong example. Indeed, it is not possible to deliver successful diabetes care without high levels of patient engagement, and there has been considerable interest and investment in patient training to improve outcomes.

From a strategic point of view, healthcare organizations have recognized this and have prioritized patient training and self-efficacy as key objectives (2). Within kidney medicine, there is evidence of a link between health literacy and outcomes; a strong example is home dialysis, whereby people who are trained to undertake their own treatment do well (3, 4). A key question is how to reliably extend these opportunities to people who undergo in-center dialysis so that they can reap the potential benefits that come from greater self-efficacy.

One approach is to develop mechanisms that encourage people who undergo in-center dialysis to have the choice to learn and engage in tasks related to their own treatment. This is described as shared hemodialysis care (SHC). Home dialysis (HD) can be broken down into approximately 14 tasks, which range from easy to more complex (Figure 1) (5). The level and complexity of tasks an individual decides to learn is flexible, and the logical approach is to start with simple aspects before progressing to more complex tasks as confidence is gained. Benefits reported by patients include a greater sense of independence and control over their own condition and, for some, the opportunity to conduct independent dialysis (6).

It is therefore important to discover the best approaches to support the delivery of SHC and how they can best be measured. The key is to test metrics that can be used to assess individual progress and to demonstrate the level of engagement that is offered by providers. Until such measures are used routinely, it will not be possible to develop evidence-based mechanisms that create optimal opportunities for SHC.

In 2016, a quality improvement collaborative was established in England, supported by the Health Foundation, with the objective of scaling up SHC for patients in center-based HD (7). The work involved multidisciplinary teams that included patient partners from 12 kidney centers. It focused on patient and nurse education, and it incorporated quality improvement measures such as rapid tests of change and peer assistance to examine and share the most effective approaches. The impact was tested through a stepped wedge cluster randomized controlled trial of approximately 600 prevalent HD patients. The primary outcome measure was the number of patients engaged in five or more treatment-related tasks. The results of that study are being prepared for publication.

In addition to quantitative assessments, which included the number of patients conducting independent dialysis by the end of the study, a logic model was developed through qualitative evaluation of the drivers and inhibitors that had an impact on successful delivery. This enabled the development of "involvement models," which described the most effective approaches to achieve both patient and staff involvement. It became clear from this work that the most successful approach to involve patients is rehabilitative and is focused on the principles of person-centered care and goal-directed dialysis (8, 9). In this model, most patients at a particular dialysis center are facilitated to be as involved as much as they wish; and training becomes part of the culture of the organization, performed by all on an ongoing basis. As for the staff involvement model with the most impact, that is one of coproduction, whereby all staff members are committed to supporting SHC.

The recent change in emphasis in dialysis targets from a focus on small solute clearance to the broader concepts of goal-directed dialysis requires a system change (9). SHC responds to that challenge by giving individuals the choice and opportunity to learn aspects of their own care and to make decisions about it irrespective of whether home dialysis is a possibility for them. The most successful approaches to this are likely based on rehabilitation and coproduction in which patient training is an integral part of the culture of the organization. ■

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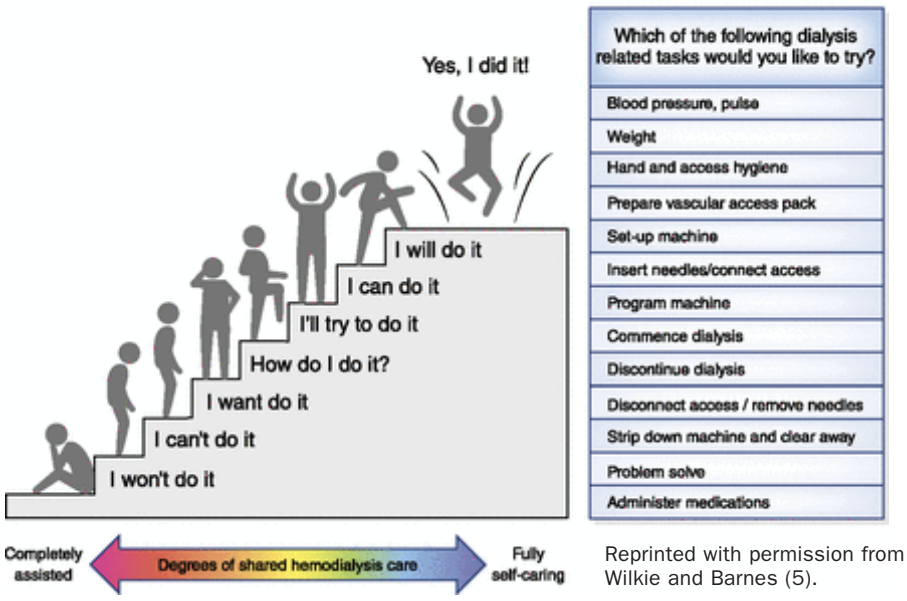
Figure 1. Small steps (tasks) within shared care provides a framework to unlock potential.



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Endothelin Receptor Antagonism in CKD

SONAR and Beyond

By Donald Kohan

On April 15, 2019, the results of the CREDENCE (1) and SONAR (2) trials were published. Both trials showed a 35% reduction in the relative risk of composite renal events in people with type 2 diabetes and kidney disease (DKD). Canagliflozin is now the first drug approved by the US Food and Drug Administration in almost two decades for slowing the progression of chronic kidney disease (CKD) in people with type 2 diabetes. By contrast, the future of endothelin receptor antagonists (ERAs) for treating DKD is uncertain. Various forums within the nephrology community have discussed aspects of atrasentan and SONAR; however, there is apparently no consensus opinion among nephrologists on what SONAR accomplished and the future of ERAs in diabetic or other forms of CKD.

SONAR was the first major DKD trial to incorporate an enrichment period; this involved all study participants receiving atrasentan for 6 weeks to identify individuals who might benefit (proteinuria reduction as a predictor of renoprotection) and in whom minimal side effects might occur (early ERA-induced fluid retention as a predictor of heart failure). Such an approach is highly relevant to the modern era of personalized medicine, whereby the goal is individualized therapy that is effective and safe. In addition, the enrichment period approach will permit correlation of initial drug response with systems biology (e.g., genomics, proteomics, metabolomics). Such analyses for SONAR will be forthcoming and may provide important insights into the biology of DKD.

There was a numerically higher incidence of heart failure events in the atrasentan treatment group in SONAR, although this did not achieve statistical significance and was much lower than in a previous trial of ERAs in DKD patients (3). This obviously indicates the need for continued vigilance for fluid retention, but is it the death knell for ERAs in DKD? Is the future of ERAs in DKD even more dismal, given the sponsor's decision to prematurely stop SONAR? It should be noted that despite the sponsor's actions, a strong renoprotective effect of atrasentan was observed. Further, given that atrasentan conferred renoprotection similar to that of canagliflozin, it begs the question whether combining canagliflozin or another sodium-glucose co-transporter 2 inhibitor (given their unique diuretic properties) and atrasentan (both on top of renin-angiotensin system [RAS] blockade) will yield additive or synergistic renoprotection in DKD while minimizing fluid retention. Hence, it is too soon to say what will happen with atrasentan in DKD; it would indeed be a shame to turn our backs at this point on what appears to be a highly renoprotective drug.

Moving beyond DKD, it is important for the kidney-community to keep in mind that ERAs are being vigorously pursued as a treatment for a variety of kidney diseases, based on an abundance of preclinical data. Relevant kidney and/or hypertension clinical trials include the following:

- Focal segmental glomerulosclerosis (FSGS). The phase 2 DUET trial found that sparsentan, a combined ERA/angiotensin receptor blocker (ARB), reduced proteinuria by ~50% compared with ARB treatment alone in people with primary FSGS (4). On the basis of those studies, the phase 3 DUPLEX trial has been launched involving 300 FSGS patients with a primary endpoint of change in eGFR slope (NCT03541174).
- IgA nephropathy. The phase 3 PROTECT trial is examining the effect of sparsentan versus an ARB on proteinuria in 280 people with IgA nephropathy (NCT03762850).
- Resistant hypertension. The phase 3 PRECISION trial examines the effect of the ERA aprocitentan (vs. placebo) on blood pressure (BP) reduction in 600 people with resistant hypertension (NCT03541174).
- Uncontrolled hypertension and CKD. The phase 3 INSPIRE-CKD trial will examine the effect of the ERA aprocitentan (vs. placebo) on BP reduction in 200 people with stage 3–4 CKD.
- Systemic sclerosis CKD. The phase 2 ZEBRA trial will report shortly on the effect of the ERA zibotentan on renal functional outcomes in people with systemic sclerosis (NCT02047708).
- Sickle cell nephropathy. A recently completed phase I trial examined the effect of the ERA ambrisentan on albuminuria (NCT02712346). The initial findings suggest that in patients using RAS blockade, ambrisentan confers greater albuminuria reduction than does placebo.

To date, fluid retention–related adverse events have not been reported to be an issue in the above-mentioned non-DKD trials. It is notable that most of the patients in these non-DKD studies are less likely to have significant cardiovascular comorbidities than are the patients in SONAR (the latter had a mean eGFR of ~43 mL/min per 1.73 m^2, and fluid retention or hypervolemia was present in 32.3% and 36.6% of the placebo and atrasentan groups, respectively). Thus, it is possible that ERA-induced significant adverse events related to fluid retention may prove to be less of an issue in patients with lower cardiovascular disease involvement.

In summary, I believe that the future holds much promise for the use of ERAs in CKD. Although we remain very mindful of their potential for fluid retention, we as a nephrology community must remain cognizant that this class of drugs has consistently reduced proteinuria, on top of RAS blockade, in the majority of CKD patients in whom they have been tried, and that the renoprotective effect of atrasentan in DKD parallels that of canagliflozin. Looking toward the future, there remain a wide variety of kidney diseases for which ERAs may exert a therapeutic benefit on top of RAS blockade, either as a single add-on agent or together with sodium-glucose co-transporter 2 inhibitors.

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