Published in final edited form as:

Am J Kidney Dis. 2013 May ; 61(5): 694–697. doi:10.1053/j.ajkd.2013.02.347.

Treatment of Depression and Poor Mental Health Among Patients Receiving Maintenance Dialysis: Are There Options Other Than a Pill or a Couch?

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Depression is a common psychological disorder among adults receiving maintenance hemodialysis. Up to 30% of these patients either report symptoms or have a clinical diagnosis of depression.¹ Similarly, mental health and, more broadly, health-related quality of life (HRQoL) are well below general population averages in maintenance hemodialysis patients.² Depression and poor mental health are associated with a higher risk of hospitalization and death in this population.^{3–10} Moreover, depressed hemodialysis patients are more likely to not adhere to dietary and fluid restrictions, to withdraw from dialysis therapy, and to commit suicide.^{11–13} With improvements in health care treatment and delivery, care goals for hemodialysis patients have evolved beyond just survival to include patients' overall well-being.¹⁴ Hence, it is incumbent upon nephrologists to be vigilant in managing depression and poor mental health in hemodialysis patients.

In this issue of *AJKD*, a timely study by Unruh et al¹⁵ reports the effects of frequent in-center and nocturnal hemodialysis on the outcomes of self-reported depressive symptoms and mental health among participants in the Frequent Hemodialysis Network (FHN) Trials. The FHN Trials were prospective 1-year randomized controlled trials of hemodialysis patients in the United States and Canada.¹⁶ Of 332 total patients, 245 were randomly assigned to either frequent (6 times per week) or conventional (3 times per week) daily in-center hemodialysis and 87 were randomly assigned to either frequent (6 times per week) or conventional (3 times per week) nocturnal hemodialysis, generally provided at home.¹⁷ It has been noted previously that frequent hemodialysis improved the 2 coprimary composite clinical outcomes of these trials, namely death or change in ventricular mass and death or change in a physical health composite score.¹⁷

In the present report, which focused on secondary outcomes, self-reported depressive symptoms were measured by the Beck Depression Inventory (BDI) and assessed at baseline, 4 months, and 12 months.¹⁵ A higher BDI score indicates a greater likelihood of depression,¹⁸ and a BDI score higher than 14 approximates a diagnosis of major depression in the setting of end-stage renal disease.¹⁹ Assessed at similar times, self-reported mental health was measured by the RAND Short-Form Health Survey and defined using the mental health composite score, a mathematical summary of 4 subscales: emotional well-being, role

limitation due to emotional problems, energy/fatigue, and social functioning.²⁰ The mental health composite score is normalized to a mean score of 50, and lower scores are consistent with poorer mental health. Unsurprisingly, at baseline, mean BDI score was approximately 12 and mental health composite score was approximately 45, which is consistent with the high prevalence of depression and poor mental health in hemodialysis patients. The primary analyses focused on mean changes in BDI and mental health composite scores from baseline to month 12 between the frequent- and conventional-treatment groups. Although there was not a significant difference in mean change in BDI score between the treatment groups, frequent daily hemodialysis led to significantly larger increases in mean mental health composite scores than did conventional hemodialysis, reflecting an improvement in the mental health of patients in this group. The authors also examined categorical cutoffs for elevated depressive symptoms (BDI score >15) and poor mental health (mental health composite score <43) and found important improvements in both in the frequent-daily-dialysis group, contrasting with unchanged scores in the conventional-dialysis participants. No significant changes were found in these metrics between the frequent- and conventional-dialysis groups in the nocturnal trial.

Although there were significant improvements in mental health, frequent hemodialysis did not result in a statistically significant reduction in depressive symptoms compared with conventional hemodialysis, which for the nocturnal trial may be attributed in part to small sample size and reduced power. However, on close inspection of these findings, it is noteworthy that favorable signs for reduced depressive symptoms and improved mental health were observed consistently in the frequent-hemodialysis group in both trials, which suggests a benefit conferred by frequent hemodialysis. An additional limitation is that the FHN Trials included relatively few patients on home hemodialysis therapy, which likely is the most viable venue for frequent hemodialysis considering the infrastructure and capacity limitations for the growing hemodialysis population in the United States. Although it is not unreasonable to extrapolate the authors' findings to frequent hemodialysis in the home setting, it is worth acknowledging that the home environment itself appears to provide additional benefits.²¹ Nonetheless, the rigorous design of the FHN Trials and inclusion of a diverse sociodemographic sample emphasize the merits of these findings and their applicability to the care of hemodialysis patients across North America.

Considering the known persistence of depression when left untreated, it is disappointing that few investigations of therapies for this disorder have been conducted in patients treated with hemodialysis. Only one other large study, the FREEDOM (Following Rehabilitation, Economics and Everyday-Dialysis Outcome Measurements) Study, examined the effect of a dialytic intervention for depression, and this report found that frequent daily (6 times per week) home dialysis was associated with a significant decrease in depressive symptoms.²² Although results from this prospective observational study may corroborate the trends observed by Unruh et al,¹⁵ a cautionary interpretation is warranted given inherent limitations with study design, including selection and ascertainment biases and lack of control arms.^{22,23} Among nondialytic therapies, small clinical trials evaluating the impact of exercise programs on depression have produced mixed results regarding improvements.²⁴⁻²⁶ A Brazilian clinical trial found that group cognitive behavioral therapy significantly reduced depressive symptoms and improved mental health in dialysis patients, but the feasibility of

implementing additional nondialysis therapy appointments across diverse American populations with a range of depression severity are unknown.²⁷ Although antidepressants appear to be efficacious in dialysis patients, the current evidence consists of a few small uncontrolled trials, and there are many obstacles to such treatment, including unwanted drug interactions, side effects, and patient refusal, especially in minority populations, who are at higher risk of depression and undertreatment.²⁸⁻³²

Similarly, clinical trials examining interventions to improve mental health in patients treated with hemodialysis are scant despite a mandate from the Centers for Medicare & Medicaid Services that dialysis facilities collect information on HRQoL.³³ In terms of dialytic interventions, the HEMO (Hemodialysis) Study found that in conventional hemodialysis treatment, neither higher dose nor membrane flux affected mental health.³⁴ Small observational studies have shown improvements across domains of HRQoL upon more frequent daily or nocturnal hemodialysis.^{35,36} The FREEDOM Study examined a single dimension of HRQoL, postdialysis recovery time, and found that 6-times-weekly daily hemodialysis led to improvements,²² which is consistent with the observations by Unruh et al.¹⁵

Considering the limitations of the existing literature, the findings from the FHN Trials make an important contribution to our knowledge. However, the study raises a number of questions. Chiefly, why would frequent hemodialysis cause improvements in mental health and depression? Moreover, would similar improvements be seen in patients with greater severity of depression and more impaired mental health? Frequent hemodialysis likely mitigates a number of biological reasons for depression and poor mental health in patients with kidney failure, including toxin and fluid accumulation and increased levels of proinflammatory cytokines.^{37,38} It is equally important to consider the potential effects of frequent hemodialysis on the perceptions of illness, psychological reactions, and lifestyle adjustments that contribute to depression and poor mental health in this population.³⁹⁻⁴¹ Delineating the latter mechanisms requires qualitative research, including conducting semistructured interviews and probing patients. There also are important unaddressed questions. Is patient participation in frequent hemodialysis sustainable in the long term? Frequent home hemodialysis has been plagued by patient burnout and discontinuation after a few years.⁴² What is the impact of frequent hemodialysis on informal caregivers? Caregiver social support has been linked to improvements in psychological health, adherence to treatment, and survival among patients treated with hemodialysis.^{37,38} Although a direct assessment of caregivers was not performed, most participants in the FHN Trials perceived substantial burden on their caregivers.⁴³

So have treatment options for depression and mental health expanded beyond pharmacologic therapy, psychotherapy, and cognitive behavioral therapy? Based on the findings by Unruh et al,¹⁵ it would appear the answer is “yes.” Although additional large well-designed clinical trials to examine this topic are needed, such research may be slow to arrive in an age of austerity.⁴⁴ Therefore, frequent hemodialysis should be considered as an additional novel approach to improve the psychosocial health of patients treated with maintenance hemodialysis, especially in patients with specific comorbid conditions (eg, increased left ventricular mass) that benefit from more frequent hemodialysis. Ultimately, a patient-

centered multi-pronged approach to treating depression and poor mental health that tailors treatment options to each patient's needs and preferences is warranted.

Acknowledgments

Support: None.

Financial Disclosure: The authors declare that they have no relevant financial interests.

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