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ASCENDING to New Heights in Our Understanding of the Treatment of Depression Among Individuals Receiving Hemodialysis

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Depression is the most common psychiatric condition among patients receiving maintenance hemodialysis. Depression negatively affects functional status and quality of life and is associated with increased treatment nonadherence, hospitalizations, and mortality (1). Despite the clinical and patient-reported significance of depression, clinicians often underrecognize and undertreat depressive symptoms (2, 3).

In 2016, the Centers for Medicare & Medicaid Services mandated that dialysis clinics screen and document follow-up plans for depression. Although these steps should increase depression recognition, clinicians must be prepared to respond to positive screening results. Guidelines recommend either cognitive behavioral therapy (CBT) or second-generation antidepressants (such as selective serotonin reuptake inhibitors [SSRIs]) as first-line treatment for major depressive disorder (4). Although studies have shown therapeutic efficacy of CBT in persons receiving dialysis, trials of SSRIs have yielded mixed results (5, 6). Patients receiving dialysis have unique risk factors (such as cardiovascular disease and polypharmacy) and life circumstances (including burdensome treatment and frequent health care visits) that plausibly alter the risk-benefit calculus of pharmacologic therapy or acceptance of CBT.

Mehrotra and colleagues (7) reported on a 2-phase randomized controlled trial in patients receiving hemodialysis. In phase 1, they examined the effects of an engagement interview versus a control visit on patients' acceptance of their depression and its treatment. In phase 2, they evaluated the effects of sertraline treatment versus chairside CBT on the severity of depressive symptoms. Patients were eligible to participate in the study if they had a score of at least 15 points on the Beck Depression Inventory-II (BDI-II) and met the criteria for major depressive episode or dysthymia. In phase 1, participants were randomly assigned to have either an engagement interview, designed to improve their acceptance of the diagnosis and treatment of depression, or a control visit. The phase 1 outcome, engagement interview efficacy, was defined as the proportion of participants who initiated depression treatment. In phase 2, participants were randomly assigned to receive sertraline treatment or 10 sessions

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of weekly CBT during hemodialysis. The phase 2 primary end point was Quick Inventory of Depressive Symptoms–Clinician-Rated (QIDS-C) score at 12 weeks. Secondary end points included patient-reported anxiety, energy and vitality, disability, and sleep, as well as treatment adherence measures.

Of 636 patients with BDI-II scores of 15 or higher, 184 and 120 participated in phases 1 and 2, respectively. In phase 1, acceptance of depression treatment did not differ between groups (estimated risk difference, 2.1% [95% CI, –12.1% to 16.4%]). Although no difference was observed, it is striking that the control visits averaged 30 minutes, just 20 minutes shorter than the average engagement interviews and much longer than standard dialysis clinical encounters. This suggests that control visits may have provided more meaningful interaction than routine care. This hypothesis is supported by more participants in the control group initiating treatment than projected, highlighting the importance of patient–clinician communication about depressive symptoms, regardless of intervention.

In phase 2, QIDS-C scores decreased from baseline to week 12 in both the CBT and sertraline groups, but 12-week depression scores were lower in the sertraline group (effect estimate vs. CBT, –1.84 [95% CI, –3.54 to –0.13]). Several secondary end points also differed between the groups, but their statistical significance was attenuated in analyses accounting for data missingness.

The study by Mehrotra and colleagues has many strengths, namely participant diversity, use of a depression screening tool less likely to be influenced by kidney failure–related somatic symptoms, minimal loss to follow-up, and rigorously collected patient-reported outcomes (8). A few limitations warrant discussion. First, the trial had no placebo group. However, patients in an observation cohort followed outside the trial did not show improvement in depressive symptoms, suggesting that some treatment was better than no treatment. Second, study outcomes were assessed at 12 weeks, the end of the acute phase of depression treatment. The effects of CBT and sertraline on symptom recurrence during the continuation and maintenance phases of treatment therefore cannot be inferred. Depression recurrence rates are high, with more than 50% of persons having a recurrence within 6 months if treatment is discontinued. Questions regarding the duration and stability of the observed responses are particularly germane considering that the treatment effects of CBT and sertraline were only modest. Moreover, achievement of clinical remission did not differ substantially between groups, with rates of 36% and 43% for CBT and sertraline, respectively. Such an incomplete response may partially explain the lack of substantial change in secondary outcomes. Combination therapy (pharmacologic and behavioral) may be needed to yield full remission.

In nondialysis populations, CBT and SSRIs have similar effects on depressive symptoms (9); however, sertraline outperformed CBT in ASCEND (A Trial of Sertraline vs. Cognitive Behavioral Therapy for End-stage Renal Disease Patients with Depression). One might posit that chairside (vs. office or group) CBT contributed to this finding. Hemodynamic shifts during dialysis may lead to cerebral hypoperfusion, resulting in reversible, peridialytic cognitive decline, which may have been undetected by trial screening (10). Of note, many patients describe being in a dialysis-associated “fog.” Such cognitive slowing might hinder

effective engagement in CBT. Although it is plausible that transient cognitive compromise hampered psychotherapy efficacy, a previous study demonstrated improvement in depressive symptoms with chairside CBT during dialysis (5). In the end, chairside CBT is a practical therapeutic strategy for depression in the dialysis setting. It involves a low burden for patients, with potential for widespread implementation if administered by properly trained clinic social workers.

Of most importance, the study provides equipoise for clinicians choosing between CBT and sertraline to treat depressive symptoms. The small differential efficacy across treatment groups is of questionable clinical significance, suggesting that clinicians may offer both therapeutic options without concern for compromising outcomes. Moreover, it emphasizes the importance of engaging patients in shared decision making while weighing such factors as individual preferences, medication side effect and interaction profiles, and comorbid conditions. Side effect considerations are particularly relevant given the difference in observed nonserious adverse events: 56 for sertraline versus 17 for CBT. Although pill burden or adverse effect concerns may sway some patients toward chairside CBT, others may prefer pharmacologic therapy because of privacy concerns or other matters (3, 8). In the end, tailoring therapies to patient preferences and clinical factors should improve adherence and thereby improve outcomes. To facilitate this process, as demonstrated by phase 1 findings, creating an opportunity for meaningful conversation about treatment options is essential. In conclusion, Mehrotra and colleagues conducted a rigorous trial that will allow dialysis clinicians to ASCEND to new heights in their therapeutic approach to depressive symptoms, a patient-prioritized outcome indeed.

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