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# Five Things to Know About Depression in Hemodialysis

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## 1. Major Depressive Disorder is the Most Common Psychiatry Disorder in Long-term Hemodialysis Patients

Major depressive disorder (MDD) is a constellation of cognitive and somatic symptoms. It is characterized by at least a 2-week episode of depressed mood and/or loss of interest in activities, along with, 4 other symptoms of depression.[1] Major depressive disorder is common among patients on intermittent hemodialysis (IHD), and early diagnosis requires a high index of suspicion.[2] Major depressive disorder prevalence in IHD patients varies from 25% (interview based) to 40% (self-reported screening questionnaires),[3] significantly higher than 2% to 10% in the general population.[4] Female sex, younger age, comorbidities, and longer dialysis duration are the risk factors for MDD in IHD patients.[5]

## 2. Major Depressive Disorder Can be a Challenging Diagnosis to Make in Intermittent Hemodialysis Patients, But Validated Screening Tools Exist

Patients rank depression as a top priority condition for which treatments need to be identified.[6] Yet, it remains underrecognized and undertreated.[7] Somatic features of depression in dialysis can be difficult to recognize due to overlapping symptoms with uremia and medication adverse effects.[8] Timely psychiatric evaluation in most institutions is limited, but validated screening questionnaires for identifying depressed IHD patients exist (Table 1).

## 3. Major Depressive Disorder Causes Worse Outcomes for Intermittent Hemodialysis Patients

Major depressive disorder or screening positive for depressive symptoms is associated with reduced dialysis compliance, adverse cardiac events, infections, hospitalizations, and mortality.[11,12] Mechanisms include poor compliance, worsened nutrition, and altered immune function.[13,14] Some studies link inflammatory biomarkers to increased severity of MDD.[14,15]

## 4. Consider Non-Pharmacological Therapies if Available in Your Institution

(A) Cognitive-behavioral therapy (CBT) is a low-risk, effective intervention in end-stage kidney disease (ESKD) patients with access to such therapies: A meta-analysis which included 226 HD patients showed that CBT was an effective method of decreasing the severity of depressive symptoms.[16] The CBT has also successfully improved quality of life, sleep quality, and adherence to fluid restrictions in patients with ESRD.[17]

(B) Increasing the frequency of dialysis can be beneficial but the effectiveness of exercise is unclear: Since the somatic symptoms of depression overlap with those of underdialysis, an intensification of dialysis should be considered among treatment options of depressive symptoms in ESKD. Exercise was found to improve depressive symptoms in 3/4 RCTs investigating exercise interventions in patients with ESKD.[18] It is unclear if depressed patients would follow through with above-

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**Table 1.** Screening Tools Validated for Identifying MDD in IHD Patients.

| Screening tool | Cut-off score studied | Sensitivity for MDD | Specificity for MDD |
|---|---|---|---|
| Beck Depression Inventory (BDI)[9] | ≥14 | 62% | 81% |
| Center for Epidemiologic Studies Depression Scale (CESD)[9] | ≥18 | 69% | 83% |
| Patient Health Questionnaire (PHQ-9)[10] | ≥10 | 91% | 92% |

Cut-off scores used in the studies cited are higher than those validated for the general population due to the overlap of somatic features of uremia and symptoms of depression.

mentioned interventions as they may lack motivation to exercise or attend more frequent dialysis.

## 5. Very Few Studies Have Examined the Safety and Efficacy of Pharmacotherapy in Treating Depression in Patients With End-Stage Kidney Disease

It is unfortunate that there are only a few small studies about the safety and effectiveness of drug treatments for depression in patients undergoing dialysis.[19] Therefore, it is still unclear whether depression treatment works well for people on dialysis and is safe, without causing serious side effects.[19]

(A) Consider sertraline as initial therapy: It is reasonable to initially trial sertraline given its proven efficacy, good tolerability, and low pharmacokinetic interactions. It is safe and effective in patients with recent CV events.[20] In a randomized, double-blind, placebo-controlled trial of 50 HD patients with depression, sertraline treatment for 12 weeks significantly improved depression symptoms (Beck Depression Inventory [BDI]) in 47.5% of the patients.[14] It can be initiated at a dose of 50 mg per day, up titrated every 2 weeks to a maximum dose of 200 mg daily.

(B) Fluoxetine is a reasonable alternative: A study involving 14 IHD patients showed that fluoxetine, at a daily dose of 20 mg, was safe and effective.[21]

(C) When using citalopram and escitalopram, it is important to exercise caution: In a Turkish study, citalopram at 20 mg was effective in treating 34 patients (across the spectrum of CKD, including IHD patients) with a reduction in BDI score and improvement in quality of life scores.[22] However, a retrospective study of 65 654 adults found that taking SSRIs (citalopram and escitalopram) were at an 18% higher risk for sudden cardiac death (due to higher QT-prolonging potential).[23]

(D) Tricyclic antidepressants and monoamine oxidase inhibitors are best avoided: Tricyclic antidepressants and monoamine oxidase inhibitors can accumulate and cause serious side effects in patients with impaired kidney function. Owing to severe drug interactions and limited utility, they should not be considered first-line treatment for depression in such patients.[23]

(E) However, there are currently no published observational studies or randomized controlled trials involving any other antidepressants besides selective serotonin reuptake inhibitors. Pharmacokinetic studies have shown that clearance is reduced for selegiline, amitriptyline, venlafaxine, desvenlafaxine, milnacipran, bupropion, reboxetine, and tianeptine. However, dialysis did not substantially remove any studied antidepressants. Combination therapies with pharmacological treatments plus CBT are understudied but likely to offer reason for optimism.

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