



# Pharmacological and psychological treatment of depression and anxiety among hemodialyzed patients – a review

Correspondence to:

Aleksandra Ćwiek  
II Psychiatric Department  
Institute of Psychiatry and Neurology  
9 Sobieskiego St.  
02-957 Warsaw, Poland  
e-mail: [aleksandrajcwiek@gmail.com](mailto:aleksandrajcwiek@gmail.com)

Aleksandra Ćwiek

Submitted: 23.09.2023

Accepted: 09.02.2024

II Psychiatric Department, Institute of Psychiatry and Neurology, Warsaw, Poland

## Abstract

**Purpose:** An overview of the current pharmacological treatment and psychosocial interventions, such as cognitive-behavioral therapy and breathing exercises, for depression and anxiety among hemodialyzed patients (HD).

**Views:** Depression and anxiety are common problems among HD patients, influencing their mortality and morbidity; however, they are often under-recognized and under-treated. Even though the topic is attracting more scientific attention there are still only few studies about methods of treatment for those disorders. Moreover, there are no clear guidelines on pharmacological therapy, which may prove to be difficult among patients with decreased renal function. Psychological interventions such as cognitive-behavioral therapy may be useful in treatment of these mental disorders among HD patients, though reports on the effects of such interventions are scarce.

**Conclusions:** This review outlines some of the current approaches to the treatment of mental disorders among HD patients that use both antidepressants and therapeutic methods. There is an urgent need for randomized clinical trials of both psychosocial and pharmacological interventions in treatment of depressive and anxiety disorders. Currently, both methods seem to be useful; however, they should be implemented with caution until clear guidelines are developed.

**Key words:** depression, anxiety, hemodialysis, end-stage renal disease.

## INTRODUCTION

Depression is a common mental disorder that is characterized by persistent sadness and lack of interest or pleasure in previously enjoyable activities [1]. Anxiety disorders are by definition a cluster of mental disorders characterized by significant and uncontrollable feelings of anxiety and fear [2]. These two mental disorders are common problems, with an estimated prevalence of about 20% of cases among hemodialyzed patients [3], and they significantly contribute to the morbidity and mortality among them [4]. The symptoms of psychiatric diseases in this context were often overlooked in the past [3], however in recent years the subject has gained more scientific attention. One of the main reasons is the fact that depression co-occurring with chronic diseases may be more resistant to treatment [5, 6], also it might have negative correlation with patients' quality of life [7]. Furthermore, it has been reported that depression among patients with end-stage renal disease, including patients undergoing hemodialysis, correlates with decreased survival rate [8] and adherence to dialysis-connected medication [9]. The main

factors that contribute to the development of depressive symptoms are reduced well-being through the need of medication, reduction of physical function, and dietary restrictions [10], all of which are aspects of daily struggles of hemodialyzed (HD) patients and may explain high prevalence of depression among them. All of this indicates the importance of identifying and treating depressive disorders and symptoms of anxiety. In order to screen patients, physicians may use one of the validated tools such as the Hamilton Depression Rating Scale (HAMD) and the Hamilton Anxiety Rating Scale (HAMS). Although they are not substitutes for psychiatric examination, these clinician-rated scales may prove to be useful in identifying the first symptoms of psychiatric disorders [4]. The purpose of this literature review is to shed more light on this matter by increasing the awareness of clinicians in these matters, as well as to demonstrate some of the proposed methods of treatment. The search included all available English-language articles reporting on depression and anxiety among hemodialyzed patients. The following databases were searched: Medline, Scopus and Web of science. In order to be included they had to meet following

criteria: a) patients had been undergoing hemodialysis, b) were over 18 years old, and c) experienced clinical depression or anxiety disorders including generalized anxiety disorder and panic disorder. The exclusion criteria were a) studies were not reported in English, and b) peritoneal dialysis was included.

## PHARMACOLOGICAL METHODS

There are many possible causes as to why it is difficult to recognize and deal with depression and anxiety among patients undergoing hemodialysis [11]. Although there are many scales which physicians can use to estimate the prevalence of major depressive disorder, there is no consensus as to which tool is the most accurate [11, 12]. In fact, studies show that the findings on prevalence of this disorder are highly depended on the method used [12]. Another problem faced by clinicians is the treatment of depression and anxiety among patients with chronic kidney disease (CKD). There are a few studies discussing psychotherapeutic and pharmacological interventions and their effectiveness [13]. Unfortunately, the data on the effectiveness of antidepressants is limited due to the lack of randomized studies on larger populations [14]. However, there are ongoing trials of sertraline, bupropion and fluoxetine treatment among dialyzed patients, which will evaluate effectiveness and adverse events, the findings of which are highly anticipated [15, 16]. Another reason for the lack of data is the fact that patients with end-stage renal disease are often excluded from the clinical trials due to safety concerns [17]. Selective serotonin re-uptake inhibitors (SSRIs) are mostly excreted by the liver and are not influenced by renal dysfunction [18]; however, the elimination half-life is prolonged and the clearance after oral intake is reduced for many antidepressants such as selegiline [19], amitriptyline [20], venlafaxine [21], desvenlafaxine [22], milnacipran [23], bupropion [24] and reboxetine [25, 26]. This may contribute to the higher prevalence of mild adverse effects of the treatment, though no study reported discontinuation as a consequence of side-effects of the therapy [14, 26]. The results of those reports suggest that the risk-benefit ratio may be different in comparison to the general population [27] and should be calculated individually. Another important matter is the challenge of adherence to treatment, as the majority of patients do not make a regular use of the treatment prescribed [18, 28]. Apart from the treatment of depressive symptoms, studies show that some SSRIs such as sertraline have anti-inflammatory effects and decrease C-reactive protein (CRP) levels [29]. It is worth noting that long-term hemodialysis treatment might be connected to increased levels of interleukin 1 (IL-1), IL-6 and CRP, which in turn contribute to negative nitrogen balance due to the catabolism of body protein, causing malnutrition and decreased appetite [30].

Since malnutrition is an important factor contributing to morbidity and mortality it is crucial to regularly assess the nutritional status of hemodialyzed patients [31, 32]. The European Renal Best Practice statement from 2014 recommends the use of selective SSRIs for 8 to 12 weeks and reevaluation after 12 weeks of therapy [11, 26].

Another matter is the treatment of anxiety disorders, which is complex and varies depending on the characteristics of the patient. The current guidelines recommend the use of SSRIs and serotonin and norepinephrine re-uptake inhibitors (SNRIs) as the first-line treatment [33]. The examples of medications commonly used in clinical practice with their indications, contraindications and side-effects are listed in Table 1. Benzodiazepines are considered to be second-line treatment for anxiety disorders, especially in generalized anxiety disorders and patients with specific phobias [34], though they should not be used in the treatment of chronic conditions due to their addictive potential [35, 36]. Anxiety treatment among hemodialyzed patients poses challenges as there are no randomized studies regarding this topic. Pharmacological treatment may be carefully implemented following individual evaluation, with consideration to dose reduction to avoid medication-dosage errors and their consequences [3].

## NON-PHARMACOLOGICAL INTERVENTIONS

Pharmacological methods seem to be important means of treatment of depression among HD patients; however, due to the lack of randomized studies and concerns arising from using antidepressants among those patients, non-pharmacological ways of treatment have been taken into consideration. There are a small number of reports investigating psychosocial interventions, which are described as non-medical interventions that are psychologically, socially, behaviorally or educationally oriented, among patients with CKD [37]. One of the most popular and well-documented non-pharmacological treatment methods is cognitive-behavioral therapy (CBT), which helps to reorganize negative thoughts and support behavioral adjustments and logical thinking [38, 39]. A study conducted in Brazil showed that CBT is an effective method of treatment among HD patients, causing a significant decrease of depressive symptoms and contributing to increased quality of life among them [40]. CBT also contributes to decreased anxiety levels. Different studies suggest that cognitive-behavioral therapy is effective after at least 6 to 9 months of treatment. A decrease in symptoms of depression here is probably achieved by encouraging patients to talk about their thoughts, and reorganizing those thoughts that might be interfering with their mood and daily behaviors, as well as creating coping strategies to deal with kidney disease, dialysis treatment,

**Table 1.** Antidepressants commonly used in medical practice with their indications, contraindications, adverse effects and the need of adjustment of dosages in case of renal dysfunction

Drug and dosage	Indications	Contraindications	Most common side-effects	Renal dysfunction
Sertraline 50-200 mg/d	Major depressive disorder Panic disorder Obsessive-compulsive disorder	Allergies Usage of monoamine oxidase inhibitors	Nausea Sexual dysfunction dizziness	No need to adjust the dosage in case of chronic kidney disease
Escitalopram 5-20 mg/d	Major depressive disorder Panic disorder Obsessive-compulsive disorder	Allergies Usage of monoamine oxidase inhibitors	Headaches Nausea Sexual dysfunction	Caution with patients with creatinine clearance < 53 ml/min, half-life may be prolonged
Fluoxetine 20-60 mg/d	Major depressive disorder Obsessive-compulsive disorder Bulimia nervosa	Allergies Usage of monoamine oxidase inhibitors Usage of metoprolol	Insomnia headache nausea diarrhea	Implement treatment with caution, there is no sufficient data
Duloxetine 30-120 mg/d	Major depressive disorder Generalized anxiety disorder Pain in diabetic neuropathy	Allergies renal dysfunction with creatinine clearance < 30 ml/min Usage if monoamine oxidase inhibitors Liver failure	Headaches Nausea Increased blood pressure Frequent urination Urinary retention Increased sweating	Patients with creatinine clearance > 30 ml/min have no need to adjust the dosage Do not use when creatinine clearance is < 30 ml/min
Venlafaxine 75-375 mg/d	Major depressive disorder Generalized anxiety disorder Social anxiety disorder Panic disorder	Allergies Usage of monoamine oxidase inhibitors	Insomnia Headaches Decreased appetite Blurred vision Increased blood pressure Nausea	No adjustments needed when creatinine clearance is > 30 mg/min Among hemodialyzed patients and with creatinine clearance < 30 mg/min reduced the dosage by 50%

and depression [40]. A large study assessed different non-pharmacological interventions such as acupuncture, acupressure, physical exercises or relaxation techniques including progressive muscle relaxation, breathing exercises, visualizations and autogenic training. It was reported that these relaxation techniques and physical exercises showed, to some extent, an improvement in depressive symptoms and anxiety levels [41]; however, the evidence produced by this study was insufficient for the determination, with high level of certainty, of the impact of the interventions concerned. The findings of this study match the results of another meta-analysis, in which authors showed the positive impact of psychosocial interventions on the treatment of both depression and anxiety among patients with CKD [42]. The outcomes were matched by yet another meta-analysis in regard of anxiety and depression, where there was no significant difference between HD patients receiving psychological interventions and the control group [43]. The assessment of the impact of psychosocial interventions is challenging, as studies on this topic are scarce. All of the studies have small sample groups and in most of them the adverse effects of some of methods were not included in the analysis. Neither was the change in suicide rate [42]. Thus, the outcomes of those reports should be treated with caution. Another interesting topic that is generally not reported is the usage of both pharmacological and psychological methods of treatment combined. Studies show that the effects

of the combination of these two methods of treatment are superior to each strategy alone in the general population [41]. However, there are no reports of the efficacy of such combined treatment among hemodialyzed patients.

There are only a few reports about non-pharmacological forms of anxiety treatment among HD patients. According to some studies, psychosocial interventions are an effective tool in reducing anxiety levels in the general population [44]. Moreover, some of the analyses suggest that CBT is the most effective method after comparing the long-term results of different interventions [45]. There are also only a small number of studies that investigate the efficacy of non-pharmacological methods in reducing anxiety levels among hemodialyzed patients, though these also underline the suggestion that CBT is probably the most effective form of treatment [46]. There is also one study that compares the efficacy of CBT versus sertraline usage in anxiety treatment among HD patients, though the results of the study have not yet been published [47]. These results must be regarded with caution, as there are no randomized trials on psychosocial interventions among HD patients and additional studies are needed. However, considering their positive effect on depressive symptoms they may be useful in increasing patients' quality of life.

## CONCLUSIONS

Even though the number of studies on this topic is gradually increasing, depression and anxiety are still largely under-recognized in hemodialyzed patients. It must be remembered that both of those problems contribute to decreased quality of life, poorer adherence to the treatment programs, and thus to higher rates of morbidity and mortality among those patients. This is why it is essential to evaluate hemodialyzed patients, so as to recognize the presence of alarming symptoms. Moreover, it is crucial to implement effective measures in reducing anxiety levels and manifestations of depression. Due to the lack of randomized studies and absence clear guidelines, how-

ever, this may prove difficult. That is why the purpose of this review was to present both pharmacological and non-pharmacological methods of treatment of depression and anxiety among hemodialyzed patients. The results of the studies discussed should be treated with caution, and the methods suggested should only be employed after the individual examination of each patient. Moreover, in the case of pharmacological treatments dose reduction may be considered due to decreased renal function found among this group of patients [48]. This study, like the limited number of studies that have preceded it, demonstrates the urgent need for randomized clinical trials of both psychosocial and pharmacological interventions in the treatment of depressive and anxiety disorders.

---

### Conflict of interest

Absent.

### Financial support

Absent.

### References

1. [https://www.who.int/health-topics/depression#tab=tab\\_1](https://www.who.int/health-topics/depression#tab=tab_1) (Accessed: 04.09.2023).
2. Diagnostic and statistical manual of mental disorders 5<sup>th</sup> edition: DSM-5. Arlington, VA Washington, D.C: American Psychiatric Association; 2013, pp. 189-195.
3. Cohen SD, Cukor D, Kimmel PL. Anxiety in patients treated with hemodialysis. *Clin J Am Soc Nephrol* 2016; 11: 2250-2255.
4. Ćwiek A, Czok M, Kurczab B, Kramarczyk K, Drzyzga K, Kucia K. Association between depression and hemodialysis in patients with chronic kidney disease. *Psychiatr Danub* 2017; 29 (Suppl 3): 499-503.
5. Kimmel PL, Peterson RA. Depression in end-stage renal disease patients treated with hemodialysis: tools, correlates, outcomes, and needs. *Semin Dial* 2005; 18: 91-97.
6. Blumenfeld M, Levy NB, Spinowitz B, Charytan C, Beasley CM Jr, Dubey AK, et al. Fluoxetine in depressed patients on dialysis. *Int J Psychiatry Med* 1997; 27: 71-80.
7. Dramer RA, Piraino B, Reynolds CF 3rd, Houck P, Mazumdar S, Bernardini J, et al. Characteristics of depression in hemodialysis patients: symptoms, quality of life and mortality risk. *Gen Hosp Psychiatry* 2006; 28: 306-312.
8. Rosenthal Asher D, Ver Halen N, Cukor D. Depression and nonadherence predict mortality in hemodialysis treated end-stage renal disease patients. *Hemodial Int* 2012; 16: 387-393.
9. Kimmel PL, Peterson RA, Weihs KL, Simmens SJ, Alleyne S, Cruz I, et al. Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. *Kidney Int* 1998; 54: 245-254.
10. Farrokhi F, Abedi N, Beyene J, Kurdyak P, Jassal SV. Association between depression and mortality in patients receiving long-term dialysis: a systematic review and meta-analysis. *Am J Kidney Dis* 2014; 63: 623-635.
11. Constantino JL, Fonseca VA. Pharmacokinetics of antidepressants in patients undergoing hemodialysis: a narrative literature review. *Braz J Psychiatry* 2019; 41: 441-446.
12. Palmer S, Vecchio M, Craig JC, Tonelli M, Johnson David W, Nicolucci A, et al. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int* 2013; 84: 179-191.
13. Natale P, Palmer SC, Ruospo M, Saglimbene VM, Rabindranath KS, Strippoli GF. Psychosocial interventions for preventing and treating depression in dialysis patients. *Cochrane Database Syst Rev* 2019; 12: CD004542. DOI: 10.1002/14651858.CD004542.pub3.
14. King-Wing Ma T, Kam-Tao Li P. Depression in dialysis patients. *Nephrology (Carlton)* 2016; 21: 639-646.
15. Friedli K, Almond M, Day C, Chilcot J, da Silva Gane M, Davenport A, et al. A study of sertraline in dialysis (ASSertID): a protocol for a pilot randomised controlled trial of drug treatment for depression in patients undergoing haemodialysis. *BMC Nephrol* 2015; 16: 172. DOI: 10.1186/s12882-015-0170-x.
16. <https://www.clinicaltrials.gov/study/NCT02238977?cond=hemodialysis&term=depression&intr=antidepressants&rank=1> (Accessed: 04.09.2023).

17. Hedayati SS, Yalamanchili V, Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney Int* 2012; 81: 247-255.
18. Lee SK, Lee HS, Lee TB, Kim DH, Koo JR, Kim YK, et al. The effects of antidepressant treatment on serum cytokines and nutritional status in hemodialysis patients. *J Korean Med Sci* 2004; 19: 384-389.
19. Lynn K, Braithwaite R, Dawling S, Rosser R. Comparison of the serum protein binding of maprotiline and phenytoin in uraemic patients on haemodialysis. *Eur J Clin Pharmacol* 1981; 19: 73-77.
20. Dawling S, Lynn K, Rosser R, Braithwaite R. Nortriptyline metabolism in chronic renal failure: metabolite elimination. *Clin Pharmacol Ther* 1982; 32: 322-329.
21. Turpeinen M, Koivuviita N, Tolonen A, Reponen T, Lundgren S, Miettunen J, et al. Effect of renal impairment on the pharmacokinetics of bupropion and its metabolites. *Br J Clin Pharmacol* 2007; 64: 165-173.
22. Wuerth D, Finkelstein SH, Ciarcia J, Peterson R, Klinger AS, Finkelstein FO. Identification and treatment of depression in a cohort of patients maintained on chronic peritoneal dialysis. *Am J Kidney Dis* 2001; 37: 1011-1017.
23. Royer RJ, Albin H, Barrucand D, Salvadori-Failler C, Kamoun A. Pharmacokinetic and metabolic parameters of tianeptine in healthy volunteers and in populations with risk factors. *Clin Neuropharmacol* 1988; 11 Suppl 2: S90-S96.
24. Worrall SP, Almond MK, Dhillon S. Pharmacokinetics of bupropion and its metabolites in haemodialysis patients who smoke. A single dose study. *Nephron Clin Pract* 2004; 97: c83-c89. DOI: 10.1159/000078635.
25. Dawling S, Lynn K, Rosser R, Braithwaite R. The pharmacokinetics of nortriptyline in patients with chronic renal failure. *Br J Clin Pharmacol* 1981; 12: 39-45.
26. Nagler EV, Webster AC, Vanholder R, Zoccali C. Antidepressants for depression in stage 3-5 chronic kidney disease: a systematic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). *Nephrol Dial Transplant* 2012; 27: 3736-3745.
27. Palmer SC, Natale P, Ruospo M, Saglimbene VM, Rabindranath KS, Craig JC, et al. Antidepressants for treating depression in adults with end-stage kidney disease treated with dialysis. *Cochrane Database Syst Rev* 2016; 2016: CD004541. DOI: 10.1002/14651858.CD004541.pub3.
28. García-Llana H, Remor E, Selgas R. Adherence to treatment, emotional state and quality of life in patients with end-stage renal disease undergoing dialysis. *Psicothema* 2013; 25: 79-86.
29. Zahed NS, Sharifi M, Karimi M, Nikbakht H. Impact of sertraline on serum concentration of CRP in hemodialysis patients with depression. *J Renal Inj Prev* 2016; 6: 65-69.
30. Panichi V, Migliori M, De Pietro S, Metelli MR, Taccola D, Perez R, et al. Plasma C-reactive protein in hemodialysis patients: a cross-sectional, longitudinal clinical survey. *Blood Purif* 2000; 18: 30-36.
31. Miller AH, Pariante CM, Pearce BD. Effects of cytokines on glucocorticoid receptor expression and function. Glucocorticoid resistance and relevance to depression. *Adv Exp Med Biol* 1999; 461: 107-116.
32. Lowrie EG, Laird NM, Parker TF, Sargent JA. Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. *N Engl J Med* 1981; 305: 1176-1181.
33. Reinhold JA, Rickels K. Pharmacological treatment for generalized anxiety disorder in adults: an update. *Exp Opin Pharmacother* 2015; 16: 1669-1681.
34. Stein MB, Sareen J. Clinical practice. Generalized anxiety disorder. *N Engl J Med* 2015; 373: 2059-2068.
35. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. *JAMA Psychiatry* 2015; 72: 136-142.
36. Moore N, Pariante A, Bégaud B. Why are benzodiazepines not yet controlled substances? *JAMA Psychiatry* 2015; 72: 110-111.
37. Martire LM, Lustig AP, Schulz R, Miller GE, Helgeson VS. Is it beneficial to involve a family member? A meta-analysis of psychosocial interventions for chronic illness. *Health Psychol* 2004; 23: 599-611.
38. Beck AT. The current state of cognitive therapy: a 40-year retrospective. *Arch Gen Psychiatry* 2005; 62: 953-959.
39. Hedayati SS, Finkelstein FO. Epidemiology, diagnosis, and management of depression in patients with CKD. *Am J Kidney Dis* 2009; 54: 741-752.
40. Duarte PS, Miyazaki MC, Blay SL, Sesso R. Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients. *Kidney Int* 2009; 76: 414-421.
41. Kamenov K, Twomey C, Cabello M, Prina AM, Ayuso-Mateos JL. The efficacy of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in depression: a meta-analysis. *Psychol Med* 2017; 47: 414-425.
42. Kimmel PL, Weihs K, Peterson RA. Survival in hemodialysis patients: the role of depression. *J Am Soc Nephrol* 1993; 4: 12-27.
43. Pascoe MC, Thompson DR, Castle DJ, McEvedy SM, Ski CF. Psychosocial interventions for depressive and anxiety symptoms in individuals with chronic kidney disease: systematic review and meta-analysis. *Front Psychol* 2017; 8: 992. DOI: 10.3389/fpsyg.2017.00992.
44. Levy Berg A, Sandell R, Sandahl C. Affect-focused body psychotherapy in patients with generalized anxiety disorder: evaluation of an integrative method. *Journal of Psychotherapy Integration* 2009; 19: 67-85.
45. Cuijpers P, Sijbrandij M, Koole S, Huibers M, Berking M, Andersson G. Psychological treatment of generalized anxiety disorder: a meta-analysis. *Clin Psychol Rev* 2014; 34: 130-140.
46. Xing L, Chen R, Diao Y, Qian J, You C, Jiang X. Do psychological interventions reduce depression in hemodialysis patients?: A meta-analysis of randomized controlled trials following PRISMA. *Medicine (Baltimore)* 2016; 95: e4675. DOI: 10.1097/MD.0000000000004675.
47. Hedayati SS, Daniel DM, Cohen S, Comstock B, Cukor D, Diaz-Linhart Y, et al. Rationale and design of a trial of sertraline vs. cognitive behavioral therapy for end-stage renal disease patients with depression (ASCEND). *Contemp Clin Trials* 2016; 47: 1-11.
48. Yeun JY, Kaysen GA. Factors influencing serum albumin in dialysis patients. *Am J Kidney Dis* 1998; 32 (6 Suppl 4): S118-S125. DOI: 10.1016/s0272-6386(98)70174-x.