

Citalopram Versus Psychological Training for Depression and Anxiety Symptoms in Hemodialysis Patients

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Introduction. This study was designed to compare an antidepressant medication, citalopram, with psychological training in hemodialysis patients with symptoms of anxiety and depression.

Materials and Methods. A total number of 44 hemodialysis patients scored 8 and more on the Hospital Anxiety and Depression Scale (HADS) were randomly allocated to two groups to receive citalopram, 20 mg/d, for 3 months or to attend 6 sessions of 1-hour psychological training. A nephrologist and a senior psychiatry resident were responsible for training of the patients, which contained explaining the anatomy of the kidneys, causes of kidney failure, treatment modalities, the mechanism involved in hemodialysis, the required care in hemodialysis patients, stages of adaptive reaction in human, and techniques of problem solving, stress management, and muscle relaxation. Both groups completed the HADS once before and once after the treatment. The final results of the two groups were compared.

Results. Citalopram administration led to a significant decrease in the patients' depression score ($P = .001$), anxiety score ($P = .048$), and total HADS score ($P = .002$). Psychological training sessions also decreased significantly depression ($P = .04$), anxiety ($P = .03$), and total HADS scores ($P = .045$). There was no significant difference in the amount of decrease in the scores of depression ($P = .65$), anxiety ($P = .19$), and the total HADS ($P = .66$) between the two groups.

Conclusions. Psychological training and citalopram have similar effects on improving the symptoms of anxiety and depression in hemodialysis patients.

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INTRODUCTION

Physical diseases, especially their chronic and debilitating types, are associated with several psychiatric problems.¹⁻³ Kidney failure and dependence on hemodialysis are one of the chronic medical illnesses that commonly cause depression and anxiety. The prevalence rate of chronic kidney failure is 242 cases per million people worldwide, and about 8% is annually added to it.⁴ According to the latest report by the Transplant Management

and Specific Diseases Center in Iran, there are about 25 000 patients with advanced kidney failure, more than 50% of whom are currently under hemodialysis.⁵

It has been found that about 50% of hemodialysis patients suffer from all types of depression. and 5% to 20% have major depression.³ Depression is the second most common disease after hypertension among patients with end-stage renal disease (ESRD).⁶ The major risk factors of depression

in hemodialysis patients include female gender, living without a partner, low education level, low socioeconomic status, hypertension, low albumin level, and longer time on dialysis.⁷ Depression and anxiety are underestimated and less treated in hemodialysis patients.³ Several studies showed that suicide thoughts are more common in patients with hemodialysis compared to the general population and life expectancy in such patients is about one-third to one-sixth of the normal population.^{2,8} Depression in patients with ESRD is associated with higher risks of disease complications and mortality rate. An increase in mortality and complication due to depression is independent of factors such as age, race, socioeconomic status, place of residence, and other concomitant diseases.³ Depression also leads to a decrease in quality of life of these patients.^{1,9,10}

Diagnosis of depression is difficult in patients with chronic kidney disease. There is a considerable overlap between symptoms of uremia and depression, making the diagnosis challenging.¹¹⁻¹³ In other words, signs and symptoms of chronic kidney disease, the side effects of treatments (such as weight loss and loss of appetite), and associated problems such as pain are common with those of depression.³

When the patient is not trained for hemodialysis before reaching the ESRD, dialysis would be a stressful therapy for the patients and causes several psychiatric reactions.² Keramon and colleagues describe the special grief of patients with ESRD.¹³ It has been proven in various studies that the self-control sense is associated with success in job, favorable cognitive function, and a decrease in depression and anxiety in such patients.¹⁴ Some studies show that training the patients before hemodialysis can bring about an increase in their survival. The training before hemodialysis can potentially improve treatment efficacy and also patients' quality of life.^{14,15} Moreover, it has been reported that training prior to hemodialysis may postpone the need to hemodialysis by increasing the patient's cooperation, better adherence to treatment, and slowing down the progression of ESRD. Consequently, developing a specific training plan for prevention of anxiety and depression in such patients may have considerable effects on adjusting and lessening their problems.¹⁵ On the other hand, the use of antidepressants, especially

selective serotonin reuptake inhibitors (SSRIs), can be effective and safe in the treatment of depression among ESRD patient. Selective serotonin reuptake inhibitors such as citalopram, fluoxetine, fluvoxamine, and sertraline do not require dose adjustment in the presence of kidney failure, with the exception of paroxetine.¹⁶

Despite the high prevalence of ESRD in Iran and its subsequent anxiety and depression, there is no specific training or treatment protocol for hemodialysis patients, neither before nor during dialysis treatment. On the other hand, studies on the effectiveness and safety of antidepressant in ESRD patients are limited to observational reports with small sample sizes and lack of formal assessment for depression diagnosis.¹⁷ This study compares the effectiveness of citalopram and psychological training on anxiety and depression symptoms in hemodialysis patients.

MATERIALS AND METHODS

Participants

This randomized controlled trial was conducted on patients with ESRD that were currently on long-term hemodialysis at the Hemodialysis Center of Imam Khomeini Hospital, Sari, Iran. The study protocol was approved by the Ethics Committee of Mazandaran University of Medical Sciences. Patients with depressive and anxiety symptoms were included in the study. Presence of anxiety and depression was measured using the Hospital Anxiety and Depression Scale (HADS), and having scores equal to or more than 8 were considered positive for depressive and anxiety symptoms. They were excluded if they did not signed the consent form for participation, had a previous history of psychiatric disorders, they had suffered from stressors other than ESRD in the past 6 months, a new anxiety episode developed during the study, based on the stress events table by Holmz-Rahe, any change occurred in the hemodialysis schedule, other psychiatric therapies were started during the study, and they did not complete all training sessions. Based on the previous studies and the HADS scores with an average difference of 7 and subtracting the standard deviation of 4, and considering an α of 0.05 and a β of 0.2, the required sample size was calculated to be 35 patients. Meanwhile, a 25% lost to follow-up was considered and the sample size was adjusted to 44 patients.

Procedure

Participants were randomly selected from among the hemodialysis patients in the dialysis unit and randomly assigned into two groups of psychological training and citalopram. The two groups were comparable in terms of age, gender, educational level, marital status, employment, laboratory indexes, duration of and frequency of hemodialysis ($P > .05$).

The patients in the training group participated in 6 sessions of 1-hour teamwork training every other day. The content of training sessions was developed according to standard scientific methods.^{18,19} It contained explaining the anatomy of the kidneys; physiopathology and causes of kidney failure; treatment modalities with their advantages and disadvantages; the mechanism involved in hemodialysis; the required care in hemodialysis patients, stages of adaptive reaction in human; and techniques of problem solving, stress management, and muscle relaxation. The patients in the citalopram group did not attend any training session and received citalopram, 20 mg/d, for 3 months. The dosage did not change throughout the study period.

Hospital Anxiety and Depression Scale

The HADS was completed twice by the patients under the supervision of a psychiatrist, once before the random allocation of the patients and once 3 months after the start of interventions. The HADS was developed as a self-rating instrument for assessment of anxiety and depression in patients with physical and mental problems.²⁰ Being short, easily scored, and relative sensitive to changes are the advantages of this questionnaire. It is divided into an anxiety subscale and a depression subscale with 7 intermingled items for each. Each item has 4 responses with scores ranging from zero to 3, and the respondents would select one of them based on their feelings. The total score of each subscale ranges from zero to 21. Scores between 11 and 21 are considered clinically suspicious; 8

to 10, intermediate; and zero to 7, normal. This questionnaire has been translated to Persian and standardized by Montazeri and colleagues.²¹ The reliability of this scale was examined using internal consistency with Cronbach coefficient alpha of 0.86 for depression and 0.78 for anxiety subscales.

Data Analysis

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 15.0, SPSS Inc, Chicago, Ill, USA). Descriptive statistics such as central and dispersion indexes were first run and then the independent sample *t* test was applied to compare the two groups. Pre- and post-intervention scores in each group were compared using the paired *t* test. The chi-square test was used to compare qualitative variables. The level of significance was defined as .05.

RESULTS

Twenty-two patients participated in each study group. One patient in the training group was excluded due to a change in hemodialysis schedule. In the citalopram group, 1 patient was excluded due to a change in hemodialysis schedule and 2 patients because of a recent stressor. Thus, the study continued with 21 patients in the training group and 19 patients in the citalopram group. The mean age of the patients was 49.1 ± 14.5 years and 52.3 ± 15.6 years in the training and citalopram groups, respectively. In the citalopram group, 42% of the participants were men, and similarly, 45% of those in the training group were men.

The pre-intervention scores of anxiety and depression as well as the total HADS were not significantly different between the two groups. As summarized in the Table, the mean depression score before the intervention was 9.42 ± 3.11 in the citalopram group and changed to 6.26 ± 4.18 after the drug administration ($P = .001$). Regarding anxiety scores, the pre-intervention anxiety mean score was 10.00 ± 3.17 , which was reduced to 8.15 ± 5.61 after citalopram administration ($P = .048$). The total

Comparison of Depression and Anxiety Score and Total Hospital Depression and Anxiety Scale (HADS) Scores Between Hemodialysis Patients Receiving Psychological Training and Citalopram

HADS	Psychological Training			Citalopram		
	Pretest	Posttest	<i>P</i>	Pretest	Posttest	<i>P</i>
Depression	9.58 ± 3.47	7.33 ± 4.80	.04	9.42 ± 3.11	6.26 ± 4.18	.001
Anxiety	9.09 ± 2.01	7.18 ± 4.14	.03	10.00 ± 3.17	8.15 ± 5.61	.048

score of HADS in the citalopram group changed significantly after drug administration (19.47 ± 4.71 versus 14.48 ± 8.85 , $P = .002$).

In the training group, the mean depression score was 9.58 ± 3.47 , which significantly decreased to 7.33 ± 4.80 after training ($P = .04$). The pre-intervention mean anxiety score in this group was 9.09 ± 3.01 , which changed significantly to 7.18 ± 4.41 at the end of the training ($P = .03$). It was also observed that the total HADS score significantly decreased after the training (18.61 ± 5.04 versus 15.14 ± 6.06 , $P = .045$; Table).

There were no significant differences between the two groups for depression ($P = .16$), anxiety ($P = .83$), and total ($P = .55$) scores after the intervention. The mean differences of the pre- and post-intervention were not significantly different between the two groups regarding the scores for depression ($P = .65$), anxiety ($P = .19$), and the total HADS ($P = .66$).

Citalopram was well tolerated by all of the patients and no severe adverse effects were reported.

DISCUSSION

Our results confirmed that psychological training based on the standard protocols and the use of citalopram resulted in comparable decreases in the severity of depressive and anxiety symptoms of hemodialysis patients. We used the validated HADS for before-after measurements of depressive and anxiety symptoms in a randomized controlled study. One limitation of the study, however, was lack of a third group to test the effectiveness of a combination of both therapies.

Nonpharmacological therapies have been assessed by several studies among patients with chronic kidney disease. Devins and colleagues conducted a randomized clinical trial on 297 patients with predialysis stages of chronic kidney disease to compare psychological training with the routine care. Their training protocol contained 90-minute sessions of lectures and slide presentations about the natural function of kidney, changes in its function with chronic kidney disease, and information about treatment modalities of renal replacement therapy. The patients were followed each 3 weeks with a telephone interview lasting for about 10 minutes. Those who received training initiated dialysis 17 months after the start of the study, while the control group started dialysis 3

months earlier ($P < .001$).⁹ In a study by Tsay and coworkers, effects of adaptive techniques on the disease-related stressors and their association with depression and quality of life of ESRD patients were assessed. In this study, 57 patients participated in the adaptive techniques training besides their routine treatment and the other group received only routine treatment. Training sessions were held in small groups weekly for 8 weeks and the patients were followed each month. The Beck Depression Inventory questionnaire was applied in this study. They concluded that adaptive technique training decreased depression score.²² A similar study of 60 hemodialysis patients demonstrated the reduction of depressive symptoms by psychological intervention, including training about physical aspects of renal insufficiency and dialysis.²³ Lit and colleagues also showed that psychological training improved the quality of life of the patients.²³

Longer supportive psychotherapy sessions were applied by Cukor and colleagues. Psychological sessions were held monthly in the dialysis unit individually or in groups of 6 to 10 patients for one year. At the end of study, the Beck Depression Inventory scores significantly decreased in all the patients.²⁴ The investigators did not recruit a control group, and thus it was not clear to what extent the decrease in depression score was attributed to supportive psychological sessions, and the results are prone to bias because of other factors that may impact on depression scores longitudinally.

The content of psychological training programs varies between studies. Baraz and coworkers investigated the effects of self-care training on the quality of life and some laboratory indexes in patients on hemodialysis. They evaluated 32 patients and compared them with a control group after a 2-month training. Their findings showed the significant effects of self-care training on the quality of life and most of the laboratory indexes in patients.²⁵ Wicks and associates assessed insight therapy and showed that it effectively improved depression and anxiety in patients with dialysis.²⁶ Overall, a review of the association of mental-social interventions on depression in dialysis patients demonstrated that psychological interventions added to routine medical therapies can decline depression in ESRD patients. This review emphasized that further studies are required to suggest standardized diagnostic criteria of

depressive disorders.²⁷ Furthermore, the content and duration of psychological care programs should be investigated and compared in order to find the optimal treatment protocols for these patients.

Studies on antidepressant medical therapy of dialysis patients are limited. Small trials, most of which with no control group, has shown that the use of antidepressants is effective in improving depression and quality of life of dialysis patients.²⁸⁻³⁰ Especially, some selective serotonin reuptake inhibitors, such as sertraline and citalopram, are well tolerated and do not need dose adjustment. In a study by Wuertth and colleagues, patients on peritoneal dialysis were screened by the Beck Depression Inventory and medical treatment was started for those finally diagnosed with depression. Although most of the antidepressant medications were effective, not all of them were tolerated by the patients and 50% successfully completed a 12-month medical treatment.³¹ Thus, nonpharmacological preventive and therapeutic interventions can have a major role in the psychiatric care of ESRD patients.

CONCLUSIONS

A well-planned training program for decreasing anxiety and depression in dialysis patients may help considerably solve psychological problems of these patients. Meanwhile, it is necessary that therapeutic team have a deep understanding of depression and its treatment in order to present favorable services to such patients. Due to the importance of this topic and our findings, it is recommended that other studies be conducted with longer follow-up and adding another group to receive concurrent medical therapy and psychological training.

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CONFLICT OF INTEREST

None declared.

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