

The Evaluation and Comparison of the Effects and Complications of Escitalopram and Citalopram on Depression in Patients with Chronic renal Failure Undergoing Hemodialysis Referring to University Hospitals in Yazd

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Abstract

Background: This study compared the efficacy of citalopram and escitalopram in treating depression among patients with chronic renal failure undergoing hemodialysis.

Methods: This double-blind clinical trial was conducted on 46 patients diagnosed with Major Depressive Disorder (MDD) and chronic renal failure undergoing hemodialysis. The depression rating scale used was the Hamilton Depression Questionnaire. Patients were randomly assigned to two groups: the citalopram group (n=24) and the escitalopram group (n=22), and they underwent a 6-week treatment. Drug side effects were assessed and recorded at the conclusion of the study period. Demographic variables such as age, gender, duration of depression, duration of dialysis, marital status, and educational level were also collected. The data were then analyzed using statistical tests.

Results: There was no significant difference between the two groups in terms of gender distribution (p=0.404), marital status (p=0.155) and educational level (p=0.329). Also, no significant difference was found between the mean variables: age (p=0.478), duration of depression (p=0.485) and duration of dialysis (p=1.000). There was no significant difference between the mean depression score before treatment in the two groups (p = 0.107) and after treatment in the two groups (p = 0.412). But the mean depression score after treatment compared to before treatment was significantly lower in both groups (p=0.000). Also, no significant difference was found between the frequency of drug side effects in the two groups (p=0.292).

Conclusion: According to results, it can be concluded that both drugs have been shown to improve depression in in patients with chronic renal failure undergoing hemodialysis and are not different in their efficacy and side effects.

Keywords: Chronic Kidney failure, Citalopram Depression, Hemodialysis

1. Background

Chronic Renal Failure disease, defined as (eGFR) <15 mL/min/1.73 m² is the progressive and irreversible failure of renal function, which, like other chronic diseases involves all aspects of an individual's life (1,2). Dialysis and,

ultimately, kidney transplantation are the main treatments for this disease. Several factors, including physical and mental stress, undesired side-effects of medical treatments, functional limitations, and dietary restrictions, as well as unsuitable economic conditions, contribute to depression in dialysis patients (3).

Depression, considered the fourth leading cause of disability worldwide, is a clinical syndrome defined by a period of 2 weeks during which the patient experiences a depressed mood or anhedonia emotion, along with at least 5 out of 9 mental disorder symptoms in the DSM-5 (4,5). Depression is highly prevalent among chronic kidney disease (CKD) and End Stage Renal Disease (ESRD) patients (6).

Generally, based on the latest systematic studies, 20% of chronic kidney disorder patients suffer from major depressive disorder, and the prevalence of depression among hemodialysis patients in the country has been reported to be between 50% and 70% (7,8). Diagnosing and investigating depression among dialysis patients is crucial because individuals may suffer from eating disorders, weakened immune systems, non-compliance with medical diets, disease exacerbation, significant dysfunction, and a reduction in quality of life, ultimately leading to suicide if the disease is not diagnosed and depression is not treated (9-11).

Research has shown that the death and hospitalization rates are doubled among patients suffering from End Stage Renal Disease (ESRD) and undergoing chronic hemodialysis with depression compared to individuals without depression (4). Despite the prevalence of depression symptoms and depressive disorders among patients with chronic kidney disease (CKD) and ESRD, and its association with poor disease prognosis, only one percent of dialysis patients receives a diagnosis and proper treatment for depression (12). Therefore, providing strategies for better understanding and managing depression in CKD patients is a significant challenge for physicians. However, there is limited information about the immunity and effectiveness of antidepressant drugs in advanced CKD and ESRD patients (13). Guidelines suggest Selective Serotonin Reuptake Inhibitor (SSRI) drugs as the preferred antidepressant for treating depression among dialysis patients (14).

Citalopram and Escitalopram are both useful

SSRIs (Selective Serotonin Reuptake Inhibitor) for treating depression (15-19). Escitalopram is the active component of Citalopram. The optimal dose for moderate depression treatment is 20 mg of Citalopram daily and 10 mg of Escitalopram daily (20-23). Many studies support the efficiency of Escitalopram in severe depression treatment compared to Citalopram, and some studies suggest that these two drugs have similar tolerance and influence (24-26). Among the advantages of Escitalopram over other SSRIs are higher effectiveness, a faster onset of effects, higher tolerance, and fewer drug interactions (27). Unfortunately, despite the prevalence of depression and the importance of finding proper treatment for dialysis patients, only a few studies have been conducted regarding the impact of antidepressant drugs on depression symptoms and their safety. Based on current information, it is still unclear whether antidepressant drugs are effective and safe for dialysis patients, and there is insufficient data to clarify whether these drugs have been effective in treating major depressive disorder or influencing the prognosis of CKD and ESRD patients (28). Thus, the present study is a randomized double-blind clinical trial designed with a medical approach to determine the effectiveness of Citalopram and Escitalopram in treating depression in Chronic Renal Failure patients undergoing hemodialysis.

2. Methods

This is a randomized double-blind clinical trial prospective study. In this study, patients suffering from major depressive disorder and chronic renal failure undergoing hemodialysis treatment, referred to Shahid Sadoughi University hospitals, have been studied. The inclusion criteria for the study are: age range between 18 and 65, patients suffering from major depressive disorder with a score of at least 17 on the Hamilton Depression Rating Scale (HAM-D) confirmed by a psychiatrist, renal failure patients who have been dialyzed

for at least 3 months. The exclusion criteria include: systemic medical diseases (heart disease, diabetes, epilepsy, blood pressure, thyroid) interfering with drug consumption or following the plan, liver failure, hepatitis B and C, and HIV, psychiatric disorders other than depression, patients under treatment with SSRIs (at least 3 months after the treatment period), pregnancy or breastfeeding, addiction to different types of drugs or psychedelics, and the occurrence of any intolerable side effects in patients.

In addition, patients were excluded due to non-completion of the 6-week treatment

period, adverse events or intolerable side effects, worsening of their clinical condition, and non-compliance with the treatment protocol.

The sample size, considering a confidence level of 95%, power of 80%, a standard deviation of 7.75, a 7-score difference in the average of the Hamilton test in both study groups after 6 weeks of intervention, and accounting for a 20% sample dropout, is at least 25 samples evaluated in each group. Equation (Eq) (1) shows the formula of sample size determination.

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times 2S^2}{d^2}$$

Eq. (1)

The Hamilton Depression Rating Scale (HAM-D), constructed by Hamilton (1960), consists of 17 items. Nine items are in a 5-option scale (gradation from 0 to 4) used to measure depression severity, while the remaining 8 items are scored from 0 to 2 in a 3-option scale. Scores between 0 and 7 indicate no depression, scores between 8 and 16 indicate mild depression, scores between 17 and 23 indicate moderate depression, and scores ≥ 24 indicate severe depression. In addition, the reliability and validity of this scale have been investigated in many studies (24).

Subsequently, a psychiatry assistant evaluated clinical depression based on the depression criteria in DSM-5. After the primary evaluations and meeting the inclusion criteria for the study, the patients were assigned to two treatment groups, one receiving Citalopram and the other Escitalopram, according to a table of random numbers, for 6 weeks. The Citalopram dose was titrated over 7 days, increasing from

10mg to 20mg per day, and the Escitalopram dose was also increased from 5mg to 10mg per day. The drugs were selected from a single pharmaceutical company, and to double-blind the study, the pharmacist provided citalopram and escitalopram pills in a medicinal form of similar capsules, distributing these pills among the patients based on treatment groups with confidential codes.

Patients were followed up after 6 weeks of treatment, and at the end of the treatment period, the Hamilton test was reinvestigated. Side effects, including xerostomia (dry mouth), nausea, yawning, perspiration, agitation, decreased appetite, constipation, diarrhea, drowsiness, headache, and sexual problems, were measured based on a researcher-made questionnaire. Demographic variables such as age, gender, marital status, academic degree, duration of depression, and duration of dialysis were recorded. (figure 1).

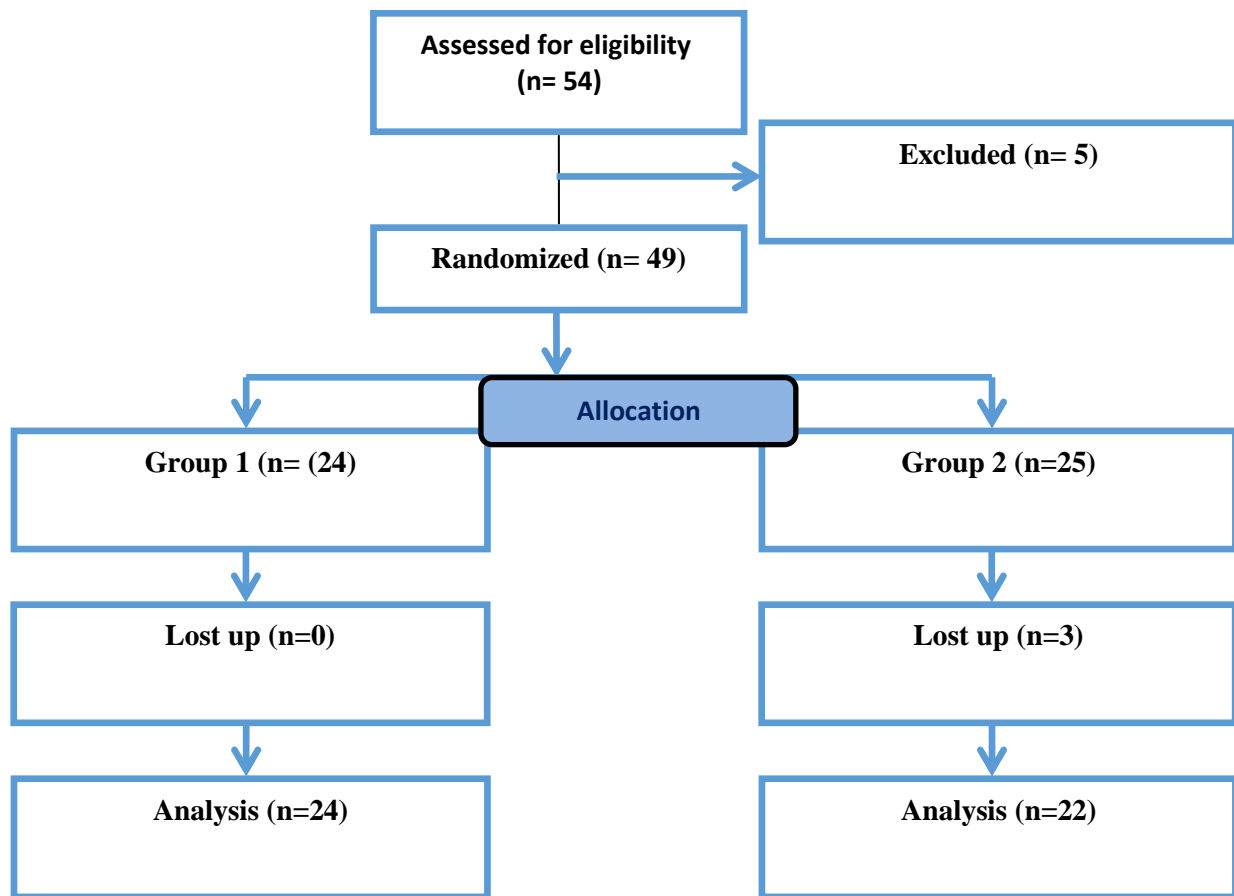


Figure 1: Consort flow chart

Statistical analysis

The collected data entered SPSS22 statistical software. Independent T-test, Mann-Whitney test, and Chi Square test were employed to compare scores between the two groups. The comparison of variables before and after intervention was done by paired sample T test. $P < 0.05$ was assumed significant.

3.Results

A total of 54 individuals entered the study of whom 5 were excluded based on the physician's opinion, and an additional 3 were excluded due to nausea as a side effect from the Escitalopram group. Ultimately, the study was conducted on 46 patients, divided into two groups: citalopram ($n=24$) and escitalopram ($n=22$). Among the 46 patients

in this study, 30 (65.2%) were male, and 16 (34.8%) were female. There was no statistically significant difference in the average age using t test ($p=0.478$), duration of depression in months ($p=0.485$), and duration of dialysis in years ($p=1.000$) between the two groups (analyzed using Mann-Whitney test).

Similarly, there was no statistically significant difference in the frequency distribution of variables, including gender ($p=0.404$), marital status ($p=0.155$), and academic degree ($p=0.329$) between the two groups, as assessed by the Chi-Square test.

Table 1 presents the study results regarding the mean depression scores before and after treatment in the two groups under investigation. Analysis using the paired t-test indicated no statistically significant difference in the average depression scores

before and after treatment between the two groups. However, analysis using the paired t-test revealed a statistically significant difference in the average depression scores before and after treatment within both

groups. In other words, the average depression scores significantly decreased in both treatment groups after treatment compared to before treatment, indicating an improvement in depression.

Table 1. Mean depression score before and after treatment in two groups

time	Group		P-value*
	citalopram	escitalopram	
before treatment	17.96±3.97	20.00±4.45	0/107
after treatment	10.17±2.98	11.00±3.81	0.412
P-value**	0/000	0/000

* t test

**Paired sample t test

Table 2- Frequency distribution of drug side effects in two groups

Side effects	Group		Total *
	citalopram	escitalopram	
No side effects	16(66.7%)	15(68.2%)	31(67.4%)
Nausea	2(8.3%)	4(18.2%)	6(13%)
yawning	2(8.3%)	0(0%)	2(4.3%)
Sweating	1(4.2%)	0(0%)	1(2.2%)
Drowsiness	2(8.3%)	0(0%)	2(4.3%)
yawning + Sweating	1(4.2%)	0(0%)	1(2.2%)
Xerostomia+ Sweating	0(0%)	1(4.5%)	1(2.2%)
Agitation + Drowsiness	0(0%)	1(4.5%)	1(2.2%)
Anorexia+Nausea+ Agitation	0(0%)	1(4.5%)	1(2.2%)
total	24(100%)	22(100%)	46(100%)
P-value	0/292		

*Chi Square test

Table 2 displays the study results regarding the frequency distribution of drug side effects in both study groups. Analysis using the chi-square statistical test showed no statistically significant difference in the

frequency distribution of drug side effects between the two groups.

Figure2 illustrates the study's results regarding the frequency distribution of side effects among all the investigated patients.

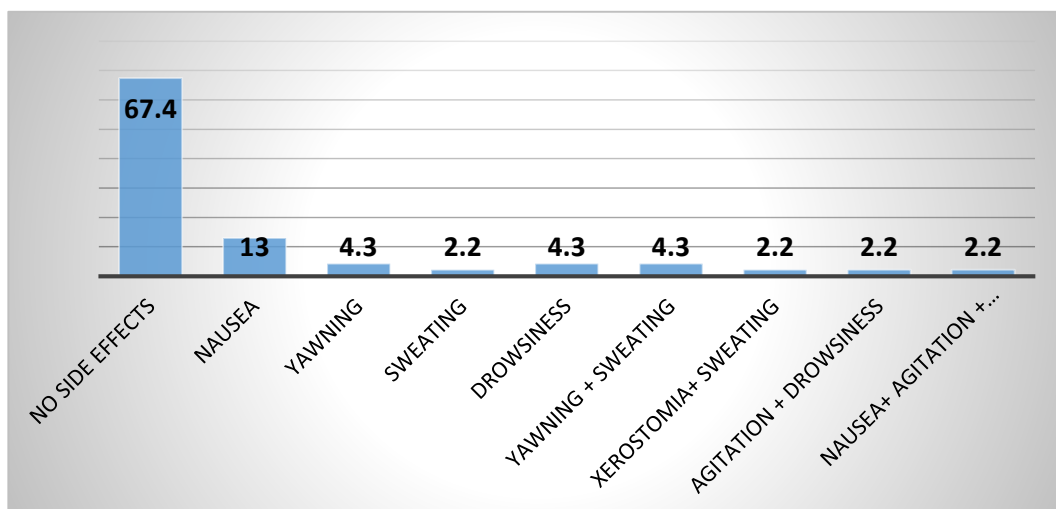


Figure 2: Frequency distribution of drug side effects in total patients (%)

4. Discussion

The results of the present study indicate that both Citalopram and Escitalopram drugs have been effective in improving depression among chronic renal failure patients undergoing hemodialysis, with no significant difference in their impact and side effects. The Hamilton questionnaire was employed in this study to assess depression among patients. Numerous studies have investigated the effects of various drugs on depression treatment in patients undergoing hemodialysis. Yazici utilized the Zung questionnaire in his study to evaluate the effectiveness and tolerance of Escitalopram among depressed patients with End-Stage Renal Disease (ESRD). The findings revealed a significant decrease in depression scores in the Escitalopram group compared to the placebo, demonstrating the effectiveness and tolerance of Escitalopram in these patients (25), consistent with our study results where Escitalopram significantly reduced depression scores after treatment compared to before treatment.

In another systematic review study, the effects of four antidepressant drugs—Fluoxetine, Sertraline, Citalopram, or Escitalopram were investigated compared to a placebo among patients with chronic renal failure undergoing hemodialysis. The results indicated that although treatment with antidepressant drugs may lead to a decline in depression scores in the long term compared to a placebo, antidepressant drugs, in general, do not have a significant impact on improving the life quality of chronic renal failure patients undergoing hemodialysis. This study demonstrated that the frequency of side effects such as hypotension, headache, sexual disorders, and nausea in patients consuming antidepressant drugs was not higher than the placebo group (14), which contrasts with the current study results where there was no statistically significant difference in the frequency of drug side

effects between the two groups. In another systematic review conducted by Nagler, the effects of antidepressant drugs on depression among CKD stage 5-3 patients were studied, revealing that the dose of some antidepressant drugs such as Selegiline, Amitriptyline, Venlafaxine, Desvenlafaxine, Milnacipran in stages 3-5 of chronic renal failure needs to be adjusted. Additionally, there was insufficient evidence about the effectiveness of antidepressant drugs against placebo among depressed patients with chronic renal disease (26). These two systematic reviews have suggested the necessity to conduct larger clinical trials to compare antidepressants.

Azorin and his colleagues compared the effect of Escitalopram and Citalopram on the treatment of severe depression disorder in three clinical studies involving 506 patients. The results revealed that Escitalopram was more effective than Citalopram in depression treatment with a faster onset (23). Also, Li demonstrated that a 6-week treatment period with a 20-40mg Citalopram dose has a similar effect and tolerance to a 20-10mg Escitalopram dose (27).

Montgomery et al. demonstrated the superior efficacy of escitalopram over citalopram in a meta-analysis, which showed that escitalopram had statistically significant better efficacy compared to citalopram (28). A key difference between our study and that of Montgomery et al. is that their meta-analysis included a general population of individuals with depression, whereas our study had a different patient population and design.

Gorman et al. also assessed the efficacy of escitalopram and citalopram in treating Major Depressive Disorder and found that escitalopram may have a faster onset and greater overall magnitude of effect in improving symptoms of both depression and anxiety in these patients (29).

The lack of significant differences between

escitalopram and citalopram in our study, when compared to Gorman et al.'s findings, could be due to differences in patient populations, a smaller sample size, limited statistical power, or potential medication interactions specific to dialysis patients.

Sánchez et al. also compared escitalopram and citalopram and found that escitalopram demonstrated greater efficacy and a faster onset of action than comparable doses of citalopram. The lower efficacy of citalopram observed in these studies may be attributed to the inhibitory effect of the R-enantiomer on the S-enantiomer, potentially through an allosteric interaction with the serotonin transporter (30).

Generally, based on the results of the present study and the mentioned ones, it can be concluded that the effect of all antidepressant drugs on depression among dialysis patients was not identical. Some, like Citalopram and Escitalopram, have improved depression among dialysis patients, while others like Selegiline, Amitriptyline, Venlafaxine, Desvenlafaxine, Milnacipran, and Fluoxetine haven't improved depression significantly.

Limitation of study: Short duration of follow-Up, and patient self-reporting bias were limitations of the study.

5. Conclusion

After treatment, the average depression score significantly decreased in both groups, indicating an improvement in patients' depression. Furthermore, there was no statistically significant difference in the average depression scores after treatment between the two groups, as well as in the frequency distribution of drug side-effects. Consequently, it can be concluded that both Citalopram and Escitalopram drugs effectively improved depression in chronic renal failure patients undergoing hemodialysis. Additionally, there is no significant difference in the effects and side-effects between these

two drugs. It seems that more studies are needed to generalize the results to all patients with hemodialysis.

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Author contributions: M.A, and A.J carried out the experiment. F.H wrote the manuscript with support from P.R, and R.H. P.R supervised the project. F.H conceived the original idea.

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