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Cognitive impairment in different hemodialysis techniques

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Abstract

Background: Cognitive impairment is one of the most common, often untreated, comorbidities affecting patients with chronic kidney disease treated with hemodialysis. Increased mortality, poor compliance, depression, and poor quality of life were all linked to cognitive impairment in the hemodialysis population. The intradialytic exercise proved to be beneficial in improving patients' quality of life, among other positive effects. Cooling dialysate has various positive effects, including improved patients' mood and decreased hypotensive episodes during hemodialysis. The study aims to assess the effect of intradialytic exercise and cool hemodialysis on cognitive function in patients on hemodialysis.

Results: The study showed no significant effect of both interventions on the patient's cognitive functions. However, cooling dialysate showed an improvement in the severity of depressive symptoms by Beck's Depression Inventory II ($p = 0.02$). On the other hand, Mini-International Neuropsychiatric Interview showed an increase of patients diagnosed with depression in the intradialytic exercise group.

Conclusions: Both interventions had no significant effect on the mean scores of the Montreal Cognitive Assessment, which are lower in our sample than in the general population (23.9–25). Potential implications include the importance of managing psychiatric comorbidities in patients on hemodialysis. Cooling dialysate can be adopted to alleviate depressive symptoms in patients on hemodialysis.

Keywords: Cognitive impairment, Hemodialysis, Cooling dialysate, Intradialytic exercise

Background

Chronic kidney disease (CKD) is a global health issue with a worldwide prevalence of 13.4% [26]. CKD is defined as the damage or the decrease in glomerular filtration rate (GFR) to less than 60 mL/min/1.73 m² for at least 3 months [44]. CKD increases the incidence of cardiovascular disease, end-stage renal disease (ESRD). ESRD is defined by a glomerular filtration rate (GFR) of less than 15 mL/min/1.73 m² [1].

Cognitive impairment (CI) is one of the most common, often untreated, comorbidities affecting patients with

chronic kidney disease treated with hemodialysis [31]. CI occurs when at least two areas of cognitive function are affected and decline when tested by a standard cognitive function test such as Montreal Cognitive Assessment (MOCA) or the Mini-Mental State Exam (MMSE) [4].

CI or overt dementia can occur in 20 to 50% of persons with moderate stages of CKD [3]. It should be noted that vascular dementia precedes CI in CKD patients [38]. Although CI can be presented early in CKD, the relationship between the severity of CKD and dementia or CI is still ambiguous. Indeed, the duration of kidney disease rather than the severity correlates with cognitive dysfunction [53]. The prevalence of depression is reported to be as high as 76.3% which adds more risk of CI in HD patients [11].

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Intradialytic exercise (IDE) is a training achieved during the HD session to intensify the patient's strength which targets many physiological and psychosocial limits [8]. Exercise programs improved depressive symptoms in patients on hemodialysis [40], and it positively affected cognitive function [27].

It was discovered that changes in intradialytic hemodynamics might cause bouts of ischemic brain damage. The cooled dialysate can be used to mitigate this effect [14]. Cooling dialysate is a procedure in which the dialysate temperature is dropped by 0.5° below core body temperature, which helps decrease intradialytic hypotension which was linked to the degree of CI in patients on hemodialysis [52].

This study was carried out to assess the effect of intradialytic exercise and individualized cool dialysate on cognitive functions in an Egyptian cohort of hemodialysis patients.

Methods

Patients

In this quasi-experimental study, with an assumed prevalence of 70% of cognitive in hemodialysis patients [36], DSSresearch.com was utilized in the calculation of sample size for studying sociodemographic and clinical variables associated with cognitive impairment in patients on hemodialysis. With an α error of 5% (95% confidence) and 20% β error (80% potent the study), we included a sample of 60 patients on hemodialysis in Mansoura Nephrology and Dialysis Unit, Internal Medicine Department, Mansoura University, Mansoura, Egypt, from December 2021 to March 2022. The patients were randomly divided into two equal groups with age and sex matched, and each included 30 patients; group A received individualized cool dialysate with a dialysate temperature of 0.5°C below core body temperature, while group B was subjected to intradialytic exercise. Adult patients aged between 18 and 60, on HD for more than 3 months, and receiving three HD sessions per week met the inclusion criteria. Patients with intellectual disability, visual or hearing impairment, pre-existing dementia, and a history of psychotic illness or a substance use disorder and those who were illiterate were not eligible for the trial. Informed written consent was obtained from all participants before their study enrollment. The Mansoura Faculty approved the study by Medicine Institutional Research Board (Code Number: MS.20.04.1106).

Individualized cool dialysate

A reduction of dialysate temperature by 0.5° below the patient's core temperature [5].

Intradialytic exercise

A gradual exercise program using a pedal cycle with an adjustable resistance level was performed. The exercise duration was calculated according to the patient's heart rate with a target heart rate of 110 BPM, considering the difference in physical fitness levels between patients and the patient's well-being. A duration of 10 to 20 min was reached, and the pedal's resistance was increased gradually. The frequency of the intervention was three times per week during the first half of the hemodialysis session for 12 consecutive weeks [46].

Both interventions were carried out every HD session, three times a week, for twelve consecutive weeks.

Clinical, cognitive function, and psychiatric assessment

A clinical assessment was done, and sociodemographic data (age, sex, education, occupation) and etiology of hemodialysis were obtained. Cognitive function and psychiatric assessment was performed for all patients before the start and after the end of the 12-week-long intervention program.

- *The Montreal Cognitive Assessment (MoCA)* [32] is a screening test that covers major cognitive domains, including attention, orientation, episodic memory, language, visuospatial ability, and executive functions [50, 51]. It is a one-page 30-point screening test administered in 10 min to identify MCI in the elderly, with a total possible score of 30 points; 26 or above points are considered normal; scores below 26 without functional impairment indicate MCI. Scores below 26 with functional impairment indicate early dementia. It includes tasks such as a trail-making test part B, clock drawing, cube copying, naming, digit span backward and forwards, selective attention, serial subtraction, sentence repetition, verbal abstraction, phonemic word fluency, a 5-word learning and delay recall task, and spatial and temporal orientation. It is a suitable cognitive screening tool for hemodialysis patients, with good sensitivity and specificity levels and covering executive functions, which appear to play an essential role in the cognitive performance of hemodialysis patients [50, 51]. The validated Arabic version of the MoCA [39].
- *The Mini-International Neuropsychiatric Interview (MINI)*: Developed by clinicians and psychiatrists in the USA and Europe for diagnosing DSM-IV and ICD-10 psychiatric disorders. It is a short structured diagnostic interview that takes about 15 min to meet the need for an accurate structured psychiatric interview for multicenter clinical trials and epidemiology studies. It gives rapid results and is the first step in outcome tracking in non-research clinical settings.

It is the validated Arabic version of the MINI [16].

- *Arabic version of the Beck Depression Inventory-second edition* (BDI-II): BDI-II is a self-report scale composed of 21 items to measure the severity of depression in light of the Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV; American Psychiatric Association, 1994) symptoms for diagnosis of depression. It can be applied to adolescents 13 years old and older [2]. It is the Arabic adaptation of BDI-II [17].

Blood sampling and laboratory tests

Before starting the first HD session of the week, blood samples were taken from the arteriovenous fistula. Routine laboratory tests for HD were done including, serum ferritin, transferrin saturation, blood hemoglobin, serum calcium, serum phosphorus, parathyroid hormone, and serum albumin [25].

Statistical analysis and data interpretation

Data were fed to the computer and analyzed using IBM SPSS Corp., released in 2013. IBM SPSS Statistics for Windows, version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using numbers and percentages. Quantitative data were described using median (minimum and maximum) and mean standard deviation for parametric data after testing normality using the Kolmogorov-Smirnov test. The significance of the obtained results was judged at the (0.05) level. Chi-square and Monte Carlo tests for comparison of 2 or more groups of qualitative data as appropriate. Student *t*-test and Mann-Whitney *U* test were used to compare two independent groups of typically and non-normally distributed data, respectively. Paired *t*-test and Wilcoxon signed rank test were used to compare pre- and post-treatment. Spearman's rank-order correlation is used to determine the strength and direction of a linear relationship between two non-normally distributed continuous variables and ordinal variables. Linear regression analysis was used to predict independent variables after log transformation of the non-normally distributed outcome. Significant predictors in the correlation were entered into a regression model with the calculation of R^2 , the quantity effect of combined variables on the desired outcome, and the prediction equation ($Y = \beta + a * x$).

Results

There was no statistically significant difference between the two groups regarding sociodemographic (age, sex, education, and occupation) or laboratory findings (Table 1). After the intervention group, B showed

a statistically significant increase in HB ($p=0.006$) and albumin levels ($p=0.049$).

The comparison of cognitive and psychiatric domains between the two groups is summarized in Table 2. There was no significant difference between the two groups before intervention regarding cognitive functions, the prevalence of psychiatric disorders, or depression severity. The mean pre-intervention score of MoCA was 23.90 ± 2.39 in group A and 24.40 ± 2.53 in group B which is below the cutoff of mild cognitive impairment. Post-intervention MoCA scores were 24.07 ± 2.38 in group A and 24.97 ± 1.94 in group B showing no statistically significant improvement compared to pre-intervention scores. Regarding psychiatric diagnosis and depression severity after both interventions, group A had a significantly lower median score of depression severity by BDI-II ($p=0.02$), while group B showed an increase in the number of patients with a psychiatric diagnosis (depression and anxiety disorders) by MINI ($p=0.038$) (Table 2).

Table 3 shows the correlation between scores of cognitive and psychiatric assessments with some sociodemographic and laboratory parameters. In group A, there was a positive correlation between MoCA scores and transferrin saturation ($r=0.405$; $p=0.048$). A strong negative correlation was found between BDI-II scores and calcium level in group A ($r=-0.597$; $p=0.003$), while group B showed a negative correlation with Hb level ($r=-0.425$; $p=0.019$), PO4 level ($r=-0.426$; $p=0.024$), and MoCA scores.

There was no statistically significant correlation between scores of BDI-II and MoCA in our study population (Table 4).

In Table 5, none of the studied factors shows significant predictors of MOCA change.

Table 6 illustrates that studied groups and change in Ca level are significant predictors of BDI-II change with prediction equation of BDI-II change = $11.23 - 6.49 * \text{Groups} - 4.18 * \text{Ca change}$ and 36.6% of the change in BDI-II change can be explained by a change in both variables ($R^2=0.366$).

Figure 1 shows no significant change in cognitive functions before and after the intervention.

Discussion

In a 60-patient cohort on hemodialysis for at least 3 months, a decline in cognitive functions was found in most patients, with a 70% prevalence before intervention. In our study, the mean age of participants was 44.57 ± 12.64 years in the cooling dialysate group and 41.0 ± 11.03 years in the intradialytic exercise group (IDE). There was no significant difference in age between the two groups. This mean age is younger than most studies about cognitive function in hemodialysis

Table 1 Sociodemographic and laboratory data of the study groups

| | | Cooling Group A N=30 | Exercise Group B N=30 | Test of significance ^{##} |
|---------------------------------|-----------------------|-------------------------|--------------------------|------------------------------------|
| Age/years, mean±SD | | 44.57±12.64 | 41.0±11.03 | $p=0.249$ |
| Sex, n (%) | | | | |
| Male | | 21 (70) | 18 (50) | $p=0.114$ |
| Female | | 9 (30) | 15 (50) | |
| Education, n (%) | | | | |
| No formal education and primary | | 10 (33.3) | 6 (20) | $p=0.169$ |
| Secondary education | | 12 (40) | 9 (30) | |
| University education or higher | | 8 (26.7) | 15 (50) | |
| Occupation, n (%) | | | | |
| Non-worker | | 6 (20) | 7 (23.3) | $p=0.374$ |
| Housewife | | 3 (10) | 5 (16.7) | |
| Employee | | 11 (36.7) | 11 (36.7) | |
| Manual worker | | 10 (33.3) | 5 (16.7) | |
| Student | | 0 | 2 (6.7) | |
| HB | Pre | 10.52±1.01 | 10.27±1.56 | $p=0.472$ |
| | Post | 11.0±0.963 | 11.05±1.79 | $p=0.903$ |
| | Paired <i>t</i> -test | $p=0.052$ | $p=0.006^*$ | |
| FERRITIN | Pre | 476.05 (13–2053) | 375 (123–2154) | $p=0.764$ |
| | Post | 448 (107–1500) | 328 (7–1864) | $p=0.502$ |
| | Wilcoxon test | $p=0.290$ | $p=0.350$ | |
| T.SAT | Pre | 22.73±6.58 | 24.09±8.85 | $p=0.545$ |
| | Post | 23.25±8.04 | 24.75±16.24 | $p=0.663$ |
| | Paired <i>t</i> -test | $p=0.752$ | $p=0.299$ | |
| Ca | Pre | 8.45±0.72 | 8.21±0.73 | $p=0.201$ |
| | Post | 8.42±0.67 | 8.48±1.02 | $p=0.807$ |
| | Paired <i>t</i> -test | $p=0.776$ | $p=0.160$ | |
| PO4 | Pre | 5.27±2.42 | 5.28±1.72 | $p=0.998$ |
| | Post | 5.74±1.59 | 5.48±1.96 | $p=0.575$ |
| | Paired <i>t</i> -test | $p=0.254$ | $p=0.545$ | |
| PTH | Pre | 345 (9–1552) | 404.5 (72–2845) | $p=0.196$ |
| | Post | 285 (6.8–4683) | 425.5 (83–2018) | $p=0.523$ |
| | Wilcoxon test | $p=0.056$ | $p=0.425$ | |
| Albumin | Pre | 4.09±0.36 | 3.93±0.324 | $p=0.324$ |
| | Post | 4.189±0.405 | 4.089±0.35 | $p=0.324$ |
| | Paired <i>t</i> -test | $p=0.093$ | $p=0.049^*$ | |

^{##} Used test: Student *t*-test and Mann-Whiney *U* test; *statistically significant

to reduce the effect of comorbidities and other risk factors of cognitive impairment and dementia. The cooling group included 21 males and 9 females, while the exercise group included 15 males and 15 females. Regarding the level of education and occupation, there was no significant difference between the two groups. The cooling group included 33.3% primary educated subjects, 40% secondary educated, and 26% university educated. On the other hand, the exercise group included 20% primary educated subjects, 30% secondary educated,

and 50% university educated. Regarding the etiology of ESRD, the cooling dialysate group included 3 patients with DM (10%), 14 hypertensive patients (46.7%), 3 patients with polycystic kidney (10%), 4 chronic glomerulonephritis patients (13.3%), 5 obstructive uropathy patients (16.7%), and one case of amyloidosis. The IDE group included 5 patients with DM (16.7%), 9 hypertensive patients (30%), 2 patients with polycystic kidney (6.7%), 8 chronic glomerulonephritis patients (26.7%), 5 obstructive uropathy patients (16.7%), and

Table 2 Cognitive function and psychiatric assessment

| | | | Cooling Group A N=30 | Exercise Group B N=30 | Test of significance*** |
|--------------------------|-----------------------|------|-------------------------|--------------------------|-------------------------|
| MOCA, mean±SD | Pre | | 23.90±2.39 | 24.40±2.53 | $p=0.43$ |
| | Post | | 24.07±2.38 | 24.97±1.94 | $p=0.113$ |
| | Paired <i>t</i> -test | | $p=0.582$ | $p=0.061$ | |
| MINI, <i>n</i> (%) | No disorder | Pre | 15 (50) | 21 (70) | $p=0.247$ |
| | Depression | | 12 (40) | 8 (26.7) | |
| | Anxiety disorders | | 3 (10) | 1 (3.3) | |
| | No disorder | Post | 14 (46.7) | 16 (53.3) | $p=0.417$ |
| | Depression | | 15 (50) | 11 (36.7) | |
| | Anxiety disorders | | 1 (3.3) | 3 (10) | |
| BDI-II, median (min-max) | Wilcoxon test | | $p=0.705$ | $p=0.038^*$ | |
| | Pre | | 15 (4–35) | 13 (1–29) | $p=0.07$ |
| | Post | | 13 (3–33) | 14 (3–34) | $p=0.953$ |
| | Wilcoxon test | | $p=0.02^*$ | $p=0.481$ | |

***Used test: Student *t*-test, Mann-Whitney, and Monte Carlo test

one case with a history of malignancy followed by nephrectomy.

In our study population, both IDE and individualized cool dialysate had no statistically significant effect on cognitive functions after a 3-month trial. Transferrin saturation was positively correlated to cognitive function, while serum phosphate and hemoglobin were associated with cognitive deterioration.

Cognitive impairment is a known complication of ESRD, with evidence supporting that it emerges early in the course of kidney disease. Dialysis patients show impairment across multiple cognitive domains, with prevalence ranging between 6.6 and 51% [18, 42]. The consequences of such impairment included poor quality of life, poor medication adherence, and increased mortality [10, 13].

Studies have attributed cognitive impairment to the existence of CKD, particularly among those on dialysis. Potential causes include metabolic abnormalities related to kidney failure and vascular diseases that have become increasingly evident in patients on hemodialysis ([3, 12]; Murray, 2008). The mean score of MoCA before intervention was 23.90 in the cooling group and 24.40 in the exercise group, with a high prevalence of cognitive impairment in the study population of 70%. These results are in harmony with Aachen University Hospital's study, which showed a mean score of 24.0 [50, 51]. A lower mean value for MoCA was found in a study that was carried on at Oxford University Hospital trust with a mean MoCA score of 23 [20]. It was revealed that patients on dialysis had significantly poorer executive function yet better memory performance than control. The study also

linked vascular issues and diseases to lower executive function [43].

Regarding the effect of cooled dialysate on cognitive functions, we found no significant difference between the mean MoCA scores before (23.90±2.39) and after intervention (24.07 ± 2.38). A randomized controlled clinical trial by Dasgupta et al. hypothesized that cooled hemodialysis would reduce the decline in cognition and improve the patient's quality of life [7]. The same was suggested by Pépin et al. [37]. An Iranian study about the effect of cold dialysis on fatigue found an improvement in the behavioral, emotional, sensational, and cognitive dimensions related to fatigue [48].

Cognitive impairment was proportional to cardiovascular instability during hemodialysis sessions [29]. In addition, radiological studies by Mizumasa et al. showed that the number of frontal lobe white matter lesions in HD patients was related to the number of hypotension episodes during HD sessions and that the increase of these lesions was an indicator of frontal lobe atrophy, which presents at a younger age in HD patients than the general population [30]. A randomized trial showed that the degree of frontal lobe atrophy was less prominent after 1 year of cool hemodialysis than in a control group that continued on 37°C hemodialyses, and a correlation was found between the degree of reduction in neurocognitive testing scores and the degree of brain injury [14]. More than half of CKD patients had silent white matter hyperintensities, which are believed to be vascular in origin in magnetic resonance imaging (MRI) studies [23, 47]. Also, due to defects in the cognitive areas of decision-making and

Table 3 Correlation between all scores of cognitive function assessment, sociodemographic, laboratory data, and BDI-II scores

| | Cooling group | | Exercise group | |
|---------------------|---------------|-------|----------------|--------|
| | ΔBDI-II | ΔMOCA | ΔBDI-II | ΔMOCA |
| ΔHb (gm/dl) | | | | |
| R | -.144 | -.201 | .026 | -.425* |
| P | .466 | .304 | .891 | .019 |
| ΔFerritin | | | | |
| R | -.101 | .129 | -.356 | .257 |
| P | .638 | .547 | .123 | .273 |
| ΔT-sat | | | | |
| R | -.071 | .408* | -.400 | -.114 |
| P | .740 | .048 | .081 | .632 |
| ΔCa | | | | |
| R | -.597** | .133 | -.274 | .153 |
| P | .000 | .485 | .159 | .436 |
| ΔPo4 | | | | |
| R | .116 | -.116 | .316 | -.426* |
| P | .547 | .547 | .102 | .024 |
| ΔPTH | | | | |
| R | .163 | -.081 | .253 | .040 |
| P | .399 | .676 | .194 | .839 |
| ΔAlbumin | | | | |
| R | -.289 | .013 | -.202 | -.169 |
| P | .129 | .948 | .302 | .390 |
| Age/years | | | | |
| R | .161 | -.226 | -.265 | .086 |
| P | .396 | .230 | .157 | .652 |
| Education | | | | |
| R | .076 | -.006 | .046 | -.044 |
| P | .690 | .977 | .809 | .817 |
| HD duration (years) | | | | |
| R | .305 | -.283 | -.260 | .023 |
| P | .107 | .137 | .165 | .902 |

r Spearman correlation coefficient

Table 4 Correlation between BDI-II and MoCA scores in both groups

| Correlation between MOCA and BDI-II | Total | Cooling group N=30 | Exercise group N=30 |
|-------------------------------------|---------------------|---------------------|---------------------|
| Pre | r=-0.006 p=0.965 | r=-0.088 p=0.642 | r=0.04 p=0.834 |
| Post | r=0.04 p=0.762 | r=0.131 p=0.489 | r=0.177 p=0.351 |

Table 5 Linear regression for prediction of MOCA change

| | β | T | p-value |
|----------------------------|-------|--------|---------|
| Constant | .526 | .477 | .637 |
| Groups | -.816 | -1.161 | .254 |
| Change in Beck score | -.045 | -.881 | .385 |
| HB change | -.244 | -.941 | .353 |
| Ferritin change | .000 | .310 | .758 |
| T-sat change | .024 | .841 | .406 |
| Ca change | .060 | .135 | .893 |
| PO4 change | .164 | .726 | .473 |
| PTH change | .001 | .681 | .500 |
| Albumin change | -.328 | -.293 | .771 |
| R²=0.118 | | | |

Cooling group coded (1), exercise group (2), education level coded (0 = illiterate and primary education, 1 = secondary education, 2 = university education or higher)

Table 6 Linear regression for prediction of BDI-II change

| | β | T | p-value |
|--|--------|--------|---------|
| Constant | 11.228 | 3.636 | .001 |
| Groups | -6.498 | -3.198 | .003 |
| Change in Beck score | -.804 | -.954 | .346 |
| HB change | -.005 | -1.177 | .247 |
| Ferritin change | -.051 | -.554 | .583 |
| Tsat change | -4.179 | -3.265 | .002 |
| Ca change | -.188 | -.253 | .802 |
| PO4 change | .001 | .374 | .710 |
| PTH. change | 4.750 | 1.324 | .194 |
| R²=0.366 | | | |
| BDI-II change = 11.23-6.49*Groups - 4.18*Ca change | | | |

Cooling group coded (1), exercise group (2), education level coded (0 = illiterate and primary education, 1 = secondary education, 2 = university education or higher)

processing speed, CI of subcortical vascular origin is suspected. Brain microbleeds or atrophy due to small vessel disease could also be involved as vascular-related risk factors, like lacunar infarcts and white matter hyperintensities [37].

Intradialytic exercise (IDE) is a training achieved during the HD session to intensify the patient's strength which targets many physiological and psychosocial limits [8]. IDE differs from resistance to aerobic exercise and stretching, using different apparatus used corresponding to the type of exercise. IDE has positively impacted the overall health and hospitalization rate of HD patients [34].

We found no significant difference between MoCA scores before (24.40 ± 2.53) and after (24.97 ± 1.94)

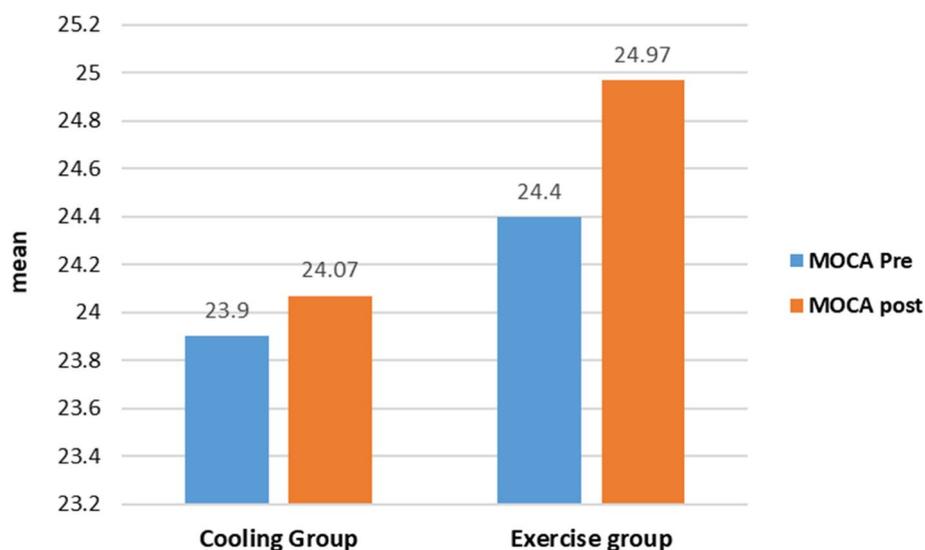


Fig. 1 Change of cognitive functions before and after intervention

our exercise program. Similar results were mentioned in a study examining the effect of exercise training in hemodialysis patients; however, the scale used was the kidney disease quality of life questionnaire, which is not specific for measuring cognitive functions [35]. On the other hand, an American study on the effect of intradialytic cognitive and exercise training on cognitive functions stated that cognitive and physical exercise is effective in preserving cognitive functions in hemodialysis compared to standard dialysis [28]. In harmony with the results of the Brazilian study by Martins et al. [27].

Using the Mini-International Neuropsychiatric Interview, we found the prevalence of depression in our study population pre-intervention to be 40% in the cooling group and 26.7% in the exercise group. This is consistent with the results of the Lebanese study by Semaan et al., which showed a 40.8% prevalence of depression [45]. A higher prevalence of depression was reported in the study conducted in the dialysis unit of the Urology and Nephrology Center, Mansoura University, Egypt, with 76.3% [11], and the Malaysian study by Kan et al. with 71.3% [22].

Regarding the severity of depressive symptoms, the results of the Beck Depression Inventory II in the cooling group showed a significant decrease in its mean score from 15 to 13. This differs from the Iranian study by Farhadi et al. that showed no effect of cool dialysate in depressive symptoms [15]. On the other hand, we found no significant change in the BDI-II scores of the exercise group. On the contrary, using the Mini-Psychiatric interview, we found no significant change in the number of

patients diagnosed as depressed in the cooling dialysate group. At the same time, there was a significant increase in the exercise group, mainly in those diagnosed with past depression before the intervention. A South Korean study showed no significant changes in depressive symptoms or diagnosis after 12 weeks of an intradialytic exercise group [19]. Meanwhile, the study by Young et al. showed a significant decrease in depression after a 12-month intradialytic exercise program [55]. Similar results were found in studies by Ouzouni et al. [33], Kouidi et al. [24], and the systematic review by Chung et al. [6].

We found no correlation between the severity of depressive symptoms and cognitive impairment. On the other hand, a South Korean study detected an inversely proportional relationship between cognitive function and depressive symptoms that concluded that CI was correlated with depression and that it is essential to detect CI and depression earlier in maintenance dialysis patients [21].

A negative correlation was found between serum phosphate and hemoglobin with cognitive functions in the exercise group; elevated phosphate level was associated with an increased risk of cognitive impairment and other neurological disorders [41]. Transferrin saturation (T-sat) was also correlated to MoCA scores; lower levels of T-sat are associated with cognitive impairment and dementia [54].

In our study, we found a negative correlation between baseline calcium level and depressive symptoms in the cooling group, which is consistent with a Spanish study that showed a protective effect of calcium against depression and anxiety in the hemodialysis population [9]. On

the other hand, a Japanese study by Tanaka et al. showed a relation between high calcium levels and poor mental health in hemodialysis patients [49].

Our study highlights the extent of cognitive and psychological deterioration in the HD population. It also shows the need for individualized exercise programs for different patients, including optimum duration and intensity of exercise. However, further studies are needed to assess the effect of pharmacological or psychological treatment in this field.

Limitations of the study

- Short duration, single-center study with a small sample and the absence of a control group must be considered
- The absence of individualized exercise programs
- Using one cognitive screening tool

Conclusions

The results revealed no significant improvement in mean scores of MoCA after either intradialytic exercise or cool hemodialysis, which were lower than the cutoff of mild cognitive impairment 23.9–25.

Factors associated with poor cognitive performance were increased age, lower education, lower albumin, and transferrin saturation. A high prevalence of depression was found in both groups (40% and 26.7%) before intervention which increased in the exercise group after intervention. The mean scores of depression severity by BDI-II were between 13 and 15 before intervention. Cooling hemodialysis showed improvement in mean depression severity scores.

Abbreviations

CI: Cognitive impairment; MoCA: The Montreal Cognitive Assessment; MINI: Mini-International Neuropsychiatric Interview; BDI-II: Beck Depression Inventory-second edition; T-sat: Transferrin saturation; PTH: Parathyroid hormone; CKD: Chronic kidney disease; IDE: Intradialytic exercise.

Authors' contributions

MMA: study design preparation, psychiatric evaluation, primary draft writing, and data collection. YS: study design preparation, psychiatric evaluation, data analysis, and manuscript revising and drafting. IHE: study method preparation, psychiatric evaluation, data analysis, and manuscript revising and drafting. MKN: designing the study intervention, medical evaluation, data interpretation, and manuscript revising. SMA: assisting in the intervention process and subject selection, monitoring patients during the intervention, and assisting in data collection. ZAG: supervising preparation of the study methods and design, analysis and interpretation of data, and manuscript drafting and revising. The final manuscript was read and approved by all authors. All authors have approved the manuscript for submission. The content of the manuscript has not been published or submitted for publication elsewhere.

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Availability of data and materials

Data are available with the request from the corresponding author.

Declarations

Ethics approval and consent to participate

Written consents were taken, and all stages of the study were fully clarified and explained to the patients who participated in our study. The ethical committee of the Mansoura Faculty of Medicine IRB approved our study (Code Number: MS.20.04.1106).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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