EFFECT OF INTRADIALYTIC AEROBIC EXERCISE ON BLOOD PRESSURE, MDA LEVELS, AND SOD IN DIABETIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS

Marcellino Mettafortuna Sephberlian[1*], Agung Susanto[1], Arifin[1], Eti Poncorini Pamungkasari[2]

Affiliation:
1. Department of Internal Medicine, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia
2. Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

Correspondence: Marcellino Mettafortuna Sephberlian, drmarcellino_ms@gmail.com, Department of Internal Medicine, Faculty of Medicine, Sebelas Maret University, Surakarta, Indonesia

Received: 1/09/2023
Accepted: 31/10/2023
Published: 31/10/2023

ABSTRACT

Introduction: Diabetic nephropathy (DKD) is a chronic kidney disease associated with diabetes mellitus patients. Hyperglycemia conditions trigger disruption of homeostasis between anti-oxidants and oxidants. An increase in free radicals triggers the body to produce superoxide dismutase (SOD). The increase in oxidants causes SOD to be unable to neutralize them optimally, thereby increasing oxidative stress. Oxidative stress can be assessed by measuring malondialdehyde (MDA). Various studies have been conducted involving intradialysis to determine whether physical exercise can reduce oxidant markers in diabetic nephropathy patients. This study aimed to determine the effect of intradialysis cycling for three months on blood pressure, MDA levels, and SOD in diabetic nephropathy patients undergoing hemodialysis (HD).
Methods: Experimental Study with a randomized controlled trial of all DKD in HD patients who met the inclusion and exclusion criteria. Patients were randomized into control and treatment groups. The treatment group was given aerobic cycling and intradialytic physical exercise in the HD room of RSUD Dr Moewardi, Surakarta, for 12 weeks. Aerobic physical exercise using a static bicycle (Adirmed Pedal Exercise Bike 931PE) is performed in the first 2 hours of the HD procedure. Physical exercise is performed in the first 2 hours of the HD procedure. Physical exercise lasts 15–30 minutes twice a week for 12 weeks. Statistical tests use a dependent t-test and Mann Whitney with $\alpha = 95\%$ and significant $p < 0.05$.
Results: Systolic and diastolic blood pressures were normally distributed, and then an independent t-test was performed with $p > 0.05$. Then the MDA and SOD levels were not normally distributed with the Wilcoxon test results for MDA levels ($p < 0.05$) and SOD levels ($p > 0.05$).
Conclusion: Intradialytic physical exercise does not affect systolic and diastolic blood pressure, can increase MDA levels statistically significant, and can increase SOD levels but not statistically significant.

Keywords: diabetic kidney disease; intradialytic; MDA; physical exercise; SOD.

INTRODUCTION

Diabetic nephropathy, or in other terms, diabetic kidney disease (DKD), is a chronic kidney disease (CKD) related to diabetes as its aetiology. Similar to CKD, DKD is also characterized by a decrease in the histological and physiological structure of the kidney that has been occurring gradually for approximately three months [1]. The prevalence of chronic kidney disease worldwide increased by 29.3% in 2017 compared to 1990 at all ages [2]. As many as half of CKD patients are caused by diabetes. The number of people with type 2 diabetes has increased along with the increase in obesity over the last 20 years [3]. Patients with DKD who have experienced a decrease in the filtration rate to the lowest level can be treated with routine treatment, namely hemodialysis (HD).

The condition of hyperglycemia in diabetic patients can affect the human kidney hemodynamically, metabolically, and inflammatoryly, so it can exacerbate the condition of kidney damage. The first hemodynamic changes are glomerular hypoperfusion and hyperfiltration, thereby increasing the albumin leakage from the glomerulus. In addition, it can trigger structural changes with thickening of the glomerular basement membrane, glomerulosclerosis, and expansion of mesangial cells, causing kidney fibrosis [4]. Immunologically, hyperglycemia triggers an imbalance between oxidants and anti-oxidants[5]. The formation of free radicals (ROS) is increasing. The body will respond to produce superoxide dismutase (SOD) through activation of Nuclear Respiratory Factor 2 (Nrf2), which is then translocated to the nucleus and binds to the Anti-oxidant Responding Element (ARE) so that it can regulate the expression of anti-oxidant genes through enzymatic return [6]. ROS contains hydroxyl radical (OH^-), peroxynitrite ($ONOO^-$), superoxide anion (O_2-), and hydrogen peroxide (H_2O_2) [7-9].

Various studies have been conducted regarding treatment to reduce MDA levels and increase SOD. One study showed that physical exercise can significantly reduce MDA levels. Physical exercise thrice a week for 12 weeks can reduce MDA levels in a study with 64 samples[10]. Another study by Abd ElKader, (2021) demonstrated that physical exercise for three months can increase SOD levels in diabetic patients. From the research data, it is hoped that it can reduce the progression of DKD [7].

Intrahemodialysis physical exercise has been widely carried out in Indonesia's big cities. However, it has not been done at the Regional General Hospital Dr Moewardi (Dr Moewardi Hospital) in Surakarta. In addition, data regarding the specific efficacy of inflammatory markers in the DKD population in Indonesia are still minimal, so it is hoped that this research can become a scientific reference in carrying out intradialysis and physical exercise.

METHODS

This study is an experimental study using the randomized controlled trial method with all DKD patients with routine management of HD in a pre-test and post-test design with a control group. This research was conducted in the HD room of Dr Moewardi Surakarta from December 2022 to March 2023. The population sampling technique is convenience sampling. The total sample was 16 patients randomized into two groups: eight in the control group and eight in the treatment group. All patients underwent a series of tests and blood pressure checks at the SOD and MDA laboratories. The control group did not receive physical exercise.

In contrast, the treatment group received aerobic physical exercise interventions for 15–30 minutes (performed within the first 2 hours of the hemodialysis procedure) with a frequency of 2 times a week for 12 weeks. According to the patient's clinical condition, aerobic exercise is done by pedalling a unique static bicycle with the feet in a sitting or lying position. Blood samples of study subjects in both groups were taken before entering the study period and at the end of the 12th week. The statistical tests used were chi-square, independent t-test, paired t-test, and Mann Whitney with a CI of 95% and p 0.05 using IBM SPSS version 25.

RESULTS

Two patients dropped out of this study due to death or not following the treatment procedure. The clinical characteristics of the control and treatment groups were relatively balanced, based on the difference test between the treatment and control groups (table 1). In this study, the pre-test systolic blood pressure treatment group obtained an average of 157.86± 16.24 and an average post-test of 143.29±26.02.

Table 1. An overview of the essential characteristics of research subjects

Variable	Group		p-value
	Treatment (n=7)	Control (n=7)	
Sex			0.286
-Male	5 (71.4%)	2 (28.6%)	
-Female	2 (28.6%)	5 (71.4%)	
Age	57.14 ±13.92	57.29 ±8.58	0.982
History of HD	3.79 ±3.92	3.96 ±5.18	0.746
BMI			0.566
-Underweight	0 (0.0%)	1 (14.3%)	
-Normoweight	4 (57.1%)	4 (57.1%)	
-Overweight	3 (42.9%)	1 (14.3%)	
-Obese	0 (0.0%)	1 (14.3%)	
Comorbid			1.000
-Yes	4 (57.1%)	4 (57.1%)	
-No	3 (42.9%)	3 (42.9%)	

*Significant α<0.05; CI95%

Table 2. Systolic blood pressure difference test between the treatment and control groups

Group	Systolic blood pressure		p-value
	Pre	Post	
Treatment	157.86 ±16.24	143.29 ±26.02	0.340
Control	170.71 ±30.02	161.29 ±8.56	0.327
p-value	0.339	0.108	

*significant α<0.05; CI95%

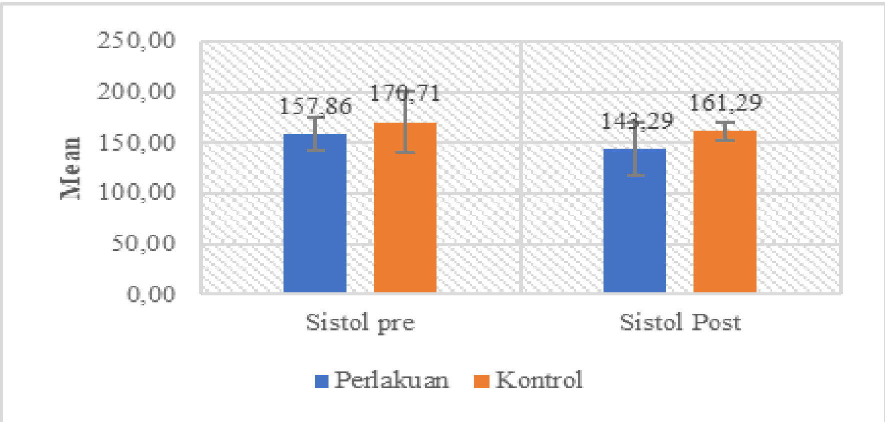


Figure 1. Bar chart of different systolic blood pressure test results between the treatment and control groups

The difference in changes in post-presystolic blood pressure in the treatment group was found to have decreased by an average of -14.57±37.16, or -9.2%, but the decrease was not statistically significant with a value of p = 0.340 (p > 0.05). Thus, the treatment of intra-hemodialysis physical exercise does not significantly influence changes in systolic blood pressure in hemodialysis patients. The control group's pre-test systolic blood pressure results obtained an average of 170.71±30.02 and an average post-test of 161.29 ±8.56. The difference in changes in post-presystolic blood pressure in the control group was found to have decreased by an average of -9.43±23.39, or -5.5%, but the decrease was not statistically significant with a value of p = 0.327 (p> 0.05), which can be seen in table 2 and figure 1. Based on the results of the above study, it was found that the systolic blood pressure comparison between the treatment and control groups in the pre-test sample obtained p = 0.339 (p> 0.05), which means it does not show a significant difference between the treatment and control groups in pre-test systolic blood pressure, and then post-test systolic blood pressure got p = 0.108 (p > 0.05), which also did not show a significant difference.

Table 3. Systolic blood pressure difference test between the treatment and control groups

Group	Diastolic blood pressure		p-value
	Pre	Post	
Treatment	'3.86 ±7.97	75.71 ±13.05	0.729
Control	1.57 ±19.42	87.71 ±17.02	0.449
p-value	0.360	0.164	

*significant α<0.05; CI95%

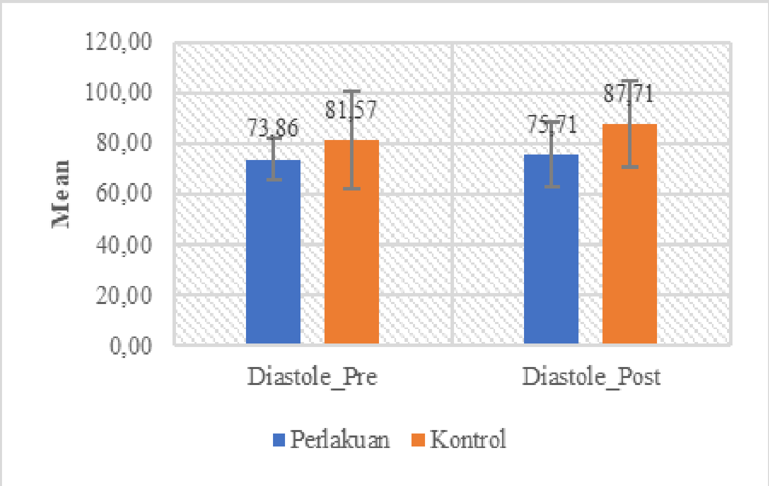


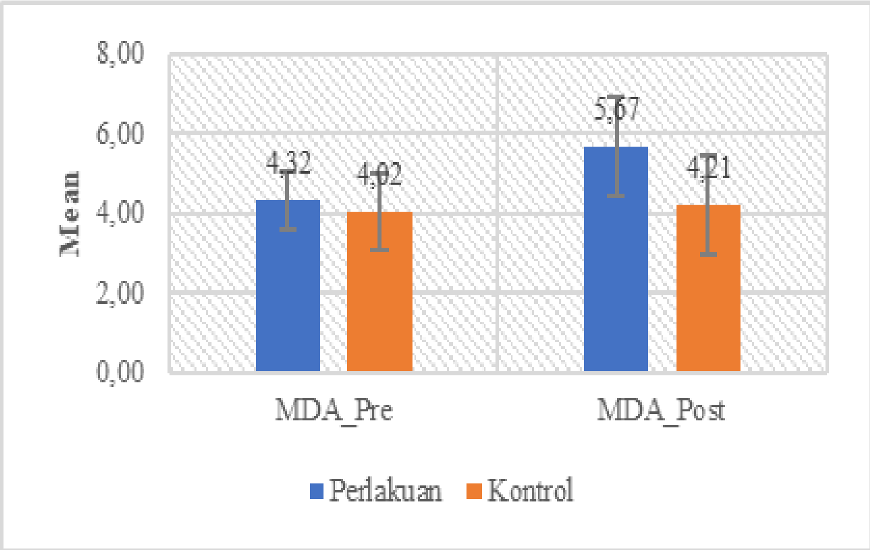
Figure 2. Bar chart of different test results for diastolic blood pressure between the treatment and control groups

Based on these tests, it was found that in the treatment group, the pre-test diastolic blood pressure results obtained an average of 73.86 ±7.97 and an average post-test of 75.71 ±13.05. The difference in changes in diastolic blood pressure in the post-pretreatment group was found to have an average increase of 1.86 ±13.55, or 2.5%, but the increase was not statistically significant with a value of p = 0.729 (p> 0.05) (Table 3 and Figure 2). Thus, treating intradialysis with physical exercise does not significantly affect changes in diastolic blood pressure in hemodialysis patients. While the results of the above study obtained an unpaired different test, the comparison of diastolic blood pressure between the treatment and control groups in the pre-test sample obtained p = 0.360 (p> 0.05), which means that there was no significant difference between the treatment and control groups in pre-test diastolic blood pressure.

Table 4. Test the difference in MDA levels between the treatment and control groups

Group	MDA		p-value
	Pre	Post	
Treatment	4.32 ±0 .73	5.67 ±1.23	0.016*
Control	4.02 ±0 ,96	4.21 ±1.23	0.731
p-value	0.602	0.077	

*significant α<0,05; CI95%



Gambar 3. Bar chart of test results for different levels of MDA between the treatment and control groups

The post-test diastolic blood pressure obtained p = 0.164 (p > 0.05) also did not show a significant difference (Table 3 and Figure 2). Thus, administering intra-hemodialysis physical exercise treatment did not affect changes in diastolic blood pressure compared to the control group, even though the tendency for an increase in diastolic blood pressure was more significant in the control group than in the treatment group.

The results of the different MDA levels tests in this study found that in the treatment group, the pre-test MDA results obtained an average of 4.32 ±0.73 and an average post-test of 5.67±1.23. The difference in changes in the MDA post-pretreatment group was found to have an average increase of 1.35 ±0.98, or 31.2%. The increase was statistically significant with a value of p = 0.016 (p <0.05) (Table 4 and Figure 3). Thus, administering intra-hemodialysis physical exercise treatment significantly increases MDA in hemodialysis patients. In the control group, the pre-test MDA results obtained an average of 4.02 ±0.96 and an average post-test of 4.21 ±1.23. The difference in post-pre-control group MDA changes was found to have increased by an average of 0.19 ±1.00, or 4.6%, but the increase was not statistically significant with a value of p = 0.731 (p> 0.05). (Table 4 and Figure 3).

Based on the results of the above study, it was found that the unpaired difference test compared MDA between the treatment and control groups in the pre-test sample obtained p = 0.602 (p> 0.05), which means that there was no significant difference between the treatment and control groups on the MDA pre-test, and the MDA post-test obtained p = 0.077 (p> 0.05) also did not show a significant difference. Then, the comparison of the difference in MDA changes did not show a statistically significant difference, with a p = 0.077 (p> 0.05). Thus, administering intra-hemodialysis physical exercise treatment increases MDA but is still not significantly different from the control group (Table 4 and Figure 3).

While the results of the above study obtained an unpaired different test, the comparison of diastolic blood pressure between the treatment and control groups in the pre-test sample obtained p = 0.360 (p> 0.05), which means that there was no significant difference between the treatment and control groups in pre-test diastolic blood pressure. The post-test diastolic blood pressure obtained p = 0.164 (p > 0.05) also did not show a significant difference (Table 3 and Figure 2). Thus, the provision of intra-hemodialysis physical exercise treatment did not affect changes in diastolic blood pressure compared to the control group, even though the tendency for an increase in diastolic blood pressure was more significant in the control group compared to the treatment group.

The pre-test SOD different test results obtained an average of 3.00 ± 1.72 and an average post-test of 3.01 ± 0.30. The difference in SOD changes in the post-pre-treatment group was found to have an average increase of 0.02 ± 1.55 or 0.6%. The increase was not statistically significant, with a p = 0.491 (p> 0.05). Thus, the administration of intra-hemodialysis physical exercise treatment did not significantly affect the increase in SOD in hemodialysis patients. In the control group, the pre-test SOD results obtained an average of 3.65 ± 1.16 and an average post-test of 2.71 ± 0.51. The difference in SOD changes in the post-pre control group was found to have decreased by an average of -0.93 ± 0.98 or -25.6%. The decrease was statistically significant, with a value of p = 0.039 (p <0.05).

Based on the results of the above study, it was found that the SOD comparison between the treatment and control groups in the pre-test sample obtained p = 0.413 (p> 0.05), which means that the pre-test value between the treatment and control groups did not show a significant difference. The post-test SOD obtained p = 0.288 (p > 0.05) also did not show a significant difference. The comparison of the difference between these changes also did not show a statistically significant difference, with a value of p = 0.229 (p>0.05). Thus, giving intrahemodialysis physical exercise treatment is not practical in increasing the SOD of hemodialysis patients.

Table 5. Test the difference in SOD levels between the treatment and control groups

Group	SOD		p-value
	Pre	Post	
Treatment	3.00 ±1.72	3.01 ±0.30	0.491
Control	3.65 ±1.16	2.71 ±0.51	0.039*
p-value	0.413	0.288	

*significant α<0,05; CI95%

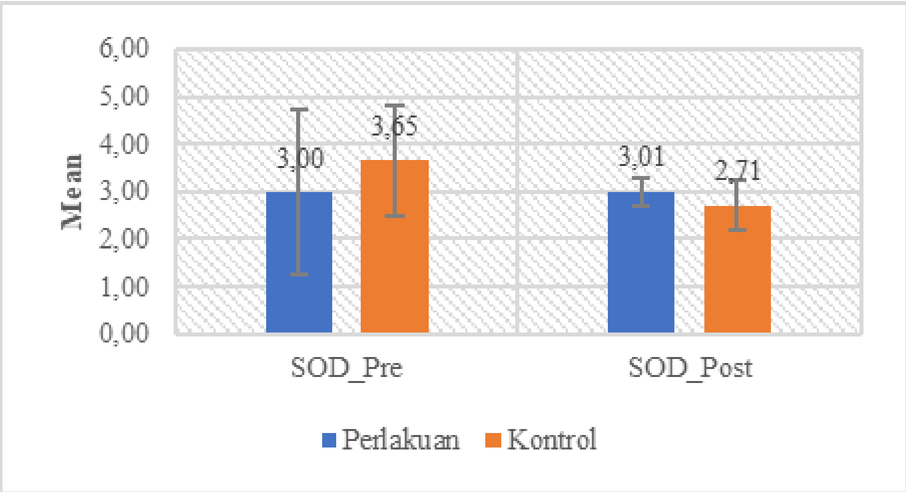


Figure 4. Bar chart of test results for different levels of SOD between the treatment and control groups

DISCUSSION

This research is related to the role of intra-hemodialysis physical exercise on oxidant and anti-oxidant levels in patients with diabetes kidney disease (DKD). The oxidants and anti-oxidant levels examined in this study were malondialdehyde (MDA) and superoxide dismutase (SDA). The subjects in this study had the same essential characteristics as male and female patients, namely seven patients each, with an average patient age of 57.21 years. These patients had been diagnosed with diabetes mellitus for an average of 16.64 years, with an average of 3.88 years having undergone hemodialysis. The subjects in this study had several differences regarding body mass index (BMI). There was one (7.1%) subject with an underweight BMI, eight (57.1%) subjects with norm weight, four (28.6%) subjects with overweight, and the remaining one (7.1%) subject was classified as obese. Out of 14 subjects, there were 8 (57.1%) with comorbidities and 6 (42.9%) without comorbidities.

This study aims to determine the effect of intradialytic physical exercise on blood pressure in end-stage DKD patients. CKD patients tend to experience increased blood pressure. Physical exercise in CKD patients can improve blood pressure and aerobic capacity; specifically, aerobic physical exercise can improve anaemia, hyperlipidemia, chronic inflammation, blood pressure, insulin resistance, decreased arterial elasticity, and decreased urea levels in the urine[11]. This study showed a decrease in systolic and diastolic blood pressure, but it was not statistically significant. Jung and Park's 2011 article shows that aerobic intradialysis physical exercise for 9 weeks can increase heart-pulmonary capacity, blood pressure, and quality of life. Similar to the article by [12] applied to 11 patients, it was found that blood pressure acutely after aerobic and resistant intra-hemodialysis had increased, but ambulatory blood pressure experienced a statistically significant decrease. In general, there is the potential for intradialysis hypotension to occur because it begins with multifactorial factors and occurs due to an aggressive decrease in circulating blood volume during a hemodialysis session. When plasma volume decreases during dialysis, blood pressure is maintained by increasing plasma refill, vascular resistance, and heart output. Intradialytic hypotension occurs when this corrective mechanism is not activated against the ultrafiltration rate (UFR). However, in patients with risk factors for IDH, there is dysregulation of physiological compensatory mechanisms, which will then result in hypotension and IDH in dialysis patients. Patients with impaired cardiac function, such as those with systolic and diastolic dysfunction, are likely to experience reduced cardiac output, which further contributes to the risk of intradialytic hypotension [13]. Obesity, smoking lifestyle, and cardiovascular risk factors can also be affected in this study, where these factors affect isolated diastolic hypertension with the target of lifestyle changes. In addition, adherence to antihypertensive medication can also be considered in the results of this study.

This study also focuses on differences in MDA levels before and after physical exercise. DKD is a condition where there is an imbalance between oxidants and anti-oxidants. Oxidant levels are responsible for the pathogenesis of DKD. The condition of DKD is associated with an increase in oxidant levels and a decrease in anti-oxidants in plasma. Oxidants in the kidneys come from the results of metabolic processes; the cytochrome P450 system produces reactive oxidative species (ROS). Exposure to hyperglycemic conditions triggers the development and accumulation of extracellular matrix proteins such as collagen I, collagen IV, and fibronectin. Increased ROS production can activate profibrotic growth factors, such as transforming growth factor beta (TGF-) and connective tissue growth factor (CTGF). Some of these cytokines can trigger fibrosis by triggering increased extracellular matrix production, resulting in fibrosis and sclerosis in the kidney [14].

In this study, malondialdehyde (MDA) levels increased in the control and treatment groups. MDA levels in the control group experienced an increase. However, in the different tests, there was no statistically significant difference ($p = 0.731$). In contrast, in the treatment group, there was also an increase in MDA levels with a more tremendous increase. Based on the different tests, a significant difference was found regarding the MDA level of the treatment group ($p = 0.016$).

A study by Esgalhado et al. (2015) showed that MDA levels in the treatment group also increased. This study measured MDA levels 30 minutes before and 60 minutes after the hemodialysis session. This study showed an increase in MDA in the treatment group, but there was no statistically significant difference. The increase in MDA is thought to be due to measurements taken after a hemodialysis session. Acute physical exercise can increase oxidative markers in hemodialysis patients [15], while chronically, its effect on oxidants is still under further research. Research [16] conducted a study on intradialytic physical exercise, which reduces oxidative stress. The results showed that oxidative stress, as measured by serum thiobarbituric acid, decreased by 38%, which is statistically significant. The study was conducted on 17 hemodialysis patients with physical exercise in the form of cycling exercise for four months. Measurements in acute conditions can cause increased oxidative stress. However, long-term exercise can stimulate the body to adapt to oxidative stress and improve physiological function. Spirlandeli et al. (2013) concluded that MDA levels would decrease after 1 hour of hemodialysis [20]. Sylviana et al. (2017) concluded that regular exercise lowers MDA levels, and MDA levels will decrease significantly 6 hours after exercise [21]. Fisher-Wellman and Bloomer (2009) added that the type of exercise, exercise intensity, duration and characteristics of the subjects tested can affect the level of oxidative stress [22].

This study examines the role of intrahemodialysis physical exercise on anti-oxidant markers in DKD patients. DKD is a physiologically dangerous condition of the patient's kidney. DKD patients will experience homeostatic disturbances between anti-oxidants and oxidants. Hyperglycemia, in general, harms the human body [17].

Hyperglycemia conditions can cause at least two changes: the first is metabolic, and the second is hemodynamic. Metabolic hyperglycemia can lead to advanced glycated end-products (AGEs), polyols, and Protein Kinase C (PKC) activation. The condition of AGEs is affected by non-enzymatic changes in glycosylation of proteins, nucleic acids, and lipids; this condition is activated after exposure to long-term hyperglycemia conditions. In patients with DKD, AGEs can cause the formation of strong bonds with proteins such as collagen that occur in kidney cells. The strong bond between collagen and protein will cause the thickening of the glomerular base, which will then trigger mesangial cells to increase extracellular matrix synthesis. In addition, the condition of AGEs is associated with decreased nitric oxide (NO) levels. NO has a protective effect on vasodilation by affecting the elasticity of blood vessels and an antiproliferative response. Activation of AGE conditions can trigger binding with AGE receptors (RAGE) on the surface of macrophages, podocytes, and mesangial cells. In the presence of AGE and RAGE, binding will cause the production of reactive oxygen species (ROS), which will then stimulate the activation of nuclear factor kappa B (NF-kB).

Furthermore, NF-kB plays a role in inducing inflammation and profibrotic cytokines and growth factors such as tumour necrosis factor-alpha (TNF-α), tumour growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF). The final impact of activation of this process will be an increase in the extracellular matrix, dilation of mesangial cells, damage to kidney tissue, and decreased kidney function (Vodošek Hojs et al., 2020). Besides that, the increased ROS levels caused by AGE activation can trigger a worsening of DKD in patients. An increase in oxidants and a decrease in anti-oxidants will accelerate atherosclerosis and other chronic complications. On the other hand, hemodialysis can increase oxidative stress in diabetic patients [18].

Understanding the poor condition of DKD patients' organ systems can trigger a search for solutions, especially regarding the problem of increasing oxidant levels and decreasing anti-oxidant levels in DKD patients. This study involved the effects of intra-hemodialysis physical exercise on anti-oxidant factors in patients with DKD. This study shows that intra-hemodialysis physical exercise can increase superoxide dismutase (SOD) levels, although it is not statistically significant. However, when viewed from the results of the final study, there were differences in the trend of changes in SOD between the control group and the treatment group. The control group tended to experience a decrease in SOD levels. In contrast, SOD levels in the treatment group tended to increase. So intra, hemodialysis physical exercise has the potential to be one of the management strategies for DKD patients to increase anti-oxidants.

This research is consistent with that of Esgalhado et al. (2015), which showed that plasma SOD levels decreased after physical exercise. Still, in this study, the decrease in SOD levels was statistically significant. This study was conducted on sixteen patients who routinely underwent hemodialysis, with a total of 11 women and an average age of 44.4 years. The physical exercises carried out in the study were carried out for 30 minutes with ten repetitions for four types of exercises for both legs. Then, blood samples were taken twice at 30 and 60 minutes after dialysis on days with and without physical exercise [19].

There are several limitations of this study. First, the inclusion and exclusion criteria were too lax. Because they were only carried out in one hospital, the sample was quite limited. Second, no other laboratory supports were examined, such as lipid profiles and sugar levels. Third, intradialytic aerobic cycling cannot be done during hemodialysis with a longer duration, such as 150 hours per week.

CONCLUSION

Aerobic combination intrahemodialysis physical exercise 2 times per week for 12 weeks did not affect systolic or diastolic blood pressure statistically, and MD levels could increase SOD levels but were not statistically significant.

ACKNOWLEDGEMENTS

There is no acknowledgement in this work.

CONFLICT OF INTEREST

The author declares there is no conflict of interest.

REFERENCES

1. Chen, T. K., Knicely, D. H. and Grams, M. E. (2019) 'Chronic Kidney Disease Diagnosis and Management', JAMA, 322(13), p. 1294. doi: 10.1001/jama.2019.14745.
2. Bikbov, B. et al. (2020) 'Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017', The Lancet, 395(10225), pp. 709–733. doi: 10.1016/S0140-6736(20)30045-3.
3. Hoogeveen, E. K. (2022) 'The Epidemiology of Diabetic Kidney Disease', Kidney and Dialysis, 2(3), pp. 433–442. doi: 10.3390/kidneydial2030038.
4. Miranda-Díaz, A. G. et al. (2016) 'Oxidative Stress in Diabetic Nephropathy with Early Chronic Kidney Disease', Journal of Diabetes Research, 2016, pp. 1–7. doi: 10.1155/2016/7047238.
5. Giacco, F. and Brownlee, M. (2010) 'Oxidative Stress and Diabetic Complications', Circulation Research, 107(9), pp. 1058–1070. doi: 10.1161/CIRCRESAHA.110.223545.
6. Niture, S. K. et al. (2010) 'Nrf2 signaling and cell survival', Toxicology and Applied Pharmacology, 244(1), pp. 37–42. doi: 10.1016/j.taap.2009.06.009.
7. Pizzino, G. et al. (2017) 'Oxidative Stress: Harms and Benefits for Human Health', Oxidative Medicine and Cellular Longevity, 2017, pp. 1–13. doi: 10.1155/2017/8416763.
8. Collin, F. (2019) 'Chemical Basis of Reactive Oxygen Species Reactivity and Involvement in Neurodegenerative Diseases', International Journal of Molecular Sciences, 20(10), p. 2407. doi: 10.3390/ijms20102407.
9. Albert-Garay, J. S., Riesgo-Escovar, J. R. and Salceda, R. (2022) 'High glucose concentrations induce oxidative stress by inhibiting Nrf2 expression in rat Müller retinal cells in vitro', Scientific Reports, 12(1), p. 1261. doi: 10.1038/s41598-022-05284-x.
10. Abd ElKader, S. M. (2021) 'Impact of Aerobic Versus Resistance Exercise Training on Glucose Control and Biomarkers of Oxidative Stress among Saudi Patients with Type 2 Diabetes', Interventions in Obesity & Diabetes, 4(5). doi: 10.31031/IOD.2021.04.000598.
11. Jung, T.-D. and Park, S.-H. (2011) 'Intradialytic exercise programs for hemodialysis patients.', Chonnam medical journal, 47(2), pp. 61–5. doi: 10.4068/cmj.2011.47.2.61.
12. Kim, J.-S. et al. (2019) 'Effect of acute intradialytic aerobic and resistance exercise on one-day blood pressure in patients undergoing hemodialysis: a pilot study', The Journal of Sports Medicine and Physical Fitness, 59(8). doi: 10.23736/S0022-4707.18.07921-5.
13. Chou, J. A., Kalantar-Zadeh, K. and Mathew, A. T. (2017) 'A brief review of intradialytic hypotension with a focus on survival', Seminars in Dialysis, 30(6), pp. 473–480. doi: 10.1111/sdi.12627.
14. Jha, J. C. et al. (2016)' Diabetes and Kidney Disease: Role of Oxidative Stress', Anti-oxidants & Redox Signaling, 25(12), pp. 657–684. doi: 10.1089/ars.2016.6664.
15. Fatouros, I. G. et al. (2008)' Acute Exercise May Exacerbate Oxidative Stress Response in Hemodialysis Patients', Nephron Clinical Practice, 109(2), pp. c55–c64. doi: 10.1159/000139990.
16. Vodošek Hojs, N. et al. (2020) 'Oxidative Stress Markers in Chronic Kidney Disease with Emphasis on Diabetic Nephropathy.', Anti-oxidants (Basel, Switzerland), 9(10). doi: 10.3390/antiox9100925.
Wilund, K. R. et al. (2010) 'Intradialytic exercise training reduces oxidative stress and epicardial fat: a pilot study', Nephrology Dialysis Transplantation, 25(8), pp. 2695–2701. doi: 10.1093/ndt/gfq106.
17. Arslan, M. et al. (2014) 'Effect of Aerobic Exercise Training on MDA and TNF- α Levels in Patients with Type 2 Diabetes Mellitus', International Scholarly Research Notices, 2014, pp. 1–5. doi: 10.1155/2014/820387.
18. Dursun, E. et al. (2005) 'Effect of haemodialysis on the oxidative stress and anti-oxidants in diabetes mellitus', Acta Diabetologica, 42(3), pp. 123–128. doi: 10.1007/s00592-005-0191-1.
19. Esgalhado, M. et al. (2015) 'Effect of acute intradialytic strength physical exercise on oxidative stress and inflammatory responses in hemodialysis patients', Kidney Research and Clinical Practice, 34(1), pp. 35–40. doi: 10.1016/j.krcp.2015.02.004.
20. Spirlandeli, A., Deminice, R. and Jordao, A. (2013) 'Plasma Malondialdehyde as Biomarker of Lipid Peroxidation: Effects of Acute Exercise', International Journal of Sports Medicine, 35(01), pp. 14–18. doi: 10.1055/s-0033-1345132.
21. Sylviana, N. et al. (2017) 'The Effect of Astaxanthin and Regular Training on Dynamic Pattern of Oxidative Stress on Male under Strenuous Exercise', Indonesian Journal of Clinical Pharmacy, 6(1), pp. 46–54. doi: 10.15416/ijcp.2017.6.1.46.
22. Fisher-Wellman, K. and Bloomer, R. J. (2009)' Acute exercise and oxidative stress: a 30 year history', Dynamic Medicine, 8(1), p. 1. doi: 10.1186/1476-5918-8-1.