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Original Research

Effects of Aerobic Exercise on Depression and CD4 Counts in People Living with HIV**Untung Sujianto¹, Madya Sulisno¹, and Richal Grace Zefanya Uly²**¹Departement of Nursing, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia²Student of Master Program in Nursing, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia**ABSTRACT**

Introduction: HIV patients often experience psychological and physical disorders which greatly affect the adherence of people living with HIV/AIDS (PLWHA). This study aimed to assess the effects of aerobic exercise on the levels of depression and CD4 cell count of HIV patients.

Methods: This study used a pre-post quasi-experimental design with a control group. The sampling technique was consecutive sampling, with a total sample of 52 HIV respondents. Depression level was measured using the Beck Depression Inventory (BDI), while CD4 count was measured using the Pyma analyser. The aerobic exercise intervention was given three times a week with a duration of 20-30 minutes each for four weeks. The collected data were analysed using a paired sample t-test and an independent sample t-test.

Results: The results showed a significant difference in the mean value of depression before and after the intervention of aerobic exercise ($M = 25.15$ and $M = 22.46$, respectively) with $p = 0.001$. Similarly, there was a significant difference in the mean of CD4 counts between the control group ($M = 303.38$) and the intervention group ($M = 305.38$) after the intervention with $p = 0.031$.

Conclusion: Aerobic exercise is effective in reducing depression levels and increasing CD4 counts in HIV patients. Immune system cells circulate more rapidly and there is a boost in the production of macrophages, cells that can attack bacteria.

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INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system and which can be contagious and deadly. HIV can occur due to several risk factors, including alternating drug injection equipment (drugs, alcohol, psychotropic substances and additives), free sex (heterosexual, homosexual) without a condom, transmission from infected mothers to children, perinatal and through transfusions (Kemenkes, 2017).

Various impacts can arise for HIV sufferers such as physical, social, emotional and spiritual problems. Most People Living with HIV/AIDS (PLWHA) experience changes in emotional status, one of which is depression. Demirel et al. (2018) stated that 31% of HIV/AIDS sufferers in Turkey experienced depression and up to 19% of them experienced mental disorders. The prevalence of depression in

Indonesia is quite high, around 17-27%. Furthermore, approximately 5-10% of the general population experiences depression. The causes of depression in PLWHA patients are low CD4 count, adherence to ART, lack of physical activity, and community stigma (Demirel et al., 2018)

HIV directly destroys CD4 T cells (Cluster of Differentiation 4) which functions as body immunity and causes a primary infection which further accelerates the decrease in the number of CD4 lymphocytes in the blood. If the virus attacks CD4 T cells until their number drops below 200 per microliter, the body's immunity will be lost and become AIDS. Dianatiasab et al. (2018) stated that a CD4 cell count of <500 cells/ml or <200 cells/ml in PLWHA will cause severe depression. Factors that influence CD4 counts in PLWHA are baseline CD4 counts, medication adherence level, depression, and tuberculosis infection (Dianatiasab et al., 2018).

The number of people infected with HIV in 2012 was 35.3 million people and increased in 2018 to 37.9 million people worldwide; most of these people were at the age of 15-49 years old (UNAIDS, 2019). In Indonesia, there were 640,443 PLWHAs in 2018. The Indonesian Ministry of Health stated that the number of HIV/AIDS cases had reached 18,442 cases in 33 provinces with 3,708 deaths (Kemenkes, 2017).

Aerobic exercise is a physical activity that uses leg and arm muscle movements which are known to have many benefits. Regular movement can increase the release of neurotransmitters that is mediated by activation of Brain-derived Neurotrophic Factor (BDNF). Increased BDNF, VEGF, and IGF-1 as neurotrophic factors in the hippocampus are useful for nerve cell growth, increase regulation of stress hormones, namely cortisol on the hypothalamic-pituitary-adrenal (HPA) axis and decrease the release of pro-inflammatory cytokines so that depressive symptoms can be reduced and cells in the immune system will circulate more quickly in the body. There may also be a boost in the production of macrophages, which are cells that attack bacteria, which can increase CD4 counts in PLWHAs (Nosrat et al., 2017).

A study by Heissel et al. (2019) found that to assess aerobic exercise activity for depression and CD4 cell count, the evaluation could be done at week four. The study showed different results between the control group (SMD = -0.84, 95% CI = -1.57, -0.11, $p = 0.02$) and the intervention group (SMD = 0.90, 95% CI = -1.63, -0.30, $p = 0.004$, $p < 0.001$). Exercise can reduce symptoms of depression and anxiety in PLWHA. This therapy can also affect the CD4 count of HIV patients (Heissel et al., 2019).

The results of the study by Nosrat et al. (2017) showed significant differences in depression levels in both groups ($F = 2.63$, $p = 0.05$) and ($F = 7.40$, $p < 0.001$), with greater increases in resistance training compared to the control. Meanwhile, a study by Dianatisanab et al. (2018) found that after the aerobic exercise intervention programme, a significant difference in CD4 cell count was found between the two groups ($p = 0.01$). This means that aerobic exercise is effective in reducing levels of depression and increasing the CD4 count of HIV patients (Nosrat et al., 2017).

This study differs from previous studies in the type and design of the study, population, number of samples, place of study, and the variables measured. The researchers conducted the quasi-experimental research with a pre-post-test design with a control group. The population involved were males and females. The number of samples was also different, namely 52 patients diagnosed with HIV stage 1 and 2. These patients had their CD4 count checked first and were assessed for depression levels using Beck Depression Inventory (BDI) before receiving aerobic exercises. Research variables have never been carried out in a study that involves two variables, namely depression and CD4 cell count.

Providing aerobic exercise interventions to increase circulation in HIV patients is easy, effective

and economical for all patients to do and has no side effects. Based on these descriptions, the researchers were interested in conducting a study to investigate the effects of aerobic exercise on depression levels and CD4 cell counts in HIV patients.

MATERIALS AND METHODS

This study used a quantitative method with a pre-post-test design with a control group. The sample size was calculated using a sample size formula to test the hypothesis for a mean of two populations (Notoatmodjo, 2005). This study involved 26 respondents each in the intervention and control groups, with a total of 52 respondents. These respondents were HIV patients undergoing outpatient treatment at the Voluntary Counselling and Testing (VCT) clinic. A consecutive sampling technique was used to recruit the samples. Consecutive sampling is a sampling technique that is performed by selecting all individuals encountered and meeting the criteria until the desired sample size is met (Jannaim & Asrizal, 2018).

The inclusion criteria of this study were: 1) HIV patients at stage 1 and II; 2) age >18 years old; 3) able to communicate well; 4) at least those who have been adhering to taking ARV drugs >6 months; 5) patients with a CD4 count >200 / ml; 6) patients who come with a companion who lives in the same house; and 7) patients who were depressed (moderate, severe).

Before conducting the research, the researcher first composed a research permit and research ethics approval letter from the Health Research Ethics Committee of the Faculty of Medicine, Diponegoro University which was addressed to the VCT Clinic Sobat Kupang. The Health Research Ethics Committee of the Health Polytechnic, Ministry of Health Kupang approved the study with a reference number of LB.02.03/1/0062/2020. After obtaining the research permit, the researchers began to conduct the study.

The researcher gave the Beck Depression Inventory questionnaire and filled it out to measure the level of depression. The instrument was written in the Indonesian language and had been tested for its validity and reliability with a Cronbach's alpha of 0.923, meaning that the measuring instrument was very reliable. The CD4 count was assessed using PIMA Analyzer before and after the intervention in both groups. The researchers identified respondents based on the predetermined criteria. The researchers explained the procedure for the research process, namely the first meeting of all samples was carried out by filling out a questionnaire on the demographic data of the respondents, assessing the level of depression, checking CD4 counts and teaching aerobic exercise techniques for 20-30 minutes.

This aerobic exercise intervention was given once at the beginning of the meeting, after which the researcher gave the SOP and the video of this exercise to be performed at home and monitored by a companion who lived in the same house as the respondents. Furthermore, the respondents filled out

Table 1. Differences in the depression level between intervention and control groups (pre- and post-test; N = 52)

Type of group	Depression category	Frequency		Mean		Mean difference	SD Difference	Dependent t-test p-value
		Before (%)	After (%)	Before (SD)	After (SD)			
Intervention	Mild	4 (15.4)	11 (42.3)	25.15	22.46	-2.69	0.14	0.001
	Moderate	16 (61.5)	10 (38.5)	(5.48)	(5.62)			
	Severe	6 (23.1)	5 (19.2)					
Control	Mild	5 (19.2)	6 (23.1)	24.12	25.00	0.88	1.00	0.179
	Moderate	16 (61.5)	13 (50.0)	(5.99)	(6.99)			
	Severe	5 (19.2)	7 (26.0)					
Independent t-test p-value				0.341	0.001			

Table 2. Differences in CD4 counts between the intervention and control groups (pre- and post-test; N = 52)

Type of group	Category	n	%	Mean		Mean difference	SD Difference	Dependent t-test p-value
				Before (SD)	After (SD)			
Intervention	Increase	19	73.1			5.00	2.66	0.031
	Standing	4	15.4	300.46	305.46			
	Decrease	3	11.5	(58.70)	(61.36)			
Control	Increase	12	34.6	302.81	303.38	0.57	-1.58	0.523
	Standing	5	19.2	(62.98)	(61.40)			
	Decrease	9	46.2					
Independent t-test p-value				0.890	0.000			

the checklist sheet that was provided by the researcher after the initial intervention. The exercise was carried out three times a week for four weeks. The aerobic exercise in this study consisted of three-movement sessions, namely: 1) Warm-up; slowly approaching the extent of joint movement, then hold for 8 counts in 10 seconds and finally relax, until the respondent feels a sufficient stretch without pain for 5-10 minutes involving the joints and muscles of the upper, in the lower body as well as the left and right sides of the body, without bouncing and breathing regularly; 2) core movements; raising hands forward, upward, sideways, backward, hand movements opening and crossing, pushing and pumping forward, upward and sideways, punching hand movements, forward, sideways, upward, downwards and crosses, one-handed or two-handed swinging motion, clapping, among others, the hands' clap, hands pat the thighs and shoulders; walk in the place, take a step or two, jump a foot or two to the side, forward and back, raise the knee, kick, back, forward, and sideways; and 3) Cooling (Grace et al., 2015).

The data was processed into a computer program system. The results were analysed using univariate and bivariate analysis. Univariate analysis was carried out on respondent characteristics data (gender, age, education, marital status, number of opportunistic infections (OIs), type of ARV, risk factors, initial CD4 count), while bivariate analysis was performed on the results of the Beck Depression Inventory value and CD4 count in the control group and the intervention group using the dependent samples t-test and independent samples t-test.

RESULTS

Respondent Characteristics

The results showed that the majority of respondents were aged 26-46 years old (n = 43; 65.4%), male (n = 27; 51.9%), high school graduates (n = 23; 44.2%), and unmarried (n = 31; 59.6%). Furthermore, 29 respondents had the type of ARV drug with the Efavirenz (EFV) based type (55.8%) and the other 23 had Nevirapine (NVP) based medicine (44.2%). As many as 51 respondents (98.1%) did not experience opportunistic infections or opportunistic infections <2, while the remaining (1.9%) had opportunistic infections ≥ 2 types of infections.

Depression Level

Before the aerobic exercise intervention

The incidence of depression among HIV patients as shown in Table 1 was 23.1% in the intervention group and 19.2% in the control group. The overall mean of depression before the intervention was 25.15, which means that the level of major depression has the lowest score of 16 and the highest score of 36. From the results of the p-value in Table 1, it could be concluded that the incidence of depression between the control group and the intervention group is equivalent or has the same variance with a p-value >0.05.

After the aerobic exercise intervention

In the intervention group, the average level of depression was mild depression (42.3%) while in the control group, the highest level of depression was moderate depression (50.0%). The mean value of depression in the intervention group was 22.46, indicating a mild level of depression level, while in the control group, the mean value was 25.00, indicating a moderate level of depression. A significant change in

the level of depression after the aerobic exercise intervention was indicated by a p-value <0.001.

Differences between the intervention and control groups

The depression level of HIV patients who received the aerobic exercise intervention decreased significantly by -2.69 with a p-value <0.05. Meanwhile, in the control group that did not receive the intervention, there was no significant change; the change was 0.88 with a p-value >0.05. Based on these results, it can be concluded that there was a significant change in the level of depression before and after the aerobic exercise in the intervention group.

CD4 Cell Counts

Before the Aerobic Exercise Intervention

The intervention group and the control group had CD4 values of >200ml/dL. The overall mean of CD4 cell count of HIV patients before the intervention was 300.4 for the intervention group and 302.81 for the control group. From the results of the p-value, it can be concluded that the incidence of depression between the control group and the intervention group is equivalent or has the same variance with p-value >0.05.

After the aerobic exercise intervention

There were differences in the CD4 counts between the control group and the intervention group after receiving aerobic exercise intervention. In the intervention group, the average CD4 count was 305.46, while in the control group, the average CD4 count was 303.38. A significant change in the CD4 cell counts after the aerobic exercise was indicated by a p-value <0.001.

Differences between the intervention and control groups

The analysis of differences in the mean values of CD4 counts between the control group and the intervention group showed that the CD4 count of HIV patients who received the aerobic exercise intervention increased significantly by 5.00 with a p-value <0.05. Meanwhile, in the control group who did not receive the aerobic exercise intervention, there was no significant change. The change was 0.57 with a p-value >0.05.

DISCUSSION

Aerobic Exercise on the Level of Depression

After the aerobic exercise intervention was carried out in the intervention group, the results of the tests showed that the depression level of HIV patients was significantly different. So, it could be concluded that aerobic exercise intervention was proven to be able to reduce depression levels in HIV patients. The results of this study are in line with the research conducted by Heissel et al. (2019) which showed that there were significant differences in the level of

depression before and after the intervention with a p-value of 0.000.

Andreany stated that there was an effect of aerobic exercise on the level of depression with a p-value of 0.0002, which means that it was significant for the level of depression. Physical exercise that is performed can increase endorphin activity. Increasing endorphins will strengthen the body's natural immunity and improve mood and encourage body activity. Psychologically, the ability to show movement during exercise will increase self-confidence and self-esteem which affects mood. Regular physical exercise can help with faster recovery from stressors, thereby decreasing depression symptoms (Al-Qahtani et al., 2018).

Conceptually, a stressful situation in an individual will stimulate the hypothalamus to release neuropeptides that will activate the ANS (Autonomic Nerve System) and the pituitary to secrete corticosteroids and catecholamine which are hormones that react to stressful conditions. Increased levels of glucocorticoids will interfere with the immune system which causes the CD4 to decrease and make individuals more susceptible to infections and health conditions.

Increased levels of glucocorticoids will interfere with the immune system which causes the patient's CD4 to decrease and makes the patient more susceptible to infection and worsening health conditions (Benton & Karnik, 2019). There are several ways to handle depression in patients, one of which is to provide training in the form of therapy, such as exercising and developing constructive copings to prevent depression in HIV patients (Safira et al., 2014).

Aerobic Exercise on the CD4 Counts

After the aerobic exercise intervention was carried out in the intervention group, the results of the tests showed that the CD4 count of HIV patients was significantly different. The results of this study are in line with research conducted by Dianatinasab et al. (2018) which showed the effect of aerobic exercise on increasing CD4 cell count (p<0.001).

Similarly, Yasirin et al. (2014) also stated in their study that there was an effect of aerobic exercise in the intervention group with a CD4 count of 1.7 cells / mm³. In the paper published by the Journal of the American Medical Association, it is stated that there is no drug now or in the future that promises to definitely provide and maintain health better than a habit of living constantly with exercises (Yasirin et al., 2014).

Metabolism is also related to endurance. Substances that function to maintain the stability of the body's immunity also come from the metabolic process. The results of protein metabolism function to maintain endurance. Protein substances come from foods that are eaten. The increase in CD4, which is part of the immune system, includes the impact of protein metabolism.

Aerobic exercise can increase metabolism in the body, including protein metabolism, so that it has an impact on the quality of the immune system. Immune system cells circulate rapidly in the body and there may also be a temporary boost in the production of macrophages - cells that attack bacteria. A decrease in CD4 cells from HIV sufferers who are not normal must be balanced with treatment in the form of drugs as well as exercise to increase metabolism in the body (Naoroibam et al., 2016). The results of this study prove the research hypothesis which states that giving aerobic exercise interventions can reduce depression levels and increase CD4 counts in HIV patients.

This study has limitations since it did not control for several confounding variables, such as other comorbidities or the use of drugs in HIV patients that may affect the patient's level of depression and CD4 cell count.

CONCLUSION

Based on the results of this study, it can be concluded that there is a significant change in the level of depression after the application of aerobic exercise between the control group and the intervention group with a p-value of < 0.05 . Similarly, there is a significant difference in CD4 cell counts between the intervention group and the control group after the intervention with a mean difference of 5.00 and 0.57, respectively. They were significant mean differences in the mean values of depression and CD4 counts between the intervention group and the control group before and after the intervention of aerobic exercises. Aerobic exercise had effects on reducing depression levels and increasing CD4 counts in HIV patients.

For the nursing profession it is recommended that nurses to be able to provide one alternative action, namely aerobic exercise in reducing depression levels and increasing CD4 cell counts. Nurses can increase their knowledge and skills by learning various non-pharmacological therapies as independent actions of nurses. Families can be involved in the exercise so that they can assist the patient in doing the exercise. For further researchers the results of this study can be used as a basis for further researchers to conduct more studies by controlling the confounding variables and adding a larger sample size with a longer period of intervention.

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