J Int Acad Phys Ther Res 2021; 12(1): 2295~2301
ISSN 2092-8475
www.iaptr.org
https://doi.org/10.20540/JIAPTR.2021.12.1.2295

Effects of Aerobic Exercise Variables on Production of Creatine Phosphokinase in Stroke Patients

Background: Physical therapy applied to stroke patients is recognized as a treatment that promotes function recovery, and it is a widely known fact that constant exercise should be performed. However, there are insufficient studies on exercise intensity and exercise time that can minimize side effects and maximize function recovery for exercise therapy.
Objectives: To determine the effect of exercise variables on CPK generation during aerobic exercise in stroke patients and to discover how to use appropriate exercise intensity and time when conducting an exercise for function recovery in stroke patients.
Design: Quasi-experimental research.
Methods: This study classified subjects into three groups (low-intensity exercise group: LIE, moderate-intensity exercise group: MIE and high-intensity exercise group: HIE) according to exercise intensity, and was further classified into two groups (10-minute exercise group: 10MG and 20-minute exercise group: 20MG) according to exercise time variables within each exercise intensity group. After, the change in CPK according to exercise intensity and time was confirmed through hematological analysis.
Results: In LIE and MIE, the CPK blood concentrations before and after exercise were increased in 10MG and 20MG, which was not statistically significant ($P>.05$). In HIE, the CPK blood concentrations before and after exercise were increased in 10MG, and it was statistically significant ($P<.05$). In HIE, the CPK blood concentrations before and after exercise were increased in 20MG, and it was statistically significant ($P<.01$). In 10MG and 20MG, the CPK blood concentrations before and after exercises were increased in all intensity group, and there was a statistically significant difference only in HIE.
Conclusion: From the results of this study, considering CPK, it will be helpful to recover and improve function if the exercise intensity setting is applied in the type of moderate intensity exercise during physical therapy interventions in stroke patients.

Keywords: *Creatine phosphokinase; Stroke; Aerobic exercise*

Youngdae Yun, PT, Prof., PhD[a]

[a]Department of Physical Therapy, Suwon Women's University, Suwon, Republic of Korea

Received : 20 January 2021
Revised : 22 February 2021
Accepted : 25 February 2021

Address for correspondence
Youngdae Yun, PT, Prof., PhD
Department of Physical Therapy, Suwon Women's University, 1098 Juseok-ro, Hwaseong-si, Republic of Korea
Tel: *** - **** - ****
E-mail: yydd1014@naver.com

INTRODUCTION

Stroke is one of the major causes of death in the world, and it can seriously cause death or disability at onset. After a stroke, rehabilitation exercises to minimize disability are critical. Stroke symptoms include muscle paralysis, weakness, and abnormal movement. There may also be limitations on function abilities, such as walking and climbing stairs.[1] Therefore, exercise for recovery and improvement of function after stroke is essential.[2]

Physical therapy for stroke can have different results depending on the intensity of treatment. However, there are studies showing that if high-intensity exercise is performed after a stroke, it has a negative effect on neurological recovery. In this regard, After inducing damage to the brain cortical area responsible for sensory movement of the rat's forelimb, the normal forelimb was fixed immediately after inducing overuse on the affected forelimb. As a result, the test showed a delay in function recovery after 2 weeks.[3] Some studies have reported increased damage to brain tissue and delayed recovery of function due to overuse after stroke.[4] As shown in the above studies, in order to maximize the effect of exercise after a stroke, it is recommended to exercise at the maximum possible intensity, but exercise with excessive intensity rather causes delay in function recovery. Therefore, it can be seen that when exercise is performed after a stroke, it is necessary to determine an appropriate exercise intensity for effective function recovery. Also, as a substance essential for supplying energy required for muscle activity during all exercises, the enzyme activity level is an important factor in exercise capacity, and these enzymes' activities change according to the type, intensity, and time of exercise.[5] The creatine phosphokinase (CPK) is the main enzyme that regulates the ATP-PC system among enzyme factors closely related to muscle activity CPK concentration in the blood increases during exercise as the cell membrane permeability increases due to intracellular hypoxia of muscle tissue and ATP depletion.[6,7] When muscle tissue is damaged during exercise, cell membrane permeability increases and CPK moves to interstitial fluid, resulting in a high blood concentration. Therefore, blood CPK concentration can be used as an index to estimate muscle damage.[8] This change in CPK activity in plasma is sensitive data on the efficient use of energy metabolism and is a good indicator of the effect of physical exercise.[9] Accordingly, studies on change in CPK activity according to exercise performance are being actively conducted in general adults and athletes. However, studies on changes in CPK activity according to variables, such as exercise intensity and time, in stroke patients who require a more careful approach toward exercise application are insufficient.

Therefore, in this study, by examining the effects of exercise intensity and time variables following aerobic exercise on CPK production in stroke patients, I propose an effective exercise method using appropriate exercise variables when applying exercise for function recovery.

SUBJECTS AND METHODS

Subjects

The studied subjects were 45 people who voluntarily wished to participate in the study through an announcement for patients admitted to Y hospital in S City and met the criteria for selecting subjects. The criteria for selection were medically diagnosed patients with stroke, and the onset period was within 6 months to 2 years. Subjects were selected with a K-MMSE score of 24 or higher, and those who can gait independently and those whose muscle tone on the affected side is less than 2 steps on the modified Ashworth scale. Subsequently, 30 subjects were finally selected through a cardiopulmonary function homogeneity test. The Ethics Committee and Institutional Review Board of Yong-in University approved this study (2-1040966-AB-N-01-20-2003-HSR-179-3).

Table 1. General characteristics of the subjects

	TENS (M ± SD)	[b]LIE (n=10)	[c]MIE (n=10)	[d]HIE (n=10)	*P*
Age (years)	[e]10MG	[a]50.40 ± 12.77	48.00 ± 8.71	49.60 ± 7.46	.927
	[f]20MG	55.20 ± 8.40	57.40 ± 9.23	58.60 ± 5.77	.880
	P	.503	.137	.235	
Height (cm)	10MG	158.60 ± 9.78	165.60 ± 7.16	168.20 ± 7.08	.196
	20MG	166.60 ± 7.98	162.80 ± 4.43	165.40 ± 6.76	.655
	P	.195	.479	.541	
Weight (kg)	10MG	57.40 ± 4.82	66.40 ± 3.36	65.40 ± 9.52	.093
	20MG	63.60 ± 11.01	59.80 ± 6.18	61.80 ± 9.47	.808
	P	.282	.069	.566	

[a]Values are presented as means±standard deviation, [b]LIE: low-intensity exercise group
[c]MIE: moderate-intensity exercise group, [d]HIE: high-intensity exercise group
[e]10MG: 10-minutes group, [f]20MG: 20-minutes group

Cardiopulmonary function homogeneity test

Forty–five subjects who agreed to participate in this study were tested for cardiopulmonary function homogeneity. Here, the heart rate was measured after exercising for 20 min at a speed of 2.6 km/h on a treadmill; subjects reaching 70-80% of the maximum heart rate (HRmax) were the final studied subjects. Heart rate was also measured using a heart rate monitor (Edge 800, Garmin Ltd, USA). The HRmax was calculated by subtracting the subject's age from 220 applied in the Karvonen method, and the heart rate and its maximum were compared. From the homogeneity test, 31 subjects were measured at 70-80% of the HRmax. However, for the convenience of classifying the study group, one subject was randomly dropped out, and 30 subjects were selected as the final studied subjects.

Classification of study groups

The studied subjects were divided into a low–intensity exercise group (LIE, n=10), a moderate–intensity exercise group (MIE, n=10), and a high–intensity exercise group (HIE, n=10) through randomized controlled trial. Within each exercise group, it was divided into a 10–minute exercise group (10MG, n=5) and a 20–minute exercise group (20MG, n=5) according to the variable of exercise time through randomized controlled trial. The general features of each group of subjects are shown in Table 1.

Intervention

The target heart rate range for determining the aerobic exercise intensity of the subjects of this study used the Karvonen method,[10] which calculates the target heart rate by multiplying the target exercise intensity by heart rate reserve and adding resting heart rate. Heart rate reserve is maximal heart rate minus resting heart rate; maximal heart rate is 220 minus age.

For the exercise intensity of each group, aerobic exercise was performed at 30-40% of the exercise intensity in the low–intensity exercise group, 50-60% in the moderate–intensity exercise group, and 70-80% in the high–intensity exercise group. Aerobic exercise was performed using a treadmill device.

While the 10–minute warm–up exercise and 10–minute main exercise were applied to the 10–minute group to maintain the target heart rate, 10–minute warm–up exercise and 20–minute main exercise were applied to the 20–minute group to maintain the target heart rate. Warm–up exercise started at a speed of 0.8Km/h, and the speed was increased by 0.2 Km/h per minute, and the exercise was continued until the target heart rate was attained. The main exercise was performed within the target heart rate range; during aerobic exercise, the subject could maintain the target heart rate using a portable heart rate monitor (Edge 800, Garmin Ltd, USA). The subject wore a heart rate sensor strap at the heart of the 3rd to 6th rib cartilage height, set the minimum target heart rate and the maximum target heart rate using a heart rate meter, and then performed the exercise to see the heart rate within the target heart rate range. A warning sound was set to sound when the subject exceeded the target heart rate range when performing an exercise. When the warning sound was heard, a physical therapist intervened to adjust the treadmill movement speed to maintain the target heart rate.

Outcome measures

The subjects' first blood sample was collected by a nurse the day after the homogeneity test, and the second blood sample was collected after the intervention. The amount of blood collected for one blood analysis was 5ml, and the blood was collected twice in total by a nurse from the median cubital vein. The blood was centrifuged at a speed of 2500 to 3000 rpm for 15 to 20 minutes using a centrifuge. Only the part necessary for the test was extracted with a serum separation tube, and the CPK blood concentration was measured using a slide–type dry biochemical analyzer (DRI–CHEM NX500i, Fusifilm Corporation, Japan).

Statistical analysis

SPSS 20.0 (SPSS Inc., Chicago, Illinois) was used for statistical analysis. The normality test was analyzed using the Shapiro–Wilk method, and the homogeneity test was analyzed using one–way ANOVA and independent t–test. The comparison of the difference before and after the intervention within each exercise time group by exercise intensity was analyzed using a paired t–test. The comparison between exercise time groups by exercise intensity was analyzed using an independent t–test. The comparison between exercise intensity groups by exercise time was analyzed using one–way ANOVA. Post–hoc analysis was analyzed using the Scheffe test. The significance level was set at .05.

RESULTS

Changes in CPK in LIE regarding exercise time

In LIE, the CPK blood concentrations before and after exercises were increased in 10MG and 20MG and were not significant ($P>.05$). The difference between the two groups of 10MG and 20MG was not also significant ($P>.05$) (Table 2).

Changes in CPK in MIE regarding exercise time

In MIE, the CPK blood concentrations before and after exercises were increased in 10MG and 20MG and were not significant ($P>.05$). The difference between the two groups of 10MG and 20MG was also not significant ($P>.05$) (Table 2).

Changes in CPK in HIE regarding exercise time

In HIE, the CPK blood concentrations before and after exercise were increased in 10MG and 20MG. The CPK in 10MG increased from 96.20±24.27 IU/ℓ to 115.80±32.86 IU/ℓ and was significant ($P<.05$). The CPK in 20MG increased from 104.60±17.12 IU/ℓ to 143.00±20.21 IU/ℓ and was significant ($P<.01$). The difference between the two groups of 10MG and 20MG was also not significant ($P>.05$) (Table 2).

Changes in CPK in 10MG regarding exercise intensity

In 10MG, the CPK blood concentrations before and after exercises were increased in all intensity groups. There was a statistically significant difference only in HIE ($P<.05$). The difference between the three groups of exercise intensity was not significant ($P>.05$, Figure 1).

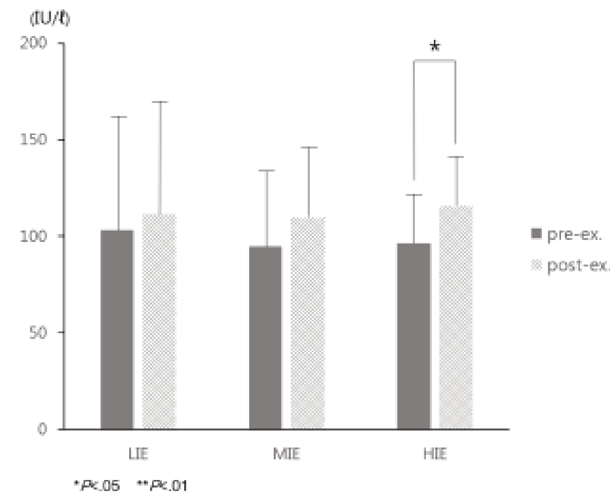

Figure 1. Changes in creatine phosphokinase in 10-minute exercise group

Table 2. Changes in creatine phosphokinase in the exercise group (IU/ℓ)

		Pre-Exercise	Post-Exercise	t	P
[b]LIE	[e]10MG	[a]103.20 ± 63.79	111.40 ± 65.57	-.650	.551
	[f]20MG	108.20 ± 47.61	118.60 ± 52.86	-2.065	.108
	t	-.162			
	P	.875			
[c]MIG	10MG	94.60 ± 39.86	109.80 ± 35.54	-1.939	.124
	20MG	100.20 ± 41.24	136.80 ± 44.26	-2.477	.068
	t	-1.206			
	P	.274			
[d]HIG	10MG	96.20 ± 24.27	115.80 ± 32.86	-3.587	.023*
	20MG	104.60 ± 17.12	143.00 ± 20.21	-5.120	.007**
	t	-2.026			
	P	.077			

*$P<.05$, **$P<.01$

[a]Values are presented as means±standard deviation, [b]LIE: low-intensity exercise group

[c]MIE: moderate-intensity exercise group, [d]HIE: high-intensity exercise group

[e]10MG: 10-minutes group, [f]20MG: 20-minutes group

Changes in CPK in 20MG regarding exercise intensity

In 20MG, the CPK blood concentrations before and after exercises were increased in all intensity groups. There was a statistically significant difference only in HIE ($P<.01$). The difference between the three groups of exercise intensity was not significant ($P>.05$, Figure 2).

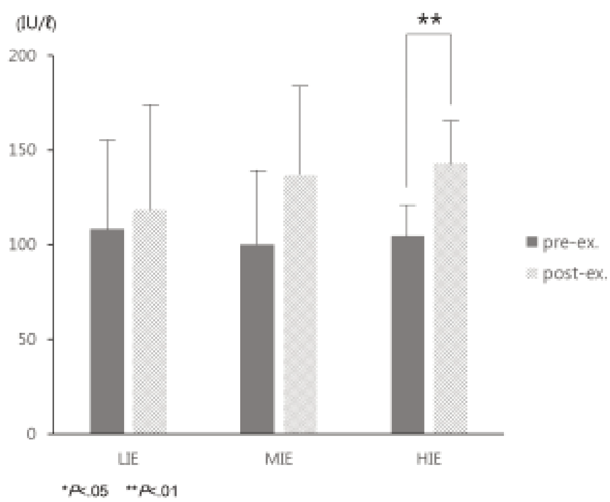

Figure 2. Changes in creatine phosphokinase in the 20-minute exercise group

DISCUSSION

Physical therapy for stroke patients aims at maximizing the patient's potential for functional recovery and minimizing the possibility of secondary disorders. Components of a physical therapy exercise program should include the type, frequency, intensity, and time of the exercise.

Typical types of aerobic exercise include cycling, treadmill, and walking. Exercise intensity should be an appropriate exercise stimulation so that the HRmax will be 60-85% and the maximum oxygen uptake (VO_2max) will be 50-80% at a frequency of 3-5 days per week. Exercise time varies regarding the intensity and frequency of exercise.[11] This exercise intensity is an important factor in achieving a physical therapy effect. Appropriate exercise intensity increases the activity of the motor cortex of the brain, which can improve the activities of daily living movements, improve functional ability, and shorten hospitalization. There is a certain correlation between stroke and exercise intensity.[12] In some previous studies, studies on the generation of metabolites were conducted by organizing an exercise program for the public or athletes. However, there are insufficient studies to suggest an appropriate exercise program composition by analyzing metabolic changes regarding exercise intensity and time variables in stroke patients. Therefore, this study classified subjects into three groups regarding exercise intensity, and were further classified into two groups regarding exercise time variables within each exercise intensity group. Subsequently, the change in CPK regarding exercise intensity and time was confirmed through hematological analysis. Changes in CPK activity increased not only in anaerobic exercise but also in aerobic exercise. Serum CPK activity in skeletal muscle was also increased by exercise. In particular, it is used as an index of muscle damage during high-intensity exercise.[13]

In this study of stroke patients, the CPK blood concentration increased in the 10- and 20-munite exercise groups in the low-intensity and moderate-intensity exercise groups, but was not significant. In the high-intensity exercise group, there was a significant difference before and after exercise in the 10- and 20-minute exercise groups. However, the difference between the exercise time groups within the high-intensity exercise group was not significant. Seifi-Skishahr has reported that as a result of performing aerobic exercise at medium- and high-intensity in the general population, CPK was significantly increased in high-intensity exercise after exercise compared to that in rest.14 It was consistent with the results of this study in stroke patients. Considering this, it is believed that CPK of stroke patients is more affected by exercise intensity than exercise time. Also, Nuttal et al. reported that the CPK concentration measured after applying resistance exercise for 6 minutes in the general population exceeded that of stability.8 This result showed that CPK was elevated even with exercise for a relatively short time. In this study of stroke patients, the CPK concentration increased after high-intensity exercise in both the 10- and the 20-minute exercise groups. Although the types of exercise differed, the results agreed with previous studies. The normal range of CPK blood concentration was 55 to 215 IU/ℓ, and it was also found that the CPK blood concentration measured after exercise did not exceed the normal range. It can be inferred that the exercise was performed within a range that did not damage the subject's muscle tissue with an appropriate study design. From the above results, it is thought that when aerobic exercise is applied to stroke patients, the change in CPK blood concentration will be more affected by exercise intensity than exercise time.

However, some studies have shown that guidelines for high CPK blood levels above 200 IU/ℓ outside the normal limit do not apply to all groups. Most CPK in the blood is transmitted from the muscles, and the CPK in the brain is rarely transmitted into the blood; therefore, people with a large amount of muscle may have high levels of CPK in the blood.[15,16] Also, some studies have reported that the normal threshold for CPK should be set to 325 IU/ℓ for white women, 504 IU/ℓ for white men, 621 IU/ℓ for black women, and 1200 IU/ℓ for black men.[17] Furthermore, blood CPK may increase depending on the intensity or amount of exercise alongside sudden stretch exercise that is unfamiliar. This is not usually a familiar exercise and is closely related to muscle damage.[18] It can be inferred that this study was conducted in a familiar environment for in-patients, and the results were within the normal range.

This study was unable to control the brain injury site, type of injury, and degree of injury in stroke patients, and did not control the daily life variables such as individual medication, daily life habits, and physical activity of the subjects. This study compared changes in CPK with exercise variables such as exercise intensity and exercise time as a one-time exercise. In the future, if various data are accumulated through research, such as exercise period or recovery time after exercise, it will be considered as clinically meaningful data.

CONCLUSION

From the above results, it was found that high intensity exercise requires attention due to an increase in CPK during physical therapy intervention in stroke patients, and the method applied in the type of moderate intensity long time exercise is appropriate exercise intensity.

REFERENCES

1. Sharp SA, Brouwer BJ. Isokinetic strength training of the hemiparetic knee: effects on function and spasticity. *Arch Phys Med Rehabil*. 1997;78(11):1231-1236.
2. Hobbs B, Artemiadis P. A review of robot-assisted lower-limb stroke therapy: unexplored paths and future directions in gait rehabilitation. *Front Neurorobot*. 2020;15:14-19.
3. Kozlowski DA, James DC, Schallert J. Use-dependent exaggeration of neuronal injury after unilateral sensorimotor cortex lesions. *J Neurosci*. 1998;16:4776-4786.
4. Humm JL, Kozlowski DA, James DC, et al. Use-dependent exacerbation of brain damage occurs during an early post-lesion vulnerable period. *Brain Res*. 1998;783:286-292.
5. Wilmore JH, Costill DL. Physical energy: fuel metabolism. *Nutr Rev*. 2001;59:13-16.
6. Stansbie D, Aston JP, Dallimore NS, et al. Effect of exercise one plasma pyruvate kinase and creatine kinase activity. *Clin Chim Acta*. 1983;132(2):127-132.
7. Leeuwenburh C, Heinecke JW. Oxidative stress and antioxidants in exercise. *Curr Med Chem*. 2001;8(7):829-838.
8. Nuttal FQ, Jones B. Creatine kinase and glutamic oxaloacetic transminase activity in serum: kinetics of change with exercise and effect of physical conditioning. *J Lab Clin Med*. 1968;71(5):847-854.
9. Brancaccio P, Maffulli N, Limongelli FM. Creatine kinase monitoring in sport medicine. *Oxford J Med & Health British Med Bulletin*. 2007;82(1):209-230.
10. Karvonen J, Vuorimaa T. Heart rate and exercise intensity during sports activities. Practical application. *Sports Med*. 1988;5(5):303-311.
11. Kollen B, Kwakkel G, Lindeman E. Functional recovery after stroke: a review of current developments in stroke rehabilitation research. *Rev Recent Clin Trials*. 2006;1(1):75-80.
12. Page SJ. The role of timing and intensity of rehabilitation therapies. *Top Stroke Rehabil*. 2006;13(1):8-9.
13. Ratamess NA, Kraemer WJ, Volek JS. Effects of heavy resistance exercise volume on post exercise androgen receptor content in resistance trained man. *J Steroid Biochemical Moles Biology*. 2005;93:35-42.
14. Seifi-skishahr F, Siahkohian M, Nakhostin-roohi B. Influence of aerobic exercise at high and moderate intensities on lipid peroxidation in

untrained men. *J Sports Med Phys Fitness*. 2008;48(4):515–521.
15. Brancaccio P, Maffulli N, Limongelli FM. Creatine kinase monitoring in sport medicine. *Br Med Bull*. 2007;82(1):209–230.
16. Kwon YW, Ko SK. The effect of different intensity with acute isocaloric exercise on inflammatory factors and CK in mentally retarded obese population. *Kor J Sports Sci*. 2012;21(2):1085–1096.
17. Moghadam–Kia S, Oddis CV, Aggarwal R. Approach to asymptomatic creatine kinase elevation. *Cleve Clin J Med*. 2016;83(1):37–42.
18. Gleeson M, Almey J, Brooks S, et al. Hematological and acute phase responses associated with delayed–onset muscle soreness in humans. *Eur Appl Physiol Occup Physiol*. 1995;71:137–142.