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THE COMPARISON OF EFFECT OF HIGH INTENSITY INTERVAL TRAINING COMPARED TO AEROBIC TRAINING ON SERUM LEVELS OF SOME OF STRESS-ACTIVATED PROTEIN KINASES AND GLUCOSE IN TYPE II DIABETIC MEN WITH PERIPHERAL NEUROPATHY

Hamideh Moamen Kahkha,Mahtab Moazami*,Najmeh Rezaeian

Deartment of physical education and sport sciences,bojnourd Branch,Islamic azad university,bojnourd,iran
Email: mikaeel.sepehrzadeh1397@gmail.com
Mahtab Moazzami*(Phd),Associate Professor of sport sciences ,university of Ferdowsi mashhad,mashhad,iran
Email:mahtab.moazami@gmail.com,moazami@um.ac.ir
Najmeh Rezaeian(Phd),Faculty of sport sciences,university of bojnourd,bojnourd,iran.
Email: Rezaeian.n@gmail.com
Address for correspondence:
Mahtab moazzami
Associate Professor of sport sciences ,Department of sport sciences,ferdowsi university of mashhad,iran

Abstract:
Aim: Sensitive peripheral neuropathy is one of the most common complications of type 1 and type 2 diabetes as a sign of progression of the disease. Extracellular signal-regulated kinases (ERK) and p38 and of course JNK are MAPKs that are involved in the development of neuropathic pain and induce pain sensitivity.therefore, the present study aimed to investigate and compare the effect of high intensity interval training and aerobic exercise on some of Stress-Activated Protein Kinases such as p38 and NF-Kβ,JNK and glucose in type II diabetic men with peripheral neuropathy.
Methods: This research is fundamental in purpose and in terms of empirical data collection. The number of patients were36people .this research has done in zahedan. Subjects randomly divided into three groups of intensity interval training and aerobic exercise and one control group. Subjects presentedm at the protocol site prior to the start of the exercise program for some initial assessments and measurements.**Results:** The normality of the data distribution has done by k-s and ANOVA with repeated measures was used to study the significant differences between groups . Data analysis was performed using SPSS software version 21 .**Conclusion:**The results showed that the positive effect of exercise on studied factors although,the intense interval training is more effective.
Key words: Stress-Activated Protein Kinases, glucose,NFKB,P38,JNK,high intensity interval training.

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Introduction:

Mitogen-activated kinase protein (MAPK), a member of the serine / threonine kinase family, is activated following the double defrilization of threonine and residual tyrosine. Various actions have been identified for MAPK. For example, MAPKs have a regulatory effect on the metabolism of macro nutrients such as carbohydrates (35). In addition, MAPKs play a central role in guiding intracellular and extracellular stimuli and causing pain sensitivity (35). Extracellular signaling kinases (ERK) and P38, and of course JNK, are among the MAPKs involved in neuropathic pain and pain sensitivity. MAPKs are activated in neuropathic pain models and, following environmental neurological damage, occur at the spinal level of ERK phosphorylation (8) and P38. Neuropathy is a common complication associated with diabetes (33). In type 2 hyperglycemia and increased free fatty acids, they can stimulate the production of active oxygen species (ROS) in mitochondria and activate stress-sensitive signals such as stress-activated kinase protein (SAPK). JNK and P38 and the (NF-Kβ) are the most important ROS-sensitive SAPK proteins. Activation of these signaling pathways is mediated not only by beta-cell dysfunction (25), but also by insulin depletion of the Insulin Receptor Substrate-1 (IRS-1) and the reduction of proteins involved in the signal pathway (5). NF-KB is a nuclear transcription factor that is found in all types of cells and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet radiation, and bacteria and antigens. Before the discovery of NF-KB, it was found that high salicylate doses reduced hyperglycemia in type 2 diabetes (28). The development of insulin resistance and type 2 diabetes then plays an anti-inflammatory factor, aspirin inhibits it (37). Activation of NF-KB involves a regulatory pathway that triggers the inflammatory process and increases nuclear transmission in diabetic neuropathic individuals Leukocytes in diabetic patients may be activated at the end of advanced screening. Leukocytes can release superoxide radicals and proteases, all of which are oxidizing, can then activate NFKB transcription in peripheral single-celled cells (14). Because sedentary lifestyle is one of the effective mechanisms in activating MAPKs and this protein, stress-activated kinases (34) and the role of physical activity and exercise in improving insulin sensitivity is clear; Therefore, physical activity and exercise may be an effective treatment for neuropathy in patients with type 2 diabetes.. It has been accepted that long-term exercise can be achieved by increasing glucose transporters (GLUT4 into the cell). Muscle and insulin-induced substrates (IRS) as well as increased muscle mass more than 75% of glucose uptake due to muscle tissue-related insulin stimulation increase the body's response to insulin and increase insulin sensitivity and in preventing obesity and complications Exercise increases muscle glucose uptake, which depends on functional changes in signaling (21). Increased levels of physical activity can improve blood sugar control and cardiorespiratory fitness in T2D patients. Traditional exercise guidelines are likely to focus on moderate to low-intensity exercise because activities such as walking are easy and relatively safe. However, such activities are the most common because they are the basis of a healthy and active life (10), which most people with type 2 diabetes do not describe (9). This is especially true for patients with type 2 diabetes, who have evidence that their chosen walking speed during exercise may be too low to achieve key health indicators (17). Therefore, more intense exercise-controlled exercise may be the most effective means of improving cardiorespiratory fitness and lowering blood sugar in type 2 diabetes. (18).

For a long time, performing aerobic exercises with low or medium intensity has been a desirable method for fat burning and weight loss (1). In this regard, the American Diabetes Association emphasizes the implementation of at least 150 minutes of moderate-intensity aerobic exercise, three days a week to lose weight, improve glucose control and reduce the risk of cardiovascular

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disease (29). In recent decades, small but intense intermittent exercises have become very popular among the people. Intense periodic exercises are quick and effective exercises. Because, in a shorter period of time.

However, according to research, no studies have ever compared the effects of intense high interval training and aerobic exercise on changes in protein kinases activated by stress JNK, P38 and NF-Kβ. Therefore, the present study aims to investigate and compare the effect of intense and aerobic exercise on serum levels of JNK, P38 and NF-Kβ and glucose in men with type 2 diabetes and neuropathy.

Methods:

After initial coordination with Zahedan Diabetes Association centers for conducting the research work, as well as information disseminated throughout the city, information were invited to qualify. Candidates were invited on a specific day and after providing a full explanation of the research process and the benefits and risks of the study and obtaining consent to participate in the present study, This study were conducted after completing the Health Assessment Questionnaires and daily physical activity and physical activity readiness for diabetic patients aged 45-55 years with neuropathic complications. This information were obtained from the medical records of the patients. The number of patients were determined according to the results of the pilot study. Subjects were randomly divided into three groups of high interval training 1 and aerobic exercise and one control group. Subjects were present at the site of the protocol prior to the implementation of the training program for some initial assessments and measurements, and in the pretest. Initial evaluations include: Anthropometric indices such as: height, weight, body mass index and body fat percentage Determine the maximum heart rate of each person using the formula (Age × 0.7- 208) (32). In order to learn how to implement training protocols and to control the familiarity factor on performance and performance, subjects participated in two sessions of relevant exercises before the start of the training period (3). The first blood sampling were performed one day before the beginning of the training period at 12- hour fasting to measure baseline (pre-intervention) blood levels in 3 groups. Workout intensity was assessed and assessed using a 10-point Borg scale and heart rate control (using a Polar Pacemaker). During the study, the subjects in the control group did not participate in any organized exercise program.forty-eight hours after the last training session, blood samples were taken again in three groups to measure blood and anthropometric indices after the end of the training period. Evaluation of blood factors evaluated using appropriate kit .

Training protocol: The training protocol implemented in the training group is as follows: Subjects in the high intensity interval group, after warming up for 5 minutes, participated in the intense running exercises. Severe intermittent exercise consisted of one minute running at 90-95% of maximum heart rate and 1-3 minute resting intervals at 50-60% of maximum heart rate. At the end of each session, 5 minutes of exercise were allowed to cool. The training protocol was administered three times in a week, in the morning for twelve weeks (12). The aerobic training group perform aerobic exercise for three sessions per week. Exercises will consist of three parts: warm-up (static and dynamic stretching for 5 minutes), aerobic exercise protocol, running and cooling (stretching for 5 minutes). In the first session, aerobic exercise is performed for 5 minutes at 40-50% of maximal heart rate and gradually increases to40 minutes at 2 minutes by 60 to 70% of maximal heart rate (31).After evaluating the number of subjects, appropriate statistical test were used to evaluate the natural distribution of the data. Analysis of variance

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(ANOVA) with repeated measures were used to study the significant differences between groups. Data analysis were performed using SPSS software version 21.

Results:.

Given the significance level of 0.001, which is less than 0.05, the null hypothesis is rejected: that is, between the effect of 12weeks of high intensity interval training and aerobic exercise on serum JNK ,p38.nfkb,and glucose levels in men with type 2diabetes, there is a significant difference. The Tuki tracking test is now being used to find out.

Table1: :anova for analysis of NF-Kβ,p38,jnk and glucose

variable	variable	Sum f squars	df	Mean square	f	sig
P38	Between groups	30865/500	2	15432/750	99/427	0/001
	Within groups	6509/500	33	197/258		
	total	37537	35			
jnk	Between groups	237/359	2	118/679	10/528	0/001
	Within groups	372/014	33	11/273		
	total	609/373	35			
NF-KB	Between grous	106/85	2	42/553	31/66	0/001
	Within groups	44/346	33	1/344		
	total	129/452	35			
glucose	Between groups	۳۴۲۸۶	2	171/43	112/91	0/001
	Within groups	5010	33	151/81		
	total					

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Table 2:Tukey were used clarifying differences between groups in glucose,p38,jnk,nfkb.

variable	groups	Mean Difference	SD	SIG
P38	cont rol - high intensi trainin g	71/25	5/73	0/001
	Control-aerobic	42/75		0/001
	High intensity interval training - aerobic	28/50		0/003
jnk	Control-high intensity interval trining	2/61	1/37	0/001
	Control-aerobic	3/64		0/012
	Aerobic-gigh intensity interval training	6/26		0/001
Nf-kb	Control-high interval training	3/13	0/473	0/001
	Control-aerobic	3/37		0/001
	Aerobic-gigh intensity	2/32		0/001

	interval training			
.Glucose	Control-high interval training	71/50		0/001
	Control-aerobic	57	5/03	0/001
	Aerobic-high intensity interval training	50/14		0/001

The results of this table show that the effect of 12 weeks of high intensity interval training on serum JNK ,p38.nfkb,and glucose levels in men with type 2 diabetesis more effective.

Discussion:

AMPK is an enzyme that acts as a fuel gauge. As phosphorylation of the kinase protein ion activated by AMP (AMPK increases glucose transport in the plasma membrane), which leads to improved glucose uptake into skeletal muscle). Activation of AMPK improves insulin sensitivity and glucose homeostasis in muscle tissue .Since muscle is the main site of glucose consumption, it seeks to stimulate insulin, thus impairing insulin sensitivity throughout the body (15). Exercise stimulates the transfer of GLUT4 to the plasma membrane. And glucose transporters increase in skeletal muscle. (7) .Exercise increases the amount of glycogen stores in the muscles as well as increases insulin sensitivity (Howley, 2008,). In this regard, several studies have reported that aerobic and resistance exercise increases GLUT4 protein in healthy and diabetic subjects (7,6). Also, preventing the expression of this protein during exercise inhibits the improvement of insulin-induced glucose transfer. Therefore, increasing GLUT4 protein to improve muscle insulin resistance. (16) In a recent study, Afzalpour et al. (2016) concluded that aerobic exercise continued to improve insulin resistance by increasing GLUT4 .n addition, in the study Recently, Mohebbi et al. (24) also reported that regular running on a treadmill with moderate to high intensity in obese mice increased the expression of GLUT4 gene in both muscles and slowed down the contraction (24). They also stated that this increase is dependent on the intensity of activity and means that It is possible that severity could affect gene expression and possibly GLUT4 protein, and this effect may be due to metabolic changes (24). As the overall level of hyperactivity and metabolic syndrome increases, interest in using HIIT training protocols for patients with Type 2 diabetes also increases. Growing evidence suggests that comparable improvements or even superiority in skeletal muscle metabolic adaptation, cardiovascular fitness, vascular function, and body composition are the result of HIIT training (20)moreover, when Exercise with different intensities will have the same muscle capacity as GLUT4 carriers, which is due to the fact that higher intensity training increases the need for glucose in the active muscle as a supplier of more energy and more accessible than fat.In connection with the effect of HIIT and aerobic exercise on serum glucose levels, we saw a decrease after these exercises, although

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the average decrease was more in the HIIT group, which is in line with the findings), Mohammad Rahimi et al. (23) Ramezani et al. (27) Yang et al. (36).In connection with the effect of HIIT and aerobic exercise on JNK levels, we saw an increase after these exercises, although the average increase was more in the group of HIIT, which is in line with the findings of Purvez et al. (26), Lawrence et al. (19), DiGraf et al. (21). The study found that between 12 weeks of HIIT and aerobic exercise on P38 serum levels There is a significant difference in men with type 2 diabetes and peripheral neuropathy, we saw an increase after these exercises However, the average increase was greater in the HIIT group, which was in line with the findings of), somvar (30), Yu (38), Lawrence et al. (19), but is not consistent with the results of purvez et al. (26), which may be the reason for the difference in the type of subjects.

In relation to the effect ofHIIT and aerobic exercise on NFKB serum levels, we saw an increase after these exercises, although the average increase was more in theHIIT group, which is in line with the findings of Anoush (4), Fashi (10),) are consistent.

Conclusion: Since inactivity is one of the effective mechanisms of activation of MAPKs and these stressactivated protein kinases (34), the role of physical activity and exercise in improving insulin sensitivity is also clear; therefore, physical activity and Exercise can be an effective therapeutic strategy for improving neuropathy in patients with type 2diabetes. The results of this study showed a positive effect of exercise on NF-Kβ, p38,JNK and glucose in patients with type 2 diabetes.

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