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*Original scientific paper*

# Influence of Physical Exercise Program on Glycemic Status and Inflammatory Parameters in Type 2 Diabetes Mellitus

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**ABSTRACT: Introduction:** Physical activity has a positive effect on the regulation of diabetes mellitus and has been shown to have benefits in improving health. **Aim:** Examine the effects of physical activity on changes in glycemic parameters (glucose, HbA1C) and inflammatory parameters (leukocyte count (WBC), CRP) before and one month after the exercise program. **Material and Methods:** The study was designed as a prospective, analytical, and observational study. **Results:** T-test of paired samples assessed the impact of physical activity on glycemic and inflammatory parameters in subjects with confirmed Diabetes mellitus type 2 and in subjects without confirmed diabetes mellitus type 2. In subjects with confirmed diabetes the value of eta squared (η2 - eta sqared) is 95%, which indicates a significant impact of physical activity on the change in glucose values and on the change of HbA1C value was indicated by the value of eta square of 93%. When it comes to inflammatory parameters, the impact of physical activity was found in the reduced number of WBC (η2 = 88%), and in CRP (η2 = 90%). In subjects without confirmed diabetes mellitus, a significant effect of physical activity on the change in glucose (η2 = 94%) and HbA1C (η2 = 77%). The influence of physical activity on the reduction of leukocyte count was proven by η2 - eta sqared test (η2 = 66%), as well as a decrease in CRP (η2 = 30%). **Conclusion:** This study showed a significant impact of physical activity on the reduction of elevated glycemic and inflammatory parameters.

**Keywords:** Diabetes Mellitus type 2, Leukocyte Count, Glycated Hemoglobin A, Physical Activity.

## INTRODUCTION

Physical activity is necessary to maintain adequate blood glucose levels and to maintain overall health in people with diabetes and prediabetes (Šulevski & Kocijan, 2019). Blood glucose levels are lowered by the action of insulin and a mechanism independent of insulin, muscle activity. Muscle contraction can increase the transport of glucose into muscle by moving the GLUT -4 type protein carrier from inside the cell to the cell membrane. Physical activity increases the permeability of the membrane to glucose by increasing the incorporation of GLUT -4 glucose into the cell membrane (Šulevski, 2019). Physical activity has many benefits when performed regularly and at moderate intensity. People with diabetes can engage in all forms of physical activity, but with caution (Šulevski & Kocijan, 2019). Decreased insulin and the presence of glucagon are necessary for an early increase in glucose production during physical activity, and increases in plasma glucagon and catecholamine levels play a central role during prolonged physical activity (Djukanovic, Raznatovic & Jovanovic, 2010). At the onset of activity, glycogen stores are abruptly depleted by the synthesis of lactate, with vasodilation, increased blood flow to the muscles, and utilization of glucose from the blood occurring after a few minutes. Lipolysis is activated and releases free fatty acids and glycerol.

The amount of glucose and fatty acids consumed depends on the type of physical activity, its intensity and duration. The longer the activity, the more important carbohydrates are as an energy source (Baretić, 2017). The ability to perform physical activity depends on the extent to which it is possible to maintain an adequate supply of oxidative substrate in muscle, or in layman's terms, to "provide fuel." The energy available to muscles can be that of fat and glucose. During moderate activity, muscles use mostly fat for fuel, and as the intensity of the activity increases, muscles use more and more glucose. Very intense activity can only be sustained if enough glucose is available for the muscles used in the exercise. When muscle glycogen is depleted, exhaustion occurs, and under these conditions the intensity of exercise must be reduced (Karas, 2014). Physical activity is the first choice in the treatment of type 2 diabetes mellitus because of its effect on metabolic disorders and its ability to modulate acute and chronic inflammatory conditions (Pedersen BK, 2009).

Possible mechanisms that could link inflammation and type 2 diabetes mellitus include disruption of insulin signaling in the liver by inflammatory molecules or proinflammatory effects on insulin or insulin resistance (Gkrania-Klotsas et al, 2010). Inflammation of central adipose tissue leads to the production of adipokines, whose release into the general circulation contributes to the overall inflammatory state (Elks CM & Francis J, 2010). The influence of physical activity on inflammatory parameters is of interest to many researchers. They explain the general inflammatory response as a consequence of the immune response to high blood glucose levels and the presence of inflammatory mediators produced by adipocytes and macrophages in adipose tissue (Berbudi, Rahmadika, Tjahjadi & Ruslami, 2020). Subclinical systemic inflammation can be detected by an increase in high-sensitivity C-reactive protein (hs-CRP) and is associated with the development of type 2 diabetes mellitus (Effoe, Correa, Chen, Lacy & Bertoni, 2015). High-sensitivity CRP is the inflammatory marker that is most widely used. A small increase in CRP increases the risk of developing cardiovascular disease in diabetics, while it indicates an increased risk of developing diabetes in healthy individuals (Ridker PM & Silvertown JD, 2008). If we talk about the role of increased leukocyte count, it is associated with the development of macrovascular and microvascular complications in type 2 diabetes mellitus, because chronic inflammation leads to increased production of cytokines and reactants in the initial phase and activation of inflammatory signaling networks (Pradhan, Manson, Rifai, Buring & Ridker, 2001). The aim of study was examine the effects of physical activity on changes in glucose, HbA1C, leukocyte count (WBC), and CRP before and one month after the exercise program.

## MATERIALS AND METHODS

We conducted the research on a sample of 60 respondents who are beneficiaries of the Center for Health Promotion and Improvement "Generation" health program. The respondents are members of the third age. Written informed consent was obtained from all subjects. Then, they were divided into 2 groups: a group of subjects with confirmed diabetes and a group of subjects without confirmed diabetes. We included subjects aged 65 to 75 years in the study and excluded subjects who were younger than 65 years and had comorbidities. The study was designed as a prospective, analytic, and observational study. Duration of the research process was from March to November 2018. Laboratory parameters of interest observed before the start of the exercise program and one month after the exercise program were: Glucose level, HbA1C, leukocyte count (WBC), and CRP. The exercise program included exercises performed 5 times per week for 30 minutes over a period of 2 months. The basic and most important goal of the exercises is to restore full function of the entire musculoskeletal system, i.e., the locomotor system. The group exercise programs include: Breathing exercises (abdominal and thoracic), exercises to maintain coordination, balance, and equilibrium, exercises to improve circulation, strengthen the upper and lower extremities, stretching ex-

ercises, and exercises for precision of fine motor skills. All respondents were educated on the benefits and proper execution of the exercises.

## RESULTS AND DISCUSSION

The study included 83.33% of female subjects and 16.67% of male subjects in the group of subjects with confirmed diabetes and 80% of female subjects and 20% of male subjects in the group of subjects without confirmed diabetes. According to statistics, the average age in the group of respondents with confirmed diabetes was 69 years, while the oldest respondent was 73 years old and the youngest respondent was 68 years old. The average age in the group of respondents without confirmed diabetes was 66 years old, while the oldest respondent was 71 years old and the youngest was 65 years old.

The effect of physical activity on measured glycemic and inflammatory parameters (glucose, HbA1C, WBC, CRP) was assessed by paired-samples T-test in subjects with confirmed type 2 diabetes mellitus and in subjects without confirmed diabetes.

We observed a statistically significant decrease in certain parameters in subjects with confirmed diabetes (Table 1). Glucose values before physical activity were M=12.58 mmol/L (SD =1.94) and after physical activity were M=5.09 mmol/L (SD =0.66), t(29)=25.63, $p < 0.001$ (two-sided), and the mean decrease in value was 7.48 with a 95% confidence interval (6.88-8.08). The value of eta squared (η2-eta squared) is 95%, indicating a significant effect of physical activity on the change of glucose values. The HbA1C level was M=10.49% before physical activity (SD =1.39) and M=5.58% after physical activity (SD =0.39), t(29)=19.65, $p < 0.001$ (two-sided), with an average reduction of 4.91 and 95% confidence interval (4.38-5.42). The significant effect of physical activity on the change of HbA1C value was indicated by the value of eta square of 93%. The number of leukocytes (WBC) before physical activity was M=13.24 x 109/L (SD =1.89) and after physical activity was M=7.06 x 109/L (SD =1.24), t(29)=15.15, $p < 0.001$ (bilateral) with a mean decrease of 6.17 with 95% confidence interval (5.34-7.01). The significant influence of physical activity on the change of WBC values is indicated by the Eta square in the value of 88%. CRP values before physical activity were M=33.35 mg/dL (SD =10.20) and after physical activity were M=3.89 mg/dL (SD =0.90), t(29)=16.47, $p < 0.001$ (bilateral) with a mean decrease of 29.46 with 95% confidence interval (25.80-33.12). The significant effect of physical activity on CRP level is evidenced by the eta square of 90% (Table 1).

**Table 1:** Influence of physical activity on the values of glycemic and inflammatory parameters before and after one month of application of the physical activity program in subjects with confirmed diabetes mellitus type 2.

| Parameter | Time | Mean | St. dev. | η2 |
|---|---|---|---|---|
| Glucose (mmol/L) | Before | 12,58 | 1,95 | 95% |
| | After | 5,09 | 0,67 | |
| HbA1C (%) | Before | 10,49 | 1,40 | 93% |
| | After | 5,58 | 0,40 | |
| WBC (109/L) | Before | 13,24 | 1,89 | 88% |
| | After | 7,06 | 1,25 | |
| CRP (mg/dL) | Before | 33,36 | 10,20 | 90% |
| | After | 3,89 | 0,90 | |

We observed a statistically significant decrease in certain parameters in subjects without confirmed diabetes (Table 2). The glucose value before physical activity was M=8.25 mmol/L (SD =0.91) and after

physical activity was M=4.31 mmol/L (SD =0.48), t(29)=21.91, p < 0.001 (two-sided) with a mean decrease of 3.94 and 95% confidence interval (3.57-4.30). The significant effect of physical activity on the change in glucose levels was confirmed by the Eta square, which was 94%. The HbA1C value obtained before physical activity was M=7.36% (SD =1.14) and after physical activity was M=4.89% (SD =0.73), t(29)=9.88, p < 0.001 (two-sided) with an average decrease in the value of 2.47 and 95% confidence interval (1.96-2.98). The effect of physical activity on significantly decreasing HbA1C levels is indicated by the Eta square, which is 77%. The leukocyte count (WBC) before physical activity was M=7.38 x109/L (SD =1.02) and after physical activity was M=5.86 x 109/L (SD =1.18), t(29)=7.52, p < 0.001 (bilateral) with an average reduction value of 1.52 and 95% confidence interval (1.11-1.94). A significant effect of physical activity on the reduction of leukocyte count is indicated by the Eta square in the value of 66%. The CRP value before physical activity is M=8.30 mg/dL (SD =7.92) and after physical activity is M=3.14 mg/dL (SD =1.37) t(29)=3, 52, p =0.001 (bilateral) with an average decrease of 5.16 and 95% confidence interval (2.16-8.15). The value of eta squared was 30%, again indicating a significant effect of physical activity on the reduction of CRP levels (Table 2).

**Table 2:** Influence of physical activity on the values of glycemic and inflammatory parameters before and after one month of application of the physical activity program in subjects without confirmed diabetes mellitus type 2.

| Parameter | Time | Mean | St. dev. | η2 |
|---|---|---|---|---|
| Glucose (mmol/L) | Before | 8,26 | 0,92 | 94% |
| | After | 4,32 | 0,49 | |
| HbA1C (%) | Before | 7,36 | 1,14 | 77% |
| | After | 4,89 | 0,74 | |
| WBC (109/L) | Before | 7,39 | 1,02 | 66% |
| | After | 5,86 | 1,18 | |
| CRP (mg/dL) | Before | 8,30 | 7,93 | 30% |
| | After | 3,14 | 1,38 | |

## DISCUSSION

According to the results of our study, a significant decrease in blood glucose levels, HbA1C levels, leukocyte count (WBC), and CRP levels was observed in subjects with confirmed type 2 diabetes mellitus after an exercise program. However, a statistically significant difference in all these parameters was also observed in subjects with unconfirmed type 2 diabetes mellitus after an exercise program.

In the analysis of the eta-Square test, the greatest influence of physical activity on the parameters glucose, HbA1C and CRP is shown in the group with confirmed diabetes. In the other group of subjects without confirmed diabetes, the greatest influence of physical activity on the reduction of glucose concentration is seen. When comparing the mean values before physical activity, the inflammatory parameters (WBC, CRP) and glycemic parameters (glucose and HbA1C) were increased in the group of subjects with confirmed diabetes. In the group of subjects without confirmed diabetes, the inflammatory parameters were within the reference interval, while the blood glucose levels were elevated. This may indicate the possible presence of inflammation in type 2 diabetes mellitus and the presence of certain complications, indicating the predictability of parameters in diabetes. Numerous authors have studied the effects of regular physical activity on CRP levels and confirmed that long-term and regular high-intensity physical activity has an anti-

inflammatory effect, which is achieved by a significant decrease in CRP levels (Herder et al, 2009; Belalcazar et al, 2010; Balducci et al, 2010). The results of the study by Kwi Baek Kim show us that a specific form of circuit training with a duration of twelve weeks can be considered an effective form of physical exercise that helps to reduce inflammatory blood factors (IL -6 and CRP) in patients with type 2 diabetes mellitus (Kim, 2014). The results of these studies correlate with the results of our study on the reduction of CRP after the use of exercise programs. Burr and colleagues note that the most important effect of physical activity is to improve glycemic status in people who are in the prediabetic stage or have type 2 diabetes mellitus (Burr, Rowan, Jamnik & Riddell, 2010). Similar results have been shown by Alvarez and colleagues, who proved that the use of high-intensity aerobic exercise leads to a reduction in blood glucose levels(Alvarez et al, 2016). On the other hand, the research results of Geirsdottir and colleagues, who performed 8 weeks of aerobic training, showed that there was no decrease in blood glucose levels (Geirsdottir et al, 2012). The results of these authors coincided with the results of our study, which showed a significant decrease in blood glucose levels after one month of using the physical activity program.

According to the results of our study, an increase in HbA1C level was observed in both groups of subjects. According to Shariq and colleagues, elevated HbA1C levels are considered independent risk factors for coronary heart disease and stroke in people with or without diabetes; and that the prognostic potential of HbA1C levels in people with diabetes is unique in its ability to assess glycemic control and therapeutic effect. (Sherwani, Khan, Ekhzaimy, Masood & Sakharkar, 2016). The nine-month study by Church and colleagues involved 262 male and female subjects with type 2 diabetes. Subjects were randomly assigned to the following groups: a) no physical activity, b) with physical strength activity, c) aerobic physical activity, and d) combination of aerobic physical activity and physical strength activity. All physical activity groups reduced the measurement of hemoglobin-related blood glucose (Church, Blair & Cocreham, 2010). Also, Umpierre and colleagues claim that aerobic physical activity, physical strength activity as well as their combination leads to a reduction in HbA1C (a measure of the amount of glucose bound to hemoglobin in red blood cells) by 0.67% over 12 weeks (Umpierre et al, 2011). The research of the authors mentioned above has similarities with the results of our research.

Loprinz and colleagues examined the association between objectively measured physical activity and inflammatory markers (white blood cell count, neutrophil count, and C-reactive protein) in adults with diabetes. The results showed that light physical activity measured with an accelerometer and moderate to vigorous physical activity were inversely related to white blood cell count and neutrophil count. From this, the authors concluded that adults with diabetes who engage in more physical activity have lower levels of inflammation, suggesting that physical activity may reduce disease progression by alleviating inflammation; an important finding because increased inflammation in people with diabetes may exacerbate disease progression (Loprinzi & Ramulu, 2013). In their work, Kashima and colleagues demonstrated elevated CRP and WBC levels in diabetic patients and proved that these parameters can be used to predict complications of diabetes and the development of chronic inflammation (Kashima, Inoue, Matsumoto & Akimoto, 2019). The findings of these authors have similarities with the results of our study on the reduction of leukocytes after physical activity. According to the study by Jekić B. et al, the authors concluded that only a small regulation of dietary and lifestyle habits can increase laboratory parameters after such a short period of time. Multidisciplinary health promotion and programs can effectively influence the growth arrest and gradual decrease in morbidity and mortality. The above conclusion is consistent with the findings and conclusions of this study (Jekić, Mihajlović & Bajić, 2019.)

## CONCLUSIONS

In our study, we observed a significant effect of physical activity on lowering elevated levels of glycemic and inflammatory parameters. Physical activity may reduce disease progression by alleviating inflammation. This is an important finding because elevated levels of inflammation can cause disease progression in people with diabetes. A multidisciplinary approach is very important in monitoring patients with type 2 diabetes mellitus and in establishing prevention programs that include risk management. The recommendation of this study is to perform the same investigation on a larger number of subjects and to include monitoring of nutritional and anthropometric parameters.

**CONFLICT OF INTEREST**
There are no conflicts of interest.
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