The role of physical activity on glucose transporter-4, fasting blood glucose level and glycated hemoglobin in type 2 diabetes mellitus patients in Medan, Indonesia

**Summary**

**Background.** Physical activity is essential to diabetic patients to improve insulin sensitivity so that diabetes can be well controlled.

**Objectives.** The purpose of this study was to analyze the effect of physical activity on glucose transporter-4 (GLUT-4), fasting blood glucose level (FBGL) and glycated hemoglobin (Hba\(_a\)) in patients with type 2 diabetes mellitus (T2DM) in Medan.

**Material and methods.** The study design was analytic with a cross-sectional approach. The study population was T2DM patients, and the number of samples was 83 people who fulfilled the inclusion and exclusion criteria. The study protocol was approved by the research ethics committee at the Faculty of Medicine, Universitas Sumatera Utara, and all participants willing to participate in the study signed written informed consent. The physical activity of T2DM patients was assessed by using a global physical activity questionnaire (GPAQ). The GLUT-4 level was assessed by using the Human GLUT-4 kit, which is ELISA method based. FBGL and Hba\(_a\) levels were determined by using the Doronad affinity + Modified HPLC method. Data was analyzed by the one-way ANOVA statistic test and processed by using SPSS.

**Results.** The results showed that physical activity affected the level of GLUT-4, FBGL and Hba\(_a\) among T2DM patients.

**Conclusions.** Medications and diet were not the main determinants of controlled BGL in diabetic patients. However, physical activity is one of the four-element points (education, dietary, physical activity, medicine) in diabetes management that must be implemented to achieve a better quality of life in diabetic patients.

**Key words:** exercise, glucose transporter type 4, glycated hemoglobin A, blood glucose.

Amelia R, Harahap J, Wijaya H. The role of physical activity on glucose transporter-4, fasting blood glucose level and glycate hemoglobin in type 2 diabetes mellitus patients in Medan, Indonesia. Fam Med Prim Care Rev 2021; 23(3): 274–278, doi: https://doi.org/10.5114/fmpcr.2021.108188.
cardiovascular system. Proper aerobic exercise improves physiological parameters, including FBGL and the lipid profile. Moreover, it can restore endothelial function and reduce arterial stiffness, which is a determinant of cardiovascular complications in T2DM. Both insulin and exercise increase glucose uptake into the skeletal muscles via GLUT-4 from the intracellular surface to the cell surface. In T2DM, there is a deficiency in the insulin receptor that results in glucose uptake and GLUT-4 translocation, and exercise therapy will repair defects of insulin receptor by providing GLUT-4 translocation [12–14].

Objectives

The aim of the study was to analyze the effect of physical activity on GLUT-4, FBGL and HbaA1c in T2DM patients in Medan.

Material and methods

Study design

The study design was analytic with a cross-sectional approach, in which the assessment of physical activity and glycemic control was performed at one time only.

Population and sample

The study population was T2DM patients in several primary health care centers in Medan (Medan Tuntungan PHC, Medan Belawan PHC, and Medan Ampras PHC), with the sample being 83 patients. The sample size was determined using a sample size formula for one population (with an accuracy of 10%, a significance of 95%). The inclusion criteria in this study were patients 35–55 years of age (assumed to perform active physical activities), those that had no contraindication to performing physical exercise, those willing to participate the research and those able to perform daily activities independently. The exclusion criteria were severe complication conditions (heart failure, kidney failure, diabetic gangrene) and the presence of comorbidities. Data collection was carried out for two months.

Data measurement

Assessment of physical activity was carried out using the Global Physical Activity Questionnaire (GPAQ). The GPAQ comprises sixteen questions that collect data from participation in physical activity in three domains: physical activity at work, traveling activity from place to place and recreational or leisure activities [9]. GPAQ measures physical activity through classification with MET (Metabolic Equivalent). MET is the ratio of the metabolic rate during activity to the metabolism rate at rest. MET is depicted in units of kcal/kg/hr. The Global Physical Activity Questionnaire has been validated to measure physical activity in the 16–84-year age range [15, 16]. According to the analysis guide attached to GPAQ, second version, the total physical activity level will be categorized into the following three categories: high performance of a heavy activity, medium-strong activity and low activity. Measurement of GLUT-4, FBGL and HbaA1c levels was carried out by examining the blood sample of T2DM patients. GLUT-4 was measured using the Human GLUT-4 ELISA Kit. The kit was based on sandwich enzyme-linked immune-sorbent assay technology. FBGL measurement was performed using a Colorimeter spectrophotometer + fully automatic method, and HbaA1c examination was performed using the Doronad affinity + modified HPLC method.

Statistical analysis

Data was processed by using SPSS 22 for Windows and is displayed in the tables and diagrams. The normality test was performed using the Kolmogorov–Smirnov test (p > 0.05). Normally distributed data is presented as mean ± SD. The one-way ANOVA was used to determine the effect of physical activity on GLUT-4, FBGL and HbaA1c (p < 0.05).

Ethical approval

This study was approved by the Research Ethics Committees of Universitas Sumatera Utara, Indonesia (approval number No: 280/KEP/USU/2019).

Results

Table 1. Baseline characteristics (n = 83)

| Characteristic | Frequency (n) | Percentage (%) |
|---------------|--------------|----------------|
| Gender        |              |                |
| male          | 16           | 19.3           |
| female        | 67           | 80.7           |
| Age group     |              |                |
| middle-aged adult (36–45 years of age) | 12 | 14.5 |
| early elderly (46–55 years of age) | 71 | 83.5 |
| Duration of illness |         |                |
| 1–5 years | 50 | 60.2 |
| 6–10 years | 20 | 24.1 |
| 11–15 years | 11 | 13.3 |
| > 15 years | 2 | 2.4 |
| Diabetes history |         |                |
| father | 15 | 18.1 |
| mother | 15 | 18.1 |
| father and mother | 8 | 9.6 |
| no one | 45 | 54.2 |
| BMI | | |
| underweight | 8 | 9.6 |
| normal weight | 41 | 49.4 |
| obese | 34 | 41.0 |
| Blood pressure (systole) | | |
| hypertension | 66 | 79.5 |
| no hypertension | 17 | 20.5 |
| Physical activity | | |
| high physical activity | 19 | 22.9 |
| medium physical activity | 13 | 15.7 |
| low physical activity | 51 | 61.4 |

Table 1 shows that most of the study subjects were female (80.7%), early elderly and totaled to 71 participants (83.5%). Based on the duration of diabetes, most have had diabetes for 1–5 years (60.2%). Based on the family history, 45 participants (54.2%) had a family history of a diabetic mother. Most diabetic patients had low physical activity, totaling as many as 51 participants (61.4%).

Table 2. Glucose transporter-4, fasting blood glucose level, HbaA1c level

| Parameter     | Mean   | Median  | SD     | Min  | Max  |
|---------------|--------|---------|--------|------|------|
| GLUT-4 (ng/ml) | 2.4    | 2.4     | 0.2    | 2.1  | 2.9  |
| FBGL (mg/dl) | 248.8  | 240.0   | 108.7  | 87.0 | 600.0 |
| HbaA1c (mg/dl) | 9.4    | 9.1     | 2.8    | 6.0  | 15.8 |

Table 2 shows that the levels of GLUT-4, FBGL and HbaA1c were normal, indicating that the participants were in good condition. The levels of all parameters were within the normal range, indicating that the participants were in good condition.
Table 2 shows the mean GLUT-4, fasting blood glucose and HbA1c levels, which were 2.4 ng/ml, 248.8 mg/dl and 9.4 mg/dl, respectively. In general, this shows poor glycemic control in diabetic patients.

Table 3 shows the results of the ANOVA test. There is a difference in the GLUT-4, FBGL and HbA1c levels based on the physical activity category of diabetic patients in Medan (p < 0.05).

| Parameter | Physical Activity          | F  | Sig |
|-----------|---------------------------|----|-----|
| GLUT-4 (ng/ml) | high physical activity | 3.518 | 0.048 |
|            | medium physical activity  |    |     |
|            | low physical activity     |    |     |
| FBGL (mg/dl) | high physical activity | 3.518 | 0.025 |
|            | medium physical activity  |    |     |
|            | low physical activity     |    |     |
| HbA1c (mg/dl) | high physical activity | 3.403 | 0.038 |
|            | medium physical activity  |    |     |
|            | low physical activity     |    |     |

Discussion

This study showed that the majority of patients had less physical activity. Physical activity is one of the pillars in the management of T2DM and the basis of treatment, as it can affect several aspects, including blood glucose concentration, insulin action and lowering cardiovascular risk factors [17]. Physical activity involves a significant large group of muscles that affect the increase in oxygen uptake and metabolic rate of active muscles. The metabolism process that takes place during physical activity can generate heat, most of which will be wasted through sweat. Sufficient physical activity can control body weight, BGL and, most importantly, can trigger activation of insulin production and make insulin work more efficiently [18, 19]. Unfortunately, physical activity is still the most frequent aspect ignored by patients. In fact, physical activity is still the most frequent aspect ignored by patients. In fact, physical activity with a ≥ 150 minutes/week duration. In moderate and intensive physical activity, mean BGL, HbA1c, total cholesterol and triglyceride levels were found to decrease after physical activity for ≥ 150 minutes/week. In addition, mean BGL, HbA1c, total cholesterol, LDL, HDL and tricyglyceride levels were found to decrease after intensive physical activity for ≥ 150 minutes/week [34, 35]. Another supporting study stated that patients undergoing aerobic physical exercise for eight weeks obtained improved blood glucose control with significantly decreased FBGL and HbA1c levels [36, 37].

Conclusions

The results of this study indicate that there is an effect of physical activity on the levels of GLUT-4, BGL and HbA1c in T2DM. Most of the T2DM patients only partook in low physical activity, which lead to uncontrolled diabetes as shown by higher mean GLUT-4, fasting blood glucose and HbA1c levels. In diabetic patients, medications and diet are not the only main means to control BGL. However, physical activity is one of the four-element points (education, dietary, physical activity, medicine) in diabetes management that must be implemented to achieve a better quality of life in diabetic patients.

Limitations of the study

This study is a cross-sectional study. The assessment of physical activity in this study is for general physical activity. The following research plan will provide regular physical exercise interventions to assess the effectiveness of regular physical exercise in increasing GLUT-4 secretion and blood sugar control in T2DM patients in Medan City.

Acknowledgments. The authors gratefully thank to The Ministry of Research, Technology, and Higher Education, for funding this study through the agreement of Research and Community Service Fund, for the Fiscal year 2018.
References

1. Turkson RKD. The impact of a nutrition and physical activity intervention programme on frailty syndrome in elderly citizens in Lesotho [doctoral dissertation]. University of the Free State; 2018.
2. World Health Organization. Global action plan on physical activity 2018–2030: more active people for a healthier world. WHO; 2018. Available from URL: https://apps.who.int/iris/bitstream/handle/10665/272772/9789241514187-eng.pdf.
3. Hamilton MT. The role of skeletal muscle contractile duration throughout the whole day: reducing sedentary time and promoting universal physical activity in all people. *J Physiol* 2018; 596(8): 1331–1340.
4. Kaupuzs A. The relationship between physical activity and exercise motivation of the first-year students from Rezekne Augstskola. *J Sports Sci* 2013; 4(1): 3–15.
5. Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. *Circulation* 2012; 126(1): 126–132.
6. Paramitha GM. Hubungan Aktivitas Fisik Dengan Kadar Gula Darah Pada Pasien Diabetes Melitus Tipe 2 di Rumah Sakit Umum Daerah Karanganyar [doctoral dissertation]. Universitas Muhammadiyah Surakarta; 2014.
7. Petersen MC, Shufman GI. Mechanisms of insulin action and insulin resistance. *Physiol Rev* 2018; 98(4): 2133–2223.
8. Lauritzen HP, Schertzer JD. Measuring GLUT4 translocation in mature muscle fibers. *Am J Physiol Endocrinol Metab* 2010; 299(2): E169–E179.
9. Messina G, Palmieri F, Monda V, et al. Exercise causes muscle GLUT4 translocation in an insulin. *Biol Med (Aligarh)* 2015; 3: 7.
10. Cunha VN, Paula Lima M de, Motta-Santos D, et al. Role of exercise intensity on GLUT4 content, aerobic fitness and fasting plasma glucose in type 2 diabetic mice. *Cell Biochem Funct* 2015; 33(7): 435–442.
11. Lissiwanti R, Cordita RN. Aktivitas fisik dalam menurunkan kadar glukosa darah pada diabetes mellitus tipe 2. *Jurnal Kebijakan* 2016; 5(3): 140–144 (in Indonesian).
12. Aggarwala J, Sharma S, Saroochi AJ, et al. Effects of aerobic exercise on blood glucose levels and lipid profile in diabetes mellitus type 2 subjects. *Al Ameen J Med Sci* 2016; 9(1): 65–69.
13. Putri EL. Hubungan antara latihan jasmani dengan kadar glukosa darah penderita diabetes. *Jurnal Berkala Epidemiologi* 2016; 4(2): 188–199 (in Indonesian).
14. Flores-Opazo M, Boland E, Garnham A, et al. Exercise and GLUT4 in human subcutaneous adipose tissue. *Physiol Rep* 2018; 6(22): e13918.
15. Obradovic M, Nesic G, Popovic A, et al. Physical activity and eating habits of students of the University of Belgrade: an epidemiological study. *Vojnosanitetski Pregled* 2020, doi: 10.2298/VSP2005100560.
16. Moharan R, Manipal S, Raj N, et al. Evaluation of physical activity and body mass index among dental professionals in Chennai City, Tamilnadu, India. *IJSRDS* 2017; 2(5): 7.
17. Haible S, Volk C, Demetriou Y, et al. Promotion of physical activity-related health competence in physical education: study protocol for the GEKOS cluster randomized controlled trial. *BMJ Public Health* 2019; 19(1): 1–5.
18. Indonesia PE. Pengelolaan dan pencegahan diabetes mellitus tipe 2 di Indonesia. Jakarta: PB Perkeni; 2015 (in Indonesian).
19. Luo B, Zhang J, Hu Z, et al. Diabetes-related behaviours among elderly people with pre-diabetes in rural communities of Hunan, China: a cross-sectional study. *BMJ Open* 2018; 8(1): e015747, doi: 10.1136/bmjopen-2016-015747.
20. Navale AM, Paranjape AN. Glucose transporters: physiological and pathological roles. *BioPhys Rev* 2016; 8(1): 5–9.
21. Amelia R, Yunanda Y. Relationship between depression and glycemic control among patients with type 2 diabetes in Medan. *Inl OP Conference Series: Earth and Environmental Science* 2018; 125(1): 012170, doi: 10.1088/1755-1315/125/1/012170.
22. Dwidarip E, Sidik A, Kep A. Pengaruh Senam Diabetes Mellitus terhadap Penurunan Kadar Gula Darah Sewaktu (GDS) Peserta Prolanis di Puskesmas Purwodiningratan [doctoral dissertation]. Universitas Muhammadiyah Surakarta; 2019.
23. Amelia R. The correlation between Body Mass Index and self-efficacy with blood glucose level in Type 2 Diabetes Mellitus. *Adv Sci Lett* 2017; 23(4): 3606–3609.
24. Flores-Opazo M, McGee SL, Hargreaves M. Exercise and GLUT4. *Exerc Sport Sci Rev* 2020; 48(3): 110–118.
25. Duarte CK, Almeida JC de, Merker AJ, et al. Physical activity level and exercise in patients with diabetes mellitus. *Rev Assoc Med Bras* 2012; 58(2): 215–221.
26. Riddell MC, Pooni R, Yavelberg L, et al. Reproducibility in the cardiometabolic responses to high-intensity interval exercise in adults with type 1 diabetes. *Diabetes Res Clin Pract* 2019; 148: 137–143.
27. Richter EA, Hargreaves M. Exercise, GLUT4, and skeletal muscle glucose uptake. *Physiol Rev* 2013; 93(3): 993–1017.
28. Esteves JV, Enguita FJ, Machado UF. MicroRNAs-mediated regulation of skeletal muscle GLUT4 expression and translocation in insulin resistance. *J. Diabetes Res* 2017; 2017: 7267910, doi: 10.1155/2017/7267910.
29. Osei-Yeboah J, Owiredu W, Norge G, et al. Physical activity pattern and its association with glycaemic and blood pressure control among people living with diabetes (PLWD) in the Ho municipality, Ghana. *Ethiop J Health Sci* 2019; 29(1): 819–830.
30. McGinley SK, Armstrong MJ, Boule NG, et al. Effects of exercise training using resistance bands on glycaemic control and strength in type 2 diabetes mellitus: a meta-analysis of randomised controlled trials. *Acta Diabetol* 2015; 52(2): 221–230.
31. Boniol M, Dragomir M, Auffer P, et al. Physical activity and change in fasting glucose and HbA1c: a quantitative meta-analysis of randomised trials. *Acta Diabetol* 2017; 54(11): 983–991.
32. Collberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016; 39(11): 2065–2079.
33. Huang JH, Cheng FC, Tsai LC, et al. Appropriate physical activity and dietary intake achieve optimal metabolic control in older type 2 diabetes patients. *J Diabetes Invest* 2014; 5(4): 418–427.
34. Meen J, Jaida Jayendrasinh M, Neeta M. Correlation between HbA1c values and lipid profile in type 2 diabetes mellitus. *IJBAP* 2013; 2(1): 47–50, doi: 10.5281/zenodo.4479182.
35. Carral F, Gutiérrez JV, Carmen Ayala M del, et al. Intense physical activity is associated with better metabolic control in patients with type 1 diabetes. *Diabetes Res Clin Pract* 2013; 101(1): 45–49.
36. Amelia R, Harahap J, Lelo A, et al. Risk analysis for cardiovascular complication based on the atherogenic index of plasma of type 2 diabetes mellitus patients in Medan, Indonesia. *Fam Med Prim Care Rev* 2020; 22(3): 197–201.

37. Banitalebi E, Kazemi A, Faramarzi M, et al. Effects of sprint interval or combined aerobic and resistance training on myokines in overweight women with type 2 diabetes: a randomized controlled trial. *Life Sci* 2019; 217: 101–109.

Tables: 3
Figures: 0
References: 37

Received: 28.02.2021
Reviewed: 17.04.2021
Accepted: 08.06.2021

Address for correspondence:
Rina Amelia, MD, PhD
Department of Community Medicine and Public Health
Faculty of Medicine
Universitas Sumatera Utara
Jl. dr. Mansyur No. 5 Kampus USU Medan
20155 Medan
Indonesia
Tel.: +62 8126444284
E-mail: rina2@usu.ac.id