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Investigation of The Effect of Combined Exercises on Glycemic Control in Individuals with Type 1 Diabetes[1]

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Abstract

The aim of the present study was to investigate the effect of the combined physical exercise program on the blood glucose (BG) of children with T1D. The study was conducted over four weeks using self-controlled clinical trials. The first two weeks were control period and the last two weeks were the experimental period. A total of 6 exercise sessions were performed 3 days a week during the experimental period. The exercise program consisted of aerobic, stretching, and resistance exercises. Each exercise session was performed for 40 minutes. A total of 15 children with T1D, whose mean age was 13.3±SD, were included in the study. The blood glucose and insulin dose data of the participants were recorded in both periods through the continuous glucose measurement system and the registry. It was determined that aerobic exercises provided a significant decrease in blood glucose ($p < .05$). There was no statistically significant difference between the mean BG values in the control (211.7±37.3) and experimental (208.7±40.4) periods ($p > 0.05$). On the other hand, a statistically significant decrease was found in the total daily insulin doses used by participants during the experimental (31.6±20.8 Unit) period ($p < 0.001$). Physical exercises had an acute positive effect on blood glucose in children with T1D. However, the effect of exercise alone is not sufficient for chronic glycemic control in T1D. For chronic glycemic control, first of all, the injected insulin doses should be carefully regulated according to carbohydrates and exercise.

Keywords:Type 1 Diabetes, Exercise, Glycemic Control.

Tip 1 Diyabetli Bireylerde Kombine Egzersizlerin Glisemik Kontrol Üzerine Etkisinin İncelenmesi

Öz

Bu çalışmada kombine egzersizlerden oluşan fiziksel aktivite programının tip 1 diyabetli (T1D) bireylerin kan glukozu (KG) üzerine etkisinin incelenmesi amaçlanmaktadır. Çalışma, dört hafta boyunca kendinden kontrollü klinik araştırmalar yöntemiyle gerçekleştirildi. Çalışmanın ilk iki haftası kontrol dönemi son iki hafta deney dönemi olarak planlandı. Deney döneminde haftada 3 gün toplam 6 egzersiz programı tasarlandı. Egzersiz programı aerobik (yürüyüş, koşu) egzersizler, germe egzersizleri ve direnç egzersizlerinden oluşturuldu. Her egzersiz programı 40 dakika süresince uygulandı. Çalışmaya yaş ortalaması 13.3±SD 15 T1D'li birey dâhil edildi. Katılımcıların kan glukoz ve insulin dozu verileri her iki dönemde de sürekli glukoz ölçüm sistemi ve kayıt defteri aracılığı ile kaydedildi. Aerobik egzersizlerin kan glukozunda anlamlı düzeyde azalma sağladığı saptandı ($p < ,05$). Kontrol (KG: 211.7±37.3) ve deneysel (KG: 208.7±40.4) dönemlerdeki ortalama KG değerleri arasında istatistiksel olarak anlamlı bir fark yoktu ($p > 0.05$). Fakat deney (31.6±20.8 Ünite) döneminde katılımcılar tarafından kullanılan toplam günlük insülin dozlarında istatistiksel olarak anlamlı bir düşüş bulundu ($p < 0.001$). Fiziksel egzersizlerin T1D'li çocuklarda kan şekeri üzerinde akut pozitif etkisi olduğu sonucuna ulaşılmıştır. Ancak T1D'de kronik glisemik kontrol için egzersizin etkisi tek başına yeterli değildir. Kronik glisemik kontrol için öncelikle enjekte edilen insülin dozları tüketilen karbonhidratlara ve yapılan egzersize göre dikkatli bir şekilde ayarlanmalıdır.

Anahtar Kelimeler: Tip 1 Diyabet, Egzersiz, Glisemik Kontrol.

[1] This study was produced from the PhD thesis.

Introduction

T1D is one of the most common chronic disease in children which brings a burden for children and their family with increased risk of acute and long-term complications. Achieving good glycemic control in diabetes management reduces the risk of complications. (Ryninks et al. 2015; Wong et al., 2011). Insulin, dietary intervention, and physical exercise are considered as three basic factors to ensure good glycaemic control. Regular physical exercise is one of the cornerstones in the management of T1D (Leclair et al., 2013; Mendoza et al., 2018). However, prolonged intense physical exercises that are not being properly structured may associated with difficulties in the blood glucose regulation (Chimen et al., 2012).

Skeletal muscles, account for 80% of blood glucose consumption, are highly determinant in regulating blood glucose levels (Boulinguiez et al., 2017). Therefore, it is very important for individuals with T1D to exercise regularly. While physical performance is improved by the contraction of the muscles in physical exercise, the exercise also increases insulin sensitivity and delays developing macro vascular complications. In addition, regular physical exercise is very beneficial for general health such as ideal body weight, body composition, psychosocial wellbeing and cardiovascular health of T1D patients (Riddell, 2017).

In order to ensure the quality of life of patients with T1D, it has been recommended to adjust insulin doses according to amount of nutrients in their meals, and do regular physical exercise (Robertson et al., 2009; Riddell, 2017). Patients with T1D should adjust the intensity of physical exercises and take into account the duration of action of insulin used and the amount of carbohydrates they consume (Shulman and Daneman, 2010).

Physical exercise is considered as a valuable tool for achieving a good glycaemic control for patients with T1D. It is thought that aerobic exercises will be more beneficial than anaerobic exercise for blood sugar regulation. However, studies investigating whether which kind of exercise would be more beneficial for better management of T1D in children are scarce. This study, which will contribute to the literature on determining safe exercise practices in children with T1D, aimed to examine the acute effect of combined (aerobic and anaerobic) exercises on blood sugar and to examine whether physical exercises have any other effect on glycemic control beyond the acute glucose-lowering effect.

Materials and Methods

In the study, the combined physical exercise program was implemented within the self-controlled clinical research method. In this context, children with T1D using the same insulin analogs but not doing regular physical exercise were included in the combined physical exercise

program consisting of aerobic and resistance exercises. The acute effect of aerobic and resistance exercises was evaluated by examining the differences between blood glucose data of participant in the beginning, middle and the end of the physical exercise sessions. To evaluate glycaemic control of patients with T1D, we compared blood glucose levels measured during observation and experimental periods. Ethical permission for the study was approved by the Clinical Research Ethics Committee of Health Sciences University Trabzon Kanuni Education and Research Hospital in Turkey Republic.The current study was conducted under the principles of the Declaration of Helsinki. Informed Consent Form was signed by T1D individuals who participated in the study and their parents.

Study Group

Five girls and ten boys with T1D, aged between 10 and 17, who were followed at the Paediatric Endocrinology Outpatient Clinic of Trabzon Kanuni Training and Research Hospital, university of Health Sciences, were included.

Inclusion Criteria

- Individuals with T1D with a diabetic history of at least 6 months
- Individuals with T1D using fast and long-acting insulin
- Individuals who were not doing regular physical exercise

Exclusion Criteria

- Individuals with T1D for 10 years or more
- Individuals with diabetic complications

Research Design

The study was designed as 14 days control and 14 days experiment periods. Daily basal and bolus insulin doses of each participant were recorded during the control and experiment periods. In both periods, the target range for blood glucose was set at 70-150 mg / dL. During the experiment period, the physical exercise program was applied 3 days/wk. Each exercise program was designed for a total of 40 minutes. The first three physical exercise programs consisted aerobic, stretching, and resistance, respectively. The last three physical exercise programs consisted resistance, stretching, and aerobic, respectively.

Control and Experiment Periods

The control period was determined as 14 days. During this period, any exercise program was not applied to the participants.The experimental period was determined as 14 days following the

control period. The exercise protocol included walking, running, stretching exercises, and resistance (calisthenic) exercises (Table 1).

Table 1

Experimental Period Program

Physical Exercise: 2 weeks / 3 days a week following the control period	
Aerobic Exercises	
Walking: Time: 10 min. / Intensity: 110 steps / min.	
Running: Time: 10 min. / Intensity: HRmax 60-70% (Karvonen)	
Stretching Exercises: Time 5 min. / Type: Static / Direction: From Leg To Head	
Resistance Exercises: Time 15 min. / Type: 5 Different Calisthenic / Resting Time: 40sec.	
Squat:	1st Set: Duration 60 sec./ Repeat: 20 / Resting: 20 sec. 2nd Set: Duration 60 sec./ Repeat: 30
Sit-up:	1st Set: Duration 60 sec./ Repeat: 15 / Resting: 20 sec. 2nd Set: Duration 60 sec./ Repeat: 20
Jump rope:	1st Set: Time 60 sec./ Repeat: 60 / Rest: 20 sec. 2nd Set: Duration 60 sec./ Repeat: 90
Push-ups:	1st Set: Type: Knees On the Ground / Duration 60 sec. / Repeat: 20 / Resting: 20 sec. 2nd Set: Type: Normal / Duration 60 sec./ Repeat: 15
Jump:	1st Set: Type: Double Foot Right-Left / Time 30 sec. 2nd Set: Type: Double Leg Forward-Back / Time 30 sec. / Rest: 20 sec. 3rd Set: Type: Right Foot Right-Left / Time 15 sec./ Left Foot Right-Left / Time 15 sec. 4th Set: Type: Right Foot Forward-Back / Time 15 sec. / Left Foot Forward-Back / Time 15 sec.

Data Collection Tools

Height of participants were measured using a Seca-stadiometer device (SECA, Germany) with a sensitivity level of ± 0.01 m. Bioelectric impedance device (Tanita BC-418, Japan) was used to determine body weights and BMI values before the study. The data regarding the participants' ages and diabetes histories were collected by the interview with the patients and their parents. Patients' HbA1c values in the most recent outpatient visit were obtained from the hospital records. During the first physical exercise program, heart rate (HR) was determined with a Polar M200 heart rate monitor wristband to determine resting HR and the individual running pace. During the experiment period, blood ketone levels were checked with Freestyle Libre ketone measurement strips. During the experiment period, high and low blood glucose levels were checked with Freestyle Libre glucometer strips. During the control and experimental periods, blood glucose data were monitored with the Freestyle Libre instant glucose measurement system, and the data obtained were transferred from the Freestyle Libre sensor program to the computer. The system automatically measures glucose levels every minute and stores readings at 15-minute intervals for 8 hours. When the sensor is read by the reader, the sensor automatically sends 8 hours of data to the reader. This system, where the blood glucose level can be determined at the desired frequency, updates the data every minute. Each sensor can be used for 14 days.

Statistical Analysis

SPSS 22 statistical analysis software program was used to analyze the data. Normality of the distribution of the data were evaluated using the Shapiro-Wilk test. Statistical analyzes were carried out using the Paired Sample t-test and Repeated Measures ANOVA protocols. The significance level was accepted as 0.05.

Results

The clinical characteristics of the participants are displayed in Table 2.

Table 2

Clinical Characteristics of the Participants.

n=15 (10 boys, 5 girls)	Mean (Sd)	Min.	Max.
Age (Year)	13.26 (2.34)	10	17
Height SDS	151.6 (14.51)	133	174
Weight (kg)	45.3 (14.50)	28	70
BMI z score	19.3 (3.60)	15	26
Duration of diabetes (year)	4.20 (2.86)	1	9
Latest HbA1c (%)	8.99 (1.69)	7.2	12.6

There was a statistically significant and gradual decrease in glucose levels during exercise 1 ($p = 0.000$, $p = 0.000$, and $p = 0.026$, respectively). There was also a statistically significant decrease in glucose levels in the middle of exercise 2 and 3 compared to the beginning. [(Exercise 2: $p = 0.001$; $p = 0.003$, respectively); (Exercise 3: $p = 0.002$; $p = 0.048$, respectively)]. However, decrease in blood glucose from the middle of Exercise 2 and Exercise 3 remain stable until the end of exercises (Exercise 2: $p = 0.947$, and Exercise 3: $p = 0.994$).

In Exercise 4 and Exercise 5, blood glucose level measured during the exercises was higher compared to pre-exercise blood glucose (Exercise 4: $p = 0.701$, and Exercise 5: $p = 0.496$), while blood glucose level measured during exercise 6 was slightly lower than those measured pre-exercise (Exercise 6: $p = 0.978$). However, none of the changes in blood glucose level during anaerobic exercises had reached a statistical significance. Whereas, a statistically significant decrease was observed in blood glucose during the aerobic exercises [(Exercise 4: $p = 0.013$; $p = 0.000$, respectively); (Exercise 5: $p = 0.041$; $p = 0.001$, respectively) (Exercise 6: $p = 0.044$; $p = 0.001$, respectively)], (Table 3).

Table 3

The Effect of the First and Last Three Exercise Programs on Blood Glucose

		Blood Glucose Avareges				
		Begining (1)	**Middle (2)**	**End (3)**	**p**	**Difference**
Aerobic-Resistance	Exercise 1	191.86±55.69	165.93±56.19	146.13±53.71	<0.05*	1>2, 1>3, 2>3
	Exercise 2	179.80±52.61	150.20±50.41	144.40±54.04	<0.05*	1>2, 1>3
	Exercise 3	210.20±36.74	190.46±39.29	185.13±40.68	<0.05*	1>2, 1>3
Resistance-Aerobic	Exercise 4	184.73±43.19	191.93±43,52	164.06±33.63	<0.05*	1>3, 2>3
	Exercise 5	168.86±60.70	179.06±53.24	138.53±45.65	<0.05*	1>3, 2>3
	Exercise 6	189.33±73.99	187.66±70.82	164.86±65.37	<0.05*	1>3, 2>3

p<0.05

In the first three exercises which goes from the aerobic towards the resistance, the mean blood glucose level gradually decreased from beginning to the end of exercise ($p < .001$; $p = 0.000$, and $p = 0.037$ respectively). In the last three exercises which goes from the resistance towards the aerobic, there was no a statistically significant change in the blood glucose level measured in the mid-time of exercise ($p = 0.593$). However, the blood glucose level in the end of the exercise was lower than those measured at the beginning and the middle of the exercise ($p = 0.005$; $p < 0.001$, respectively), (Table 4).

Table 4

Effect of Exercise on Blood Glucose in Terms of Sequence

	Blood Glucose Avareges				
	Begining (1)	**Middle (2)**	**End (3)**	**p**	**Difference**
Aerobic-Resistance	193.95±43.20	168.86±41.62	158.55±35.86	<0.05*	1>2, 1>3, 2>3
Resistance-Aerobic	180.97±46.06	186.21±44.25	155.81±40.67	<0.05*	1>3, 2>3

p<0.05

When the observation and experimental periods were compared, there was no statistically significant differences between the glucose levels ($p > 0.05$), the time spent in the target range (70-150 mg/dL), the time spent over the target range, the time spent below the target range, and number of low glucose events (Table 5). On the other hand, when the control and experimental periods were compared, a statistically significant decrease was observed in the BADID, BODID, and TODID during the experimental period ($p < 0.001$), (Table 5).

Table5

Comparison of Data from Control and Experimental Periods.

	Control Period	**Experimental Period**		
Parametre	**Mean (Sd)**	**Mean (Sd)**	t(14)	p
Glucose (mg/dl)	211.7 (37.3)	208.7 (40.4)	0.61	.55
Duration of 70-150 mg/dL (%)	27.7 (9.12)	28.1 (10.5)	-0.25	.81
Duration over 150 mg/dL (%)	68.1 (9.74)	68.7 (10.9)	-0.08	.94
Duration below 70mg/dL (%)	4.07 (3.24)	3.60 (2.66)	0.98	.34
Duration below 70mg/dL (min)	79.8 (52.3)	81.5 (19.7)	-0.11	.91
BADID	16.1 (9.9)	14.7 (10.1)	4.64	**<0.001****
BODID	20.5 (14.7)	16.9 (12.4)	5.29	**<0.001****
TODID	36.6 (23.3)	31.6 (20.8)	6.74	**<0.001****

BADID: Basal daily insulin dose; BODID: Bolus daily insulin dose; TODID: Total daily insulin dose
$p<0.001$

Discussions

In the present study evaluating the impact of the various mode of exercises on the blood glucose level in diabetic children, the aerobic session of the first three exercise programs, was related with decrease in blood glucose level. The effect of aerobic exercises on blood glucose has been reported in previous studies (Yamanouchi et al., 2002; Tansey et al., 2006; Ruzic et al. 2008; Lukacs and Barkai, 2015). Similar to our result, Ramalho et al. (2006) have shown that aerobic exercises have acute effects on the regulation of blood glucose. In resistance session of the first three exercise programs, a slightly (not statistically significant) decrease were observed in the blood glucose level during Exercise 2 and Exercise 3.

Resistance exercises were applied in the first sessions of the last three exercise programs. In these sessions, blood glucose levels did not decrease. Resistance exercises often cause hormonal and metabolic changes similar to high-intensity anaerobic exercises due to creating anaerobic condition (Ramalho et al., 2006; Yardly et al., 2013b; Robertson et al., 2009). It has been stated that increase in glucocorticoids and catecholamines during anaerobic exercises lead increase in hepatic glucose production which may result in hyperglycemia rather than decrease in blood glucose (Marliss and Vranic, 2002; Guelfi et al., 2005; Guelfi et al., 2007; Iscoe and Riddell, 2011; Yardly et al., 2013a; Yardly et al., 2013b; Garcia et al., 2015).

In the present study we evaluated blood glucose level in the exercises within the order from aerobic towards resistance and from resistance towards aerobic. Our results may bring insight into planning the type of physical exercises for individuals with T1D. Indeed, we have shown decrease in blood glucose level during the first three exercises which start with aerobic session. However, during the resistance session blood glucose remained stable after decrease from beginning to the

mid-exercise. Therefore, starting with resistance session might provide better blood glucose measurements with low risk of hypoglycaemia.

On the other hand, compared to the beginning blood glucose level, a slightly increase was observed in the middle of Exercise 4 and Exercise 5 which start with resistance session. In Exercise 6, there was a slightly decrease between the beginning and the mid-exercise glucose. This situation was attributed to anaerobic features of resistance exercises. Furthermore, in the second sessions of the last three exercise programs, compared to the beginning and the mid-exercise the decrease in the end was suggested as effect of aerobic exercises. In a previous study examining the acute effect of combined exercises consisting aerobic and resistance exercises on blood glucose, it was reported that the decrease in blood glucose during the order from aerobic towards resistance exercise was higher compared to the order from resistance towards aerobic exercises (Yardley et al., 2012). These results are exactly in line with the results of the current study. In another study, rigorous physical exercises combined with aerobic exercises had been reported regulating blood glucose acutely (Tonoli et al., 2012).The first three exercise programs of the exercise period of the current study and the acute response occurring in blood glucose during these programs was similar. Indeed, achieving a good glycemic control in T1D requires maintaining a balance among Carbohydrate (CHO) consumption, insulin dose and physical exercise (Leclair et al., 2013; Mendoza et al., 2018).

In present study, compared to the control period of the study the decrease in blood glucose during the experimental period was not statistically different. As patients we recruited had a poor glycemic control (The latest average HbA1c values 8.99%), lack of achieving a better glycemic control during exercise period was attributed to poor compliance to the feeding plan.In many cross-sectional studies conducted on large patient groups, regular exercises have been shown to decrease HbA1c (Herbst et al., 2006; Carral et al., 2013; Beraki et al., 2014). While, in some studies, it has been stated the role of exercise yet to be verified in achieving optimal glycemic control (Riddell and Iscoe, 2006, Tunar et al., 2012, Kennedy et al., 2013).

In the current study, it was found that the duration of stay below 70 mg/dL during both the control and the experimental period was similar. The risk of hypoglycemia in intermittent high-intensity exercises is lower than moderate-intensity aerobic exercises (Guelfi et al., 2005; Garcia et al., 2015). In a study investigating the effect of exercises on nocturnal hypoglycemia, all participants were found to have low blood glucose levels during those days of aerobic exercises, and it was reported that some of the participants developed hypoglycaemia (Tsalikian et al., 2005). The findings of this study revealed that nocturnal hypoglycemia is common on exercise days. In the present study, nocturnal hypoglycemia events were not seen in the experimental periods. This situation might be due to short duration and intensity of exercises as well applying the physical exercise as combination of various exercises.

It has been reported in many studies that exercise improves insulin sensitivity thereby glycemic control of individuals with T1D (Zinman et al., 1984; Mosher et al., 1998; D'Hooge et al., 2011). In similar, we observed a statistically significant decrease in the total daily insulin doses used by participants during the experimental period compared to the observation period.

Physical exercise in individuals with diabetes has been reported increase insulin sensitivity, improve glycemic control, decrease cardiovascular complications, prevent stroke, osteoporosis, even reduces the risk of certain types of cancer (e.g. colon, breast, prostate). However, children and adolescents with T1D are participating in exercises less frequently than healthy children (Yates and Davies, 2012; Nadella, 2017). In addition, our results revealed, a combination of regular physical exercise, a balanced CHO consumption and intricately adjusted insulin doses require to keep blood glucose level within the targeted limits and achieve a good glycemic control in patients with T1D.

Plasma insulin level, duration, and intensity of exercise, type of exercise, and the presence of counter-regulatory hormones are the factors affecting blood glucose levels during exercise (Riddell and Iscoe, 2006). Managing these factors requires knowledge and experience. In addition to the basic treatment protocols of individuals with T1D, the CHO counting method and structured regular physical exercise account for the cornerstones of the diabetes management.

Conclusions and Recommendations

The results showed that blood glucose averages decreased significantly in the aerobic part of the combined exercise session compared to the resistance part. In this context, it can be said that resistance exercises as a part of the exercise session will prevent the risk of severe hypoglycemia. In other words, starting exercises with a resistance session may provide a low risk of hypoglycemia. Individuals with T1D should adjust their insulin dose or CHO consumption after physical exercises to reduce fluctuations in blood glucose during and after the aerobic, anaerobic, or combined exercises they participate in. Children and adolescents with T1D need to be trained about which exercise forms are appropriate for them and to gain regular exercise habits, providing cardiovascular health, physical well-being, and glycemic control. In addition, especially, children and adolescents with T1D and their parents, physical education teachers and coaches should be involved in processes under the leadership of their healthcare professionals in order to gain healthy lifestyle behaviours and achieve optimal glycemic control. There are several recommendations in the literature for exercise practices in T1D. Accordingly, individuals with T1D are recommended 5 days a week or every day aerobic exercises. Besides, it was emphasized that resistance exercises should be a part of the physical exercise programs.

Ethics Committee Permission Information

Ethics evaluation committee: Clinical Research Ethics Committee of Health Sciences University Trabzon Kanuni Education and Research Hospital

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Authors' contributions

Design of the Research: TC, NG

Data Collection: TC

Statistical Analysis: TC, HB, NG

Preparation of the Article: TC, MK, HB

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