

Metabolic Effects of Fasting in Adolescents with Diabetes Type 1

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ARTICLE INFO

Article type:
Original article

Article History:
Received: 09 Apr 2018
Accepted: 22 May 2018
Published: 02 Jul 2018

Keywords:
Adolescents
Blood glucose
Diabetes mellitus
Fasting
Ramadan

ABSTRACT

Type I diabetes mellitus is a common chronic disease in adolescents. According to statistics, 12,243 diabetic Muslims fast in thirteen Islamic countries, 43% of whom have type I diabetes. This longitudinal study was conducted on volunteer adolescents with type I diabetes aged 13-18 years for 15 days using the census method. Three days before Ramadan and during the last three days of the study period, changes in the insulin dose, HbA1C, lipid profile, and body mass index (BMI) were evaluated. Among 10 volunteer patients, eight individuals could complete Ramadan fasting. Blood glucose analysis indicated a significant difference between the reported blood glucose levels ($P < 0.001$). The highest blood glucose level was reported by the patients at 12 PM (mean: 204.33 mg/dL), and the lowest blood glucose level was reported before Iftar (mean: 120.43 mg/dL). No significant difference was observed in the levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol, HbA1C, and triglyceride (TG) before and after fasting, and the only significant difference was denoted in the BMI of the patients ($P = 0.002$). According to the results, fasting could be a safe, feasible option for the adolescents with type I diabetes under specific circumstances, such as the provision of intensive training before Ramadan, raising their awareness, and supervision of patients by specialist. Our findings demonstrated that with the exception of BMI, fasting had no effects on other biochemical parameters

► Please cite this paper as:

Dashty S, Vakili R, Nematy M, Dadgar Moghadam M, Mohammadi E. Metabolic Effects of Fasting in Adolescents with Diabetes Type 1. *J Fasting Health*. 2017; 5(4): 172-177. Doi: 10.22038/jfh.2018.31010.1112

Introduction

For Muslims, fasting is a religious duty in the 9th month of the lunar calendar, which continues for 29-30 days (1). Duration of fasting depends on the time of year that coincides with Ramadan. When Ramadan is in summer, the duration of fasting is up to 20 hours per day. While fasting, Muslims avoid eating, drinking, smoking, sexual intercourse, and medication use from dawn (Sahur) to sunset (Iftar) (2, 3).

Nowadays, more than 415 million individuals have diabetes, and the number of diabetic patients is predicted to be more than 629 million by the next 25 years (4). According

to the epidemiological findings regarding diabetes and Ramadan, 12,243 diabetic Muslims patients fast in thirteen Islamic countries (5). According to the American Diabetes Association (ADA), 43% of diabetic patients fast during Ramadan in Muslim countries, and these patients are often at the risk of hypoglycemia, hyperglycemia, and diabetic ketoacidosis (DKA).

Type I diabetes mellitus is a common chronic disease in adolescents, which is associated with reduced insulin due to the destruction of pancreatic beta cells. Type I

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diabetes mellitus normally occurs in adolescents, while a quarter of the cases are diagnosed in adults (6).

Despite the risks of fasting in diabetic patients, many young patients with type I diabetes insist on fasting in Ramadan (7, 8). Fasting leads to changes in the lifestyle, which alter the biochemical parameters. Some of the major risks of fasting for diabetic patients include hypoglycemia, hyperglycemia, and ketoacidosis attacks. Severe complications of diabetes are DKA and hyperosmolar nonketotic coma, which lead to long-term complications such as cardiovascular diseases, stroke, foot ulcers, and eye damage (7, 9). Symptoms of type I diabetes are excessive thirst, fatigue, severe hunger, frequent urination, weight loss, and impatience.

During the holy month of Ramadan, changes in the sleep and meal patterns of diabetic patients affect their circadian rhythm, which alters the blood cortisol levels and body temperature (10-13). Furthermore, morning cortisol levels are lower in fasting individuals compared to non-fasting individuals, while cortisol levels are higher in the afternoon. Altered cortisol circadian rhythm while fasting accounts for the overall weakness of some diabetic Muslims during Ramadan (10).

In the patients with type I diabetes that choose to fast, time and conditions of breaking the fast and recognizing the signs of hypoglycemia and hyperglycemia could be helpful in the management of the possible adverse effects of fasting. In addition, these patients should constantly monitor their blood glucose level; if the level reaches below 70 mg/dL (3.9 mmol/L), fasting must be discontinued. In the patients with the blood glucose level of 70-90 mg/dL (3.9-5 mmol/L), hourly monitoring must be performed (3, 13, 15). Moreover, fasting should be discontinued if the blood glucose level increases to more than 300 mg/dL (16.6 mmol/L) or in the presence of the symptoms of hyperglycemia, hypoglycemia, dehydration, and acute illness (14).

According to the literature, pre-fasting training for patients with type I diabetes should be focused on the possible risks of fasting, type of nutrition, activity rate, daily blood glucose measurements, and types of medications. Such training interventions could

significantly reduce the complications of fasting in diabetic patients (15, 16).

Previous studies have suggested that adolescents with type I diabetes (depending on the exclusion criteria) are faced with no barriers against fasting, and fasting might even improve some of the biochemical parameters of these patients. The mentioned exclusion criteria encompass the differences between the adolescents with type I diabetes who suffer from the daily complications of fasting and those who are able to fast (7, 9, 17).

The present study aimed to investigate the possibility of fasting in the adolescents with type I diabetes and assess the subsequent metabolic effects on biochemical parameters.

Material and methods

Selection of the patients

In this longitudinal study, the sample size was determined using the census method, in Mashhad city of Iran at the Ramadan of 1396 solar hijri year (2017 AD). Two months before the holy month of Ramadan, adolescent volunteers for fasting (aged 13-18 years) were invited to participate in the study. Duration of fasting was 15 days in Ramadan in proportion to religious hours. Informed consent was obtained from the volunteers prior to participation, including the awareness of the benefits, disadvantages, and possible risks of fasting. Moreover, the participants were allowed to withdraw from the study at any given time. The research was registered at the Organizational Ethics Committee of Mashhad University of Medical Sciences, Iran (code: 950664).

Volunteers and tutorials

Selection of the volunteers was performed through publishing an announcement in the Department of Pediatric Endocrinology and Diabetes at Imam Reza Hospital in Mashhad, Iran. Parental consent was obtained for the participation of the volunteers in the research, including the awareness of the benefits (possible controlling of the blood glucose levels and improvement of biochemical parameters), disadvantages, and risks of fasting (possible hypoglycemia and DKA).

One month before fasting, the patients and their families received training on the risks of fasting. The training program

consisted of the descriptions of the frequency of glucose monitoring while fasting, dietary regimen, daily exercise, insulin dose adjustment, and risk factors for fasting. Patients were asked to monitor their blood glucose before Iftar, before Sahur, at 12 PM, and upon experiencing the signs and symptoms of hypoglycemia. Furthermore, the patients were advised to adhere to a complex carbohydrate diet at Sahur and use simple carbohydrates with fiber at Iftar. Caffeine-based drinks (e.g., tea and coffee) had to be avoided due to the diuretic effects of caffeine. Normal rate of sports activities was also recommended, and the intensive exercise was forbidden due to the increased risk of hypoglycemia and dehydration.

Insulin adjustment and nutritional instructions

Patients underwent multiple daily injections (MDIs) with insulin before Ramadan. Insulin dose of the patients changed in Ramadan due to the altered meal patterns. During Ramadan, use of NovoRapid insulin (pre-lunch and pre-breakfast) changed to pre-Iftar use, and pre-dinner NovoRapid changed to pre-Sahur use. In addition, long-acting Lantus insulin was prescribed at 10 PM (similar to before Ramadan).

With regard to the adjustment of the insulin dose, the patients received 70-90% of the pre-Ramadan insulin dose, which contained 60% Lantus at 10 PM and 40% NovoRapid at Sahur and Iftar. Lantus was reduced by 10% to 30% for all the patients, with the exception of one case (no need for insulin dose change). Regular insulin dose while fasting was adjusted by the patients based on the amount of their meals and blood glucose levels. All the patients were closely monitored daily and examined for the possible complications of fasting.

Patients were advised to use complex carbohydrates at Sahur and simple carbohydrates with fiber after Iftar. Caffeine-based drinks (e.g., tea and coffee) had to be avoided due to the diuretic effects of caffeine. Normal rate of sports activities was also recommended, and the intensive exercise was forbidden due to the increased risk of hypoglycemia and dehydration.

Exclusion criteria and measurable parameters

The present study was conducted on adolescents with type I diabetes mellitus aged 13-18 years. Exclusion criteria were as follows: 1) evidence of recent infections; 2) hypoglycemia or DKA within three months before Ramadan; 3) hemoglobin A1C level of >10%; 4) microvascular complications (e.g., nephropathy and retinopathy); 5) prehypertension (stage 1 or 2) and hypertension based on guidelines (18); 6) simultaneous celiac disease; 7) concurrent thyroid disorders; 8) lack of patient consent for participation and 9) symptoms of hypoglycemia with the blood glucose level of <70 or >300 mg/dL. In the presence of the mentioned criteria, the patient was obliged to break the fast.

Volunteers attended the Nutrition Clinic at Ghaem Hospital in Mashhad before and after fasting for the measurement of the BMI (body weight divided by the square of the body height). Three days before fasting and during the last three days of the fasting period (total: 15 days), blood samples (3-4 cc) were obtained from the patients at the laboratory of Imam Reza Hospital to evaluate the changes in biochemical parameters, including TG, LDL, HDL, and HbA1C.

Statistical analysis and sample size

Data analysis was performed in SPSS version 24. Qualitative variables were expressed as number and percentage, and quantitative variables were presented as mean and standard deviation (descriptive indices). Paired t-test was used for the comparative analysis of the parameters before and after Ramadan, and repeated measures analysis was used to assess the changes in the blood glucose level during 15 days of fasting. In all the statistical analyses, P-value of less than 0.05 was considered significant. In addition, the sample size of the study was census-based.

Results

In total, 10 patients with type I diabetes were enrolled in the study, including six males and four females, within the age range of 13-18 years (mean age: 16.125 years). Mean history of type I diabetes was seven years in the volunteers. One patient was excluded from the study due to simultaneous celiac disease and diabetes,

and one case was excluded due to hypoglycemia on the first day of fasting. Other patients (n=8) were able to complete the research and fasted for 15 days with no complications. All the patients received the same MDIs with insulin (Lantus and NovoRapid).

Blood glucose analysis

The results of blood glucose analysis indicated a significant difference between the reported blood glucose levels ($P<0.001$) (Table 1). The highest blood glucose level was reported

Table 1. Changes in blood glucose level before Iftar, before Sahur, and at 12 PM

Blood Glucose	Mean (mg/dL)	Standard Deviation
Before Iftar	120.43	13.85
Before Sahur	142.11	31.10
12 PM	204.33	10.32

Table 2. Paired comparison of reported blood glucose in study groups

	Mean	Standard Deviation	P-value
Before Iftar	120.43	13.85	0.001
12 PM	204.33	10.32	
Before Sahur	142.11	31.10	0.002
12 PM	204.33	10.32	
Before Sahur	142.11	31.10	0.135
Before Iftar	120.43	13.85	

by the patients at 12 PM with the mean of 204.33 mg/dL, and the lowest blood glucose level was reported before Iftar with the mean of 120.43 mg/dL. Moreover, the results of repeated measures analysis showed significant changes in the blood glucose level during fasting (before Iftar, before Sahur, and at 12 PM) ($P<0.001$).

According to the information in Table 2, paired comparison of the blood glucose levels before Iftar (group 1), before Sahur (group 2), and at 12 PM (group 3) showed a significant difference between groups 1 and 3 ($P<0.001$) and groups 2 and 3 ($P=0.002$), while no significant difference was observed between groups 1 and 2 in this regard ($P=0.135$).

Analysis of biochemical parameters

Changes in the biochemical parameters were evaluated in an analysis before and after fasting (Table 3). The results indicated no significant differences in the levels of TG, LDL, HDL, cholesterol, and HbA1C between the pre-fasting and post-fasting phases.

Assessment of the changes in the body weight of the patients before and after fasting showed the weight loss of about one kilogram. According to the statistical analyses, BMI of the patients changed significantly ($P=0.02$) (Table 4).

Table 3. Analysis of biochemical parameters before and after Ramadan

Biochemical Parameters	Mean	Standard Deviation	T	P-value
Triglyceride (pre-fasting)	103	63.22	2.151	0.06
Triglyceride (post-fasting)	80	39.44		
Cholesterol (pre-fasting)	156.62	22.34	0.14	0.89
Cholesterol (post-fasting)	155.62	35.12		
LDL (pre-fasting)	86.25	28.14	-1.192	0.09
LDL (post-fasting)	95.125	29.09		
HDL (pre-fasting)	58	19.80	-0.15	0.87
HDL (post-fasting)	59	15.25		
BMI (pre-fasting)	21.87	2.12	2.79	0.02
BMI (post-fasting)	21.47	2.04		
HbA1C (pre-fasting)	9.45	3.49	1.16	0.28
HbA1C (post-fasting)	8.87	2.61		

LDL: low-density lipoprotein; HDL: high-density lipoprotein; BMI: body mass index

Table 4. Statistical analysis of weight changes during Ramadan fasting

	Weight before Fasting (Kg)	Weight after Fasting (Kg)	P-value
Mean	57.43	56.37	0.02
Standard Deviation	8.27	8.26	
Minimum	39.5	38.5	
Maximum	66	65	

Discussion

Many young Muslims with type I diabetes are willing to fast during Ramadan despite their disease, some of whom insist on fasting without the approval of their physician (19-21). For fasting with minimal complications, native guidelines must be developed to adjust the insulin dose in diabetic patients. Therefore, we decided to prepare an appropriate insulin dietary regimen for the Iranian adolescents with type I diabetes and measure the effects of fasting on some biochemical parameters in these patients, hoping to facilitate Ramadan fasting for these individuals.

A major concern in the present study was the harmful changes in biochemical parameters due to fasting and possible complications. In this regard, a study by El Hawri et al. (2016) was conducted on adolescents with type I diabetes, and a direct correlation was observed between the reduction of fructosamine and number of fasting days. Furthermore, cholesterol and LDL were reported to increase significantly with the increased number of fasting days. This is inconsistent with the findings of the current research, and the discrepancy could be due to the difference in the sample sizes. In addition, the P-value considered for cholesterol in our study was 0.89, which is significantly higher compared to the value in the mentioned research. The hypothesis might be true in the case of LDL, the P-value for which was determined at 0.09.

In another study, Mazidi et al. (2014) denoted no correlation between fasting and blood cholesterol level. Some of the main complications associated with fasting in patients with type I diabetes are hyperglycemia, hypoglycemia, and ketoacidosis attacks. With the exception of hypoglycemia in one case, the patients in the present study experienced no complications. This finding is consistent with the study by Kaplan and Afandi (2015). It should be noted that working while fasting could give rise to the mentioned complications, and our subjects were adolescents.

In line with the research by Vakili et al. (2016), our findings indicated that adolescents with type I diabetes are able to fast during Ramadan if they are regularly monitored by a physician and receive the necessary training on

the proper use of equipment and medications.

Conclusion

According to the results, changes in biochemical parameters and metabolic effects of fasting in adolescents with type I diabetes could be controlled through pre-Ramadan intensive training, raising their awareness, providing native guidelines for the adjustment of the insulin dose, and close monitoring of the patients by a specialist. Furthermore, fasting could improve the BMI in the adolescents with type I diabetes.

Acknowledgments

Hereby, we extend our gratitude to Mashhad University of Medical Sciences, the Nutrition Clinic of Ghaem Hospital, and Department of Pediatric Endocrinology and Diabetes at Imam Reza Hospital in Mashhad, Iran for assisting us in this research project.

Conflict of interest

None.

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