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The Impact of Fasting during Ramadan on the Glycemic Control of Patients with Type 2 Diabetes Mellitus

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Key words
- ramadan
- diabetes

Abstract

Background: Millions of Muslims fast from dawn until dusk during the annual Islamic holy month of Ramadan. Most of the studies evaluating biochemical changes in diabetic patients during Ramadan showed little changes in the glycemic control. In this study, our aim was to assess the impact of fasting during Ramadan on glycemic control in patients with type 2 diabetes.
Methods and design: We examined 122 patients with type 2 diabetes (82 female, 40 male, age 56.93±9.57 years) before and after the Ramadan. 66.4% of the patients were treated with oral antidiabetic (OAD) alone, 6.5% with a combination of insulin plus OAD and 19.7% with insulin alone. 88 of 122 patients fasted during Ramadan (26.98±5.93 days). Weight, body mass index (BMI), waist circumference, blood pressure, fasting plasma glucose (FPG), postprandial glucose (PPG), fructosamine, HbA1c, fasting insulin and lipid parameters were measured.
Results: The frequencies of both severe hyperglycemia and hypoglycemia were higher in the fasting group, but the difference was not significant (p=0.18). Weight, BMI, waist circumference, blood pressure, FPG (143.38±52.04 vs. 139.31±43.47 mg/dl) PPG (213.40±98.56 vs. 215.66+109.31 mg/dl) , fructosamine (314.18±75.40 vs. 314.49±68.36µmol/l), HbA1c (6.33±0.98 vs. 6.22±0.92%) and fasting insulin (12.61±8.94 vs. 10.51±6.26µU/ml) were unchanged in patients who fasted during Ramadan. Microalbuminuria significantly decreased during Ramadan (132.85±197.11 vs. 45.03±73.11 mg/dl).
Conclusions: In this study, we concluded that fasting during Ramadan did not worsen the glycemic control of patients with type 2 diabetes.

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Introduction

Millions of Muslims fast from dawn until dusk during the annual Islamic holy month of Ramadan, which duration varies between 29 and 30 days. During the fast, Muslims are required to abstain from eating, drinking, use of oral and subcutaneous medications, and smoking from predawn to after sunset. If the person is sick or fasting may affect the health of faster, Islam exempts that subject from fasting. Nevertheless, a significant number of patients with diabetes insist on fasting during Ramadan against the advice of their doctors and the permission of religious authorities. However, in a large epidemiological study which included 12243 diabetic individuals from 13 Islamic countries, 42.8% of the patients with type 1 diabetes and the 78.7% of patients with type 2 diabetes fasted for at least 15 days during Ramadan [1].
Prolonging fasting, lifestyle changes and medical challenge that the patients create for themselves may cause acute complications, such as hypoglycemia and hyperglycemia in subjects with diabetes during Ramadan. Most of the studies that evaluating biochemical changes in diabetic patients during Ramadan showed little changes in the glycemic control [2–7], however the EPIDIAR study demonstrated a high rate of acute complications [1]. In the current study, our aim was to assess the impact of fasting during Ramadan on glycemic control and acute complications in patients with type 2 diabetes and also to define the lifestyle changes and treatment modifications during Ramadan.

Material and Methods

This study included 122 patients with type 2 diabetes who were evaluated before (2 weeks prior to the start of Ramadan) and after the Ramadan. At the first visit, the following information was recorded: age, gender, duration of diabetes, edu-

cation level, daily physical activity, smoking, complications and comorbidities, current treatment, weight, height, waist circumference (WC) and blood pressure. Peripheral arterial disease was diagnosed by physical examination.

After the Ramadan, all the patients were invited to the hospital within 2 weeks. Number of fasting days, number and time of self-reported hypo- and hyperglycemic episodes, measurements of blood pressure and any history of hospital admission during the Ramadan were recorded. Hypoglycemia was defined as symptoms that were perceived by the patient as hypoglycemia and urged him/her to break fast with or without documented low blood glucose. Severe hyperglycemia was defined as a self-reported blood glucose level ≥ 300 mg/dl. Changes in lifestyle (physical activity, food/fluid intake, sleep patterns) and changes in treatment during Ramadan were asked and blood pressure, weight and WC were evaluated. Fasting plasma glucose (FPG), postprandial glucose (PPG), fructosamine, HbA1c, fasting insulin, lipid parameters, creatinine and microalbuminuria were measured before and after the Ramadan.

Statistical analysis

SPSS version 19.0 software (SPSS, Chicago, IL, USA) was used for statistical analysis. Results were expressed as mean ± standard deviation. The Mann-Whitney U test was used to compare the continuous variables and the Chi-square test was used to compare categorical variables. McNemar test was used to compare the number of glycemic complications. P-value of less than 0.05 was considered to be statistically significant.

Results

We enrolled 122 patients with type 2 diabetes in the current study. Their mean ± SD age was 56.93 ± 9.57 years and 67.2% were female. Mean duration of diabetes was 5.73 ± 5.1 years. The demographic and clinical features of the study population are shown in **Table 1**. 66.4% of patients were treated with OAD alone (26.7% monotherapy; 25.6% bitherapy), 7.4% with a combination of OAD plus exenatide, 6.5% with a combination of insulin plus OAD (100% glinides and metformin; 37.5% sitagliptin), and 19.7% with insulin alone. A proportion of 19.7% patients received metformin alone. 28.7% of the patients received sulphonilureas, 14.8% glinides, 36.9% sitagliptin or vildagliptin and 19.7% pioglitazone. The proportion of OADs and insulin were similar in the fasting and nonfasting group.

88 patients (72.1%) fasted during Ramadan and the mean number of fasting days was 26.98 ± 5.93 (9–30). 71.6% of patients completed 30 days of fasting and 89.8% fasted at least 15 days. Changes concerning lifestyle and treatment during Ramadan are shown in **Table 2**. Physical activity, sleep duration, food intake and sugar intake were unchanged in approximately one-half of the study population. However fluid intake increased in most of the patients (61.4%) during the Ramadan. Insulin and OAD doses were maintained in 33.3% and 74.1% of the patients, respectively.

64.8% of the patients unchanged the frequency of self glucose monitoring. During Ramadan 17% of the patients who fasted, experienced at least 1 episode of hypoglycemia, however this ratio was 10.2% before Ramadan. 5.7% of the patients recorded one or more severe hyperglycemia before Ramadan, compared with 11.4% during Ramadan. The frequencies of both complications were higher in the fasting group, but the difference was not

Table 1 Demographic and clinical features of the patients.

	Patients (n = 122)
age (years)	56.93 ± 9.57 (34–77)
gender (% women)	82 (67.2%)
duration of diabetes (years)	5.73 ± 5.1 (1–23)
education level (%)	
no primary education	32 (26.2%)
secondary or higher education	90 (73.8%)
daily physical activity	
sedantary or light activity (%)	34 (27.9%)
moderate activity (%)	83 (68%)
heavy activity (%)	5 (4.1%)
smoking (%)	14 (11.5%)
presence of hypertension (%)	89 (73%)
presence of dyslipidemia (%)	88 (72.1%)
diabetes complication (%)	
neuropathy	41 (33.6%)
retinopathy	14 (11.5%)
nephropathy	28 (23%)
coronary artery disease	24 (19.7%)
peripheral arterial disease	0
cerebrovascular disease	1 (0.8%)
foot ulcer	0

± Refers to standard deviation

Table 2 Changes in lifestyle and medication during Ramadan.

	Patients who fasted (%) (n = 88)
physical activity	
more	18.2%
less	21.6%
same	60.2%
sleeping duration	
more	30.7%
less	18.2%
same	51.1%
food intake	
more	36.4%
less	15.9%
same	47.7%
fluid intake	
more	61.4%
less	13.6%
same	25%
sugar intake	
more	46.6%
less	4.5%
same	48.9%
insulin dose	
ıncreased	–
decreased	61.1%
maintained	33.3%
stopped	5.5%
OAD dose	
ıncreased	3.5%
decreased	22.4%
maintained	74.1%
stopped	–
self glucose monitoring	
ıncreased	15.9%
decreased	19.3%
maintained	64.8%

significant (p = 0.18). The frequency of hyperglycemia was higher in the patients using insulin than those not using (p = 0.004), however the frequency of hypoglycemia was not different. Only 1.6% of the patients were admitted to hospital during Ramadan and the reason was severe hypoglycemia in most of the patients. Frequencies of glycemic complications occurring before and during Ramadan in both fasted and not fasted groups are shown in **Table 3**.

A significant association with the frequency of severe hyperglycemia was observed for a change in insulin dose (20% of patients reporting severe hyperglycemia had decreased their dose compared with 84.6% of those without severe hyperglycemia) (p = 0.033). We did not find such a relationship between hypoglycemia and changes in insulin dose. In addition, there was not an association between a change in OAD dose, the level of physical activity, sleep duration and acute glycemic complications. The proportion of subjects changing food or fluid intake was not significantly different in subjects with severe hyperglycemia and hypoglycemia and in those without. However, the frequency of hyperglycemia was found to be associated with changing sugar intake during Ramadan (90% of patients reporting severe hyperglycemia had increased sugar intake compared with 41% of those without severe hyperglycemia) (p = 0.014).

The mean weight and body mass index (BMI) of the patients were 89.86 ± 17.20 kg and 36.32 ± 15.33 kg/m^2 respectively. Weight, waist circumference and blood pressure were not different before and after the Ramadan (p > 0.05) (**Table 4**). At the beginning of the study, the mean HbA1c level of the patients was 6.33 ± 0.98% and fructosamine 314.18 + 75.40 µmol/l. After the Ramadan, FPG (143.38 ± 52.04 vs. 139.31 ± 43.47 mg/dl), PPG (213.40 ± 98.56 vs. 215.66 + 109.31 mg/dl), HbA1c (6.33 ± 0.98 vs. 6.22 ± 0.92%), fructosamine (314.18 ± 75.40 vs. 314.49 ± 68.36 µmol/l) and fasting insulin levels (12.61 ± 8.94 vs. 10.51 ± 6.26 µU/ml) were similar in patients who fasted during Ramadan (**Table 4**). Although total cholesterol, LDL- cholesterol and triglyceride levels did not change, HDL cholesterol decreased during Ramadan. Serum creatitine and albumin levels and microalbuminuria significantly decreased during the Ramadan. All the changes in metabolic and clinical parameters are shown in **Table 4**.

Table 3 Number of glycemic complications.

	Before Ramadan	During Ramadan	p
patients who not fasted (n = 34)			
hypoglycemia, n (%)	3 (8.8)	6 (17.6)	0.375
severe hyperglycemia, n (%)	8 (23.5)	9 (26.5)	1
patients who fasted (n = 88)			
hypoglycemia, n (%)	9 (10.2)	15 (17)	0.18
severe hyperglycemia, n (%)	5 (5.7)	10 (11.4)	0.18

Discussion

Our study shows that fasting during Ramadan did not worsen the glycemic control in patients with type 2 diabetes. We demonstrated that glycemic parameters and frequencies of glycemic complications did not change significantly during Ramadan.

Numerous studies using small groups of diabetic patients showed little changes in anthropometric and biochemical measurements during Ramadan [3–7]. In a study, significant reductions in the mean body weight and fructosamine values were found [3]. Similarly, Katibi IA et al. showed improvement in fasting blood sugar upon during fasting in 76% of the patients [7]. However the other studies did not demonstrate such an improvement in the glycemic control of patients with type 2 diabetes [5,6]. In the present study, glycemic parameters such as FPG, PPG, HbA1c, fructosamine and fasting insulin levels were not found different after the Ramadan. Also, the mean body weight and waist circumference of the patients did not change during Ramadan in our study.

The EPIDIAR study which includes 12 243 type 1 and type 2 diabetic patients demonstrated a high rate of acute complications [1]. In this study, patients with type 2 diabetes experienced at least one episode of severe hyperglycemia and hypoglycemia requiring hospitalization, 4% and 2% respectively during Ramadan. Also in another study including 493 diabetic patients, about 14.6% of the patients experienced mild hypoglycemia, 3.2% had severe hypoglycemia and 11.2% had severe hyperglycemia during Ramadan [8].

In our study, frequencies of glycemic complications increased during Ramadan, but it was not significant. If the study popula-

Table 4 Changes in metabolic and clinical parameters in patients who fasted during Ramadan.

	Before Ramadan n = 88	After Ramadan n = 88	p
weight (kg)	89.86 ± 17.20	89.22 ± 16.68	0.069
BMI (kg/m^2)	36.32 ± 15.33	35.71 ± 11.47	0.305
waist circumference (cm)	106.97 ± 15.57	106.06 ± 14.04	0.535
systolic blood pressure (mmHg)	140.03 ± 20.92	140.01 ± 19.93	0.620
diastolic blood pressure (mmHg)	81.50 ± 12.72	79.62 ± 10.17	0.187
fasting plasma glucose (mg/dl)	143.38 ± 52.04	139.31 ± 43.47	0.758
postprandial glucose (mg/dl)	213.40 ± 98.56	215.66 ± 109.31	0.634
HbA1c (%)	6.33 ± 0.98	6.22 ± 0.92	0.057
fructosamine (Normal: 205-285 µmol/l)	314.18 ± 75.40	314.49 ± 68.36	0.114
fasting insulin (µU/ml)	12.61 ± 8.94	10.51 ± 6.26	0.200
total cholesterol (mg/dl)	199.55 ± 58.97	188.84 ± 41.26	0.122
LDL cholesterol (mg/dl)	119.16 ± 38.46	114.65 ± 34.26	0.177
HDL cholesterol (mg/dl)	45.73 ± 11.64	43.52 ± 10.52	0.002
triglyceride (mg/dl)	149.90 ± 74.89	157.65 ± 83.15	0.657
urea (mg/dl)	37.89 ± 11.86	36.59 ± 13.31	0.289
creatinine (mg/dl)	0.80 ± 0.18	0.75 ± 0.16	0.001
microalbuminuria (mg/dl)	132.85 ± 197.11	45.03 ± 73.11	< 0.001
albumin (gr/dl)	4.69 ± 0.49	4.23 ± 0.23	< 0.001

± Refers to standard deviation

tion were larger, the differences might be significant. 26.2% of the patients were using insulin at the beginning of the Ramadan. During the Ramadan, 61.1% of the patients decreased the dose of insulin and 5.6% of them stopped. Excessive reduction in dosages of insulin may prevent the high frequencies of hypoglycemia, nevertheless this may increase the frequency of hyperglycemia. When we evaluated the impact of changes in insulin treatment on the frequencies of glycemic complications, a significant association with the incidence of hyperglycemia was observed for a change in insulin dose, but hypoglycemia not. The frequency of hyperglycemia was higher in the patients using insulin than those not using. It may be associated with the reductions in insulin dose.

Few clinical trials have compared the efficacy and safety of antihyperglycaemic agents in fasting patients with type 2 diabetes during Ramadan. In 2 studies, the proportion of patients with at least one hypoglycaemic episode was significantly lower with a DPP-4 inhibitor than with sulphonilureas [10–12]. In another study, the incidence of confirmed symptomatic hypoglycaemia was lower in the repaglinide group compared with the glibenclamide group (2% vs. 4%) [13]. In other smaller trials, no differences were observed in the incidence of hypoglycaemic events between a sulphonylurea and active comparators (repaglinide, insulin glargine) [14,15]. In our study, we did not find an association between the OADs and acute glycemic complications. In the current study, major proportion of the patients using OADs maintained the OAD dose during Ramadan. Only 22.4% of the patients decreased the OAD dose, mostly the sulphonylureas and glinides. Changes in OAD dose did not affect the episodes of both glycemic complications. Most of the patients unchanged the frequency of self glucose monitoring during Ramadan. If they monitored their blood glucose levels more often, then the frequencies of glycemic complications would be different.

Approximately 50% of the patients did not change their lifestyle during Ramadan. However, when patients did change their lifestyle, the tendency was to decrease physical activity, increase sleep duration, and food and sugar intake. The changes in lifestyle generally did not have an impact on the frequencies of glycemic complications. Only, the frequency of hyperglycemia was found to be associated with changing sugar intake during Ramadan.

73% of the patients were hypertensive and the systolic and diastolic blood pressure did not change during the Ramadan. Lipid parameters were unchanged except HDL cholesterol. Serum urea levels were not different after the Ramadan, however albumin, creatinine levels and microalbuminuria decreased. In conclusion, fasting during Ramadan in patients with type 2 diabetes did not afffect the body weight, blood pressure, glycemic parameters and the frequency of acute glycemic complications. Approximately one-half of the patients did not change their lifestyle during Ramadan. Patients with diabetes who insist on fasting should be assessed before Ramadan and educated related to physical activity, meal planning, glucose monitoring, and dosage and timing of medications.

Conflict of interest: None.

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