The effects of long term fasting in Ramadan on glucose regulation in type 2 Diabetes Mellitus

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Abstract. – INTRODUCTION: For Ramadan fasting, observing Muslims do not eat or drink between sunrise and sunset during Ramadan, Islam's holy month of the year according to the lunar calendar. In 2011, fasting patients with diabetes fasted for an average of 16.5 hours per day, having 2 meals between sunset and sunrise for a month. We aimed to evaluate the impact of extended fasting on glucose regulation and observe possible complications of extended fasting in type 2 diabetes mellitus patients

PATIENTS AND METHODS: We conducted a randomized, retrospective, observational study. Patients who presented at the Diabetes Clinic during the 15 days before and after Ramadan in August 2011 Istanbul, whose hemoglobin A1c, fasting plasma glucose, postprandial plasma glucose, weight and height value examinations and follow-up were completed were included in the study.

FINDINGS: Seventy-six diabetes patients who fasted during Ramadan (fasting group) and 71 patients with diabetes who did not fast (non-fasting group) were included in the study. These two groups with similar demographic characteristics were compared before and after Ramadan. HbA1c, fasting and postprandial plasma glucose, body mass index, weight and adverse events were evaluated. No statistically significant difference was observed among the fasting and the non-fasting groups. There was no difference between the pre and post-Ramadan values of the fasting group.

CONCLUSIONS: We could not find any negative effects of extended fasting on glucose regulation of patients with diabetes who are using certain medications. No serious adverse event was observed. We failed to demonstrate benefits of increasing the number of meals in patients with diabetes.

Key Words:
  Extended daily fasting, Type 2 diabetes mellitus, Nutrition frequency, Ramadan.

Introduction

The most important treatment approach for type 2 diabetes mellitus (DM) is regulation of patients' diet from the time of diagnosis until the end of their lives[1]. The most common therapeutical recommendations were frequent food intake and regulation diet contents. Diets of patients with diabetes ought to be planned carefully in light of their individual nutrition habits, preferences, life styles and social and cultural lives[2]. For example, because many Muslims fast daily during the month of Ramadan, it is important to know whether abstaining from food and drink has detrimental effects on plasma glucose regulation, and which anti-diabetic drugs are safe and effective. Ramadan fasting for practicing Muslims is abstaining from eating and drinking from dawn until sunset for one month per lunar year and eating only two main meals at night (from sunset until dawn). Among patients with diabetes, hypo- or hyperglycemia, diabetic coma, dehydration or thrombosis are common complications resulting from long-term fasting that stem from the disease itself and/or the medications used. Some studies on impacts of long-term fasting on diabetic patients showed improved glucose regulation and no or minimal increase in adverse effects such as hypo- or hyperglycemia, diabetic coma, dehydration or thrombosis[3-8]. These studies may suggest an alternative approach for patients with diabetes who need to fast due to life style or religious beliefs. However, no study to date in the published literature has compared the diabetes regulation parameters of fasting (extended as in Ramadan) and non-fasting patients with type 2 diabetes.

This study aims at understanding how extended fasting (16.5 hours) impacts the type 2 DM patients' glucose regulation and the other possible complications related to fasting. We examined type 2 DM patients who fasted a mean of 16.5 hours a day and type 2 DM patients who ate 6 times a day for comparison purposes. Our purpose was to study the effects of fasting on type 2 DM patients by comparing the laboratory and clinical values from before and after Ramadan.

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Patients and Methods

This study was conducted on type 2 DM patients who were being followed in our Hospital's Outpatient Diabetes Clinic, who either had fasted a mean of 16.5 hours a day or were eating their normal diets during the 29 days of the month of Ramadan in August 2011 Istanbul. Baseline HbA1c levels were measured in order to better comprehend the last 3 months' and particularly the last month's diabetes regulation condition. Pre- and post-Ramadan variables of the patients, who had similar demographic characteristics, used similar medications and had similar baseline HbA1c levels, were examined. Their fasting plasma glucose post-prandial plasma glucose, HbA1c levels; the body weights and BMIs (body-mass indexes) were measured within the 15 days before and then within the following 15 days of Ramadan. Patients with type 1 diabetes, incomplete fasting, insufficient medical records, serious cardiovascular, renal, hepatic, or cerebrovascular disease and pregnant or lactating women were excluded. All included patients were asked about whether they fasted or not, if they had any disorder during Ramadan, their glucose levels when they experienced disorders (if any), and their demographic findings. The same dietitian followed all study patients.

Procedures related to this study were performed after Bezmialem Vakif University Ethic Committee approved the study protocol and approval of hospital administration for searching patients' records.

Blood laboratory tests were performed between 08.00-09.00 AM in Bezmialem Vakif University Hospital Laboratory after 12 hours fasting. Post prandial plasma glucose levels were measured two hours after the beginning of breakfast. Glucose levels were measured with glucose oxidase technique (Roche Diagnostics GmbH, Mannheim, Germany) and HbA1c levels were measured with turbidimetric inhibition immunoassay (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Besides descriptive statistics (mean, median and standard deviation), t test, and paired samples t test were used to compare normally distributed parameters, and Kruskal-Wallis and Mann-Whitney U-test were used to compare non- normally distributed parameters. Categorical data were compared with the chi-square test. Two-tailed p values < 0.05 were accepted as significant.

Results

Total of 2730 cases were reviewed for the study, 147 type 2 DM patients of them completed the study. The patients were divided into two homogenous groups with similar baseline age, gender, weight, BMI and taking similar drugs. Of the 147 patients included in the study, 76 patients (19 males, 57 females) in the fasting group did not eat or drink for a mean of 16.5 hours per day, whereas 71 patients (23 males, 48 females) in non-fasting group maintained their normal diets during the 29 days of Ramadan ($p = 0.32$). Before Ramadan, no significant differences between two groups in age, gender, BMI, initial weight, duration of diabetes, baseline HbA1c, and fasting plasma glucose and post-prandial plasma glucose levels (Table I).

Table I. Demographic distribution of fasting and non-fasting groups.

	Fasting (n=76) mean ± SD	Non fasting (n=71) mean ± SD	p
Age (years)	57.4 ± 10.1	57.6 ± 11	0.94
BMI (kg/m²)	32.6 ± 5.7	32.6 ± 6.4	0.98
Initial weight (kg)	82.6 ± 14.6	82.3 ± 15.2	0.91
Diabetes age (years)	11.2 ± 7.1	11.3 ± 7.3	0.92
Pre Ramadan HbA1c (%)	7.9 ± 1.6	8 ± 1.7	0.94
Pre Ramadan HbA1c (mmol/mol)	86.4 ± 17.5	87.4 ± 18.6	
Pre Ramadan FPG (mmol/l)	7.9 ± 2.9	8.2 ± 2.9	0.6
Pre Ramadan PPG (mmol/l)	11.2 ± 5.4	11.6 ± 5	0.64

Body mass index (BMI), hemoglobin A1c levels before Ramadan (pre Ramadan HbA1c), fasting plasma glucose levels before Ramadan (pre Ramadan FPG), post-prandial plasma glucose levels before Ramadan (pre Ramadan PPG).

Table II. Comparison of HbA1c, FPG, PPG, and body weight in fasting and non-fasting groups.

	Fasting (n = 76) mean ± SD post Ramadan	Non fasting (n = 71) mean ± SD post Ramadan	p
HbA1c (%)	7.7 ± 1.4	7.9 ± 1.3	0.12
HbA1c (mmol/mol)	84.2 ± 15.3	86.4 ± 14.2	
FPG (mmol/l)	7.4 ± 2.7	7.2 ± 2.3	0.91
PPG (mmol/l)	10.5 ± 4.5	10.3 ± 4.2	0.92
Weight (kg)	82.7 ± 14.1	83 ± 15.2	0.92

Mean ± standart deviation (mean ± SD), values before Ramadan (pre Ramadan), values after Ramadan (post Ramadan), Hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), the value of significance comparing values of fasting and non fasting group (*P*).

The post-Ramadan HbA1c, fasting plasma glucose, post-prandial plasma glucose and weight were compared between the demographically similar fasting and non-fasting groups and no significant differences were found (Table II).

Within the fasting group, when the pre and post-Ramadan, fasting plasma glucose, post-prandial plasma glucose and weight were compared, it was observed that only fasting plasma glucose level decreased significantly ($p = 0.047$) (Table III).

In the fasting during Ramadan group, the patients were divided into 4 groups based on the medications they were on: 12 patients used pre-mixed insulin and metformin (pre-met), 13 patients used long-acting insulin and metformin (long-met), 18 patients used only metformin (metformin), and 17 patients used metformin, pioglitazone, acarbose (multi-drug). There were no significant differences between pre- and post-Ramadan values of these four groups' HbA1c, fasting plasma glucose, post-prandial plasma glucose and weight (Table IV).

With respect to adverse events, there were 2 patients (1 in fasting group and 1 in non-fasting group) who experienced severe hypoglycemia (blood glucose < 50 mg/dL) and mild hypoglycemia (blood glucose 50-70 mg/dL). Mild hyperglycemia (blood glucose 200-350 mg/dL) was observed in 28 and 24 patients in fasting and non-fasting groups, respectively, and 3 patients in the fasting group and 1 patient in non-fasting group developed severe hyperglycemia (blood glucose > 350 mg/dL). There were no significant differences between the two groups in terms of hyperglycemia ($p = 0.97$). No appearancy of thrombosis, diabetic ketoacidosis, hyperosmolar non-ketotic coma, and dehydration were reported.

Discussion

Type 2 DM patients were evaluated in this study after a month long practice of extended fasting, and the findings revealed that fasting patients experienced the expected complications like hypoglycemia, hyperglycemia, diabetic coma, dehydration and thrombosis at rates similar to that of the non-fasting diabetic patients. We tried to determine how Ramadan fasting impacted diabetes regulation extended by evaluating

Table III. Comparison of HbA1c, FPG, PPG and body weight in fasting group.

	Fasting (n = 76) mean ± SD pre Ramadan	Fasting (n = 76) mean ± SD post Ramadan	p
HbA1c (%)	7.9 ± 1.6	7.7 ± 1.4	0.37
HbA1c (mmol/mol)	86.4 ± 17.5	84.2 ± 15.3	
FPG (mmol/l)	7.94 ± 2.94	7.4 ± 2.7	0.047
PPG (mmol/l)	11.2 ± 5.4	10.5 ± 4.5	0.15
Weight (kg)	82.6 ± 14.6	82.7 ±14.1	0.73

Mean ± standard deviation (mean ± SD), values before Ramadan (pre Ramadan), values after Ramadan (post Ramadan), Hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), the value of significance comparing before and after Ramadan in fasting group (*P*).

Table IV. The effects of drugs on HbA1c, FPG, PPG and body weight in the fasting group during Ramadan.

Insülin	OAD	Variables	Pre Ramadan	Post Ramadan	p
Premix	Metformin	HbA1c (%)	8.3 ± 1.8	8.1 ± 1.1	0.66
		HbA1c (mmol/mol)	90.7 ± 19.7	88.5 ± 12	
		FPG (mmol/l)	9.35 ± 2.7	8.3 ± 2.3	0.15
		PPG (mmol/l)	14.7 ± 0.6	12.6 ± 4.8	0.13
		Weight (kg)	81.7 ± 11.6	81.5 ± 10.8	0.83
Long acting	Metformin	HbA1c (%)	8.22 ± 1.5	7.7 ± 1.2	0.34
		HbA1c (mmol/mol)	89.8 ± 16.4	84.2 ± 13.1	
		FPG (mmol/l)	6.6 ± 2.6	5.8± 1.4	0.18
		PPG (mmol/l)	9.5 ± 4	9.1 ± 3.6	0.72
		Weight (kg)	77.3 ± 12.3	78.1 ± 11.6	0.38
No insulin	Metformin	HbA1c (%)	6.9 ± 0.7	6.9 ± 0.8	0.7
		HbA1c (mmol/mol)	75.4 ± 7.7	75.4 ± 8.7	
		FPG (mmol/l)	6.3 ± 1.4	6 ± 0.9	0.27
		PPG (mmol/l)	8.7± 2.1	8.35 ± 2.1	0.48
		Weight (kg)	80 ± 15.7	80.2 ± 16.2	0.74
No insulin	Multi-drug	HbA1c (%)	8 ± 1.5	7.6 ± 0.9	0.33
		HbA1c (mmol/mol)	87.4 ± 16.4	83.1 ± 9.8	
		FPG (mmol/l)	8.9 ± 3	7.5 ± 1.7	0.1
		PPG (mmol/l)	11.2 ± 6.1	10.66 ± 3.9	0.7
		Weight (kg)	83.2 ± 10.5	83.5 ± 10.4	0.55

The values before Ramadan (pre Ramadan), the values after Ramadan (post Ramadan), oral antidiabetic (OAD), Hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), Metformin, pioglitazone, acarbose, and/or sulphonylurea (multi-drug), insulin glargine or detemir (long acting insulin), insulin aspart-insulin aspart protamine (30-70) mix or insulin lispro-insulin lispro protamine (25-75) (premix insulin).

HbA1c, fasting plasma glucose and post-prandial plasma glucose and weight changes. These results were also compared to those of the non-fasting control group who followed a dietary plan outlined by the dietitian, eating 3 main meals and 3 snacks. While not yielding significant results, HbA1c level decreased more in the fasting group than in the non-fasting group. When the pre- and post-Ramadan values were compared, a significant decrease in the fasting plasma glucose was observed in the fasting group.

Due to the possible adverse event risks, diabetes patients are not recommended to fast by their physicians. Still, in the EPIDAR study, performed in 10 Muslim countries, 43% of type 1 and 79% of the type 2 DM patients preferred to fast for extended hours during Ramadan[3]. These results show that a considerable portion of Muslim patients with diabetes is affected by extended fasting. Studies show that fasting throughout Ramadan increases risks for hypoglycemia, hyperglycemia, ketoacidosis, dehydration or a thrombotic tendency in type 2 DM patients[9,10]. However, many studies have shown no such risks but rather improvements in glycaemic control during long-term daily fasting in type 2 DM patients[4,11-14]. In our study the fasting group patients, despite the extended abstinence of food and drinks during a day (16.5 hours), did not show any disruption of glucose control, and more importantly did not experience a significant increase in adverse events like hypoglycemia, hyperglycemia, and diabetic coma.

There is no consensus on what kind of treatment should be given to the type 2 DM patients who choose to fast during Ramadan due to religious beliefs. How a safe treatment for type 2 DM patients who fast during Ramadan should be is a crucial question. In our study, four groups of anti-diabetic drugs (metformin alone, metformin plus premixed insulin, metformin plus long-acting insulin analogue, multidrug oral anti-diabetic) were compared in fasting type 2 DM patients, and none of them had significant glucose regulation changes during the period. Considering other studies on this topic, findings of the studies on premixed insulin, insulin glargine, vildagliptin, gliclazide, glimepiride support our findings[6-9,15,16].

One criticism to our report is that our study population was composed of older patients and it makes it difficult to generalize our findings to the young and general type 2 diabetic population. Moreover, fewer complications might have been observed for those with high risk of hypoglycemia and in need of more frequent food intake might have avoided fasting.

Conclusions

We could not find any negative effects of extended fasting on glucose regulation of type 2 DM patients who are using certain medications. We found that the frequency of the possible adverse events caused by extended fasting (i.e., hypoglycemia, dehydration, diabetic coma, and thrombosis) were similar to those of other diabetes patients. We failed to demonstrate benefits of increasing the number of meals in Type 2 DM patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

1) Woo JI, Ho ST, Sham A, Sea MM, Lam KS, Lam TH. Diet and glucose tolerance in a Chinese population. Eur J Clin Nutr 2003; 57: 523- 530.

2) Franz MJ, Bantle JP, Beebe CA, Brunzell JD, Chiasson JL, Garg A, Holzmeister LA, Hoogwerf B, Mayer-Davis E, Mooradian AD, Purnell JQ, Wheeler M. Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications. Diabetes Care 2002; 25: 148-198.

3) Salti I, Bénard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C, Jabbar A; EPIDIAR study group. A population-based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: results of the epidemiology of diabetes and Ramadan 1422/2001 (EPIDIAR) study. Diabetes Care 2004; 27: 2306-2311.

4) Cesur M, Corapcioglu D, Gursoy A, Gonen S, Ozduman M, Emral R, Uysal AR, Tonyukuk V, Yilmaz AE, Bayram F, Kamel N. A comparison of glycemic effects of glimepiride, repaglinide and insulin glargine in type 2 diabetes mellitus during Ramadan fasting. Diabetes Res Clin Pract 2007; 75: 141-147.

5) Khatib FA, Shafagoj YA. Metabolic alterations as a result of Ramadan fasting in non-insulin dependent diabetes mellitus patients in relation to food intake. Saudi Med J 2004; 25: 1858-1863.

6) Hassanein M, Hanif W, Malik W, Kamal A, Geransar P, Lister N, Andrews C, Barnett A. Comparison of the dipeptidyl peptidase-4 inhibitor vildagliptin and the sulfonylurea gliclazide in combination with metformin, in Muslim patients with type 2 diabetes mellitus fasting during Ramadan: results of the VECTOR study. Curr Med Res Opin 2011; 27: 1367-1374.

7) Salti I. Diabetes and Ramadan Study Group. Efficacy and safety of insulin glargine and glimepride in subjects with type 2 diabetes before, during and after the period of fasting in Ramadan. Diabet Med 2009; 26: 1255-1261.

8) The Glimepride in Ramadan (GLIRA) Study Group. The efficacy and safety of glimepride in the management of type 2 diabetes in Muslim patients during Ramadan. Diabetes Care 2005; 28: 421-422.

9) Mattoo V, Milicevic Z, Malone JK, Schwarzenhofer M, Ekangaki A, Levitt LK, Liong LH, Rais N, Tounsi H; Ramadan Study Group. A comparison of insulin lispro Mix25 and human insulin 30/70 in the treatment of type 2 diabetes during Ramadan. Diabetes Res Clin Pract 2003; 59: 137-143.

10) Al-Arouj M, Assaad-Khalil S, Buse J, Fahdil I, Fahmy M, Hafez S, Hassanein M, Ibrahim MA, Kendall D, Kishawi S, Al-Madani A, Nakhi AB, Tayeb K, Thomas A. Recommendations for management of diabetes during Ramadan. Diabetes Care 2010; 33: 1895-1902.

11) Bravis V, Hui E, Salih S, Mehar S, Hassanein M, Devendra D. Ramadan Education and Awareness in Diabetes (READ) program for Muslims with type 2 diabetes who fast during Ramadan. Diabet Med 2010; 27: 327-331.

12) Temizhan A, Donderici O, Oguz D, Demirbas B. Is there any effect of Ramadan fasting on acute coronary heart disease events? Int J Cardiol 1999; 70: 149-153.

13) Pinelli NR, Jaber LA. Practices of arab american patients with type 2 diabetes mellitus during Ramadan. J Pharm Pract 2011; 24: 211-215.

14) Ahmedani MY, Haque MS, Basit A, Fawwad A, Alvi SF. Ramadan Prospective Diabetes Study: the role of drug dosage and timing alteration, active glucose monitoring and patient education. Diabet Med 2012; 29: 709-715.

15) Zargar AH, Siraj M, Jawa AA, Hasan M, Mahtab H. Maintenance of glycaemic control with the evening administration of a long acting sulphonylurea in male type 2 diabetic patients undertaking the Ramadan fast. Int J Clin Pract 2010; 64: 1090-1094.

16) Devendra D, Gohel B, Bravis V, Hui E, Salih S, Mehar S, Hassanein M. Vildagliptin therapy and hypoglycemia in Muslim type 2 diabetes patients during Ramadan. Int J Clin Pract 2009; 63: 1446-1450.