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The Effect of Ramadan on Glycaemic Control in Type 2 Diabetic Patients

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Abstract

Background: People with type 2 diabetes fasting during Ramadan have significant increases in glycaemic excursions. Therefore, diabetes management in Ramadan should target glycaemic variability to empower people with diabetes to fast safely for prolonged periods. For this purpose, we planned to evaluate the glucose variability that might occur during the month of Ramadan by monitoring the treatments and blood glucose levels in our patients.

Aim: The current study aimed to evaluate the glucose variability that might occur during Ramadan.

Study Design: Methodological study analyzing the glucose variability during Ramadan.

Methods: One hundred patients, diagnosed with Type 2 diabetes and wanted to fast during Ramadan, were recruited. Patients were divided into three groups: the metformin group, the multiple oral anti-diabetic (OAD) group, and the insulin group. During Ramadan, the patient's capillary blood glucose was monitored and recorded five times per day (before sahur, 11 am, 5 pm, before iftar and two hours after iftar). Biochemical data, pre- and post-Ramadan fasting glycated haemoglobin (HbA1c) levels, and glucose measurements were compared between the three groups.

Results: There was no significant difference between the three group in terms of age, gender, body mass index (BMI), or diabetic complications. Diabetic nephropathy frequency,

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fasting plasma glucose, and HbA1c levels were significantly lower in the metformin group. There was no significant association between HbA1c changes among the three groups. There was also a significant association between before sahur, 11 am, 5 pm, and iftar blood glucose levels among the three groups. A higher risk of post-iftar excursions was observed in insulin-treated patients.

Conclusion: Patients on insulin treatment were less tolerant of fasting and had an increased risk for hypoglycaemia. The insulin group required more frequent warnings regarding the acute and chronic complications that may develop due to fasting.

Keywords: blood glucose measurements, Ramadan fasting, type 2 diabetes mellitus,

INTRODUCTION

The month of Ramadan is a holy month for Muslims. Fasting during this month is one of the five basic conditions of Islam imposed on all Muslims. During fasting, Muslims avoid any oral intake, including medication from sunrise (Sahur) to sunset (Iftar). According to a demographic study conducted in 2009, 23% of the world's 6.8 billion people, i.e., 1.57 billion people, have an Islamic faith and this rate increases by 3% each year (1). In the EPIDIAR study conducted in 13 Muslim countries, it was observed that 78% of patients with type 2 diabetes preferred to fast for at least 15 days during Ramadan (2).

People with type 2 diabetes fasting during Ramadan have significant increases in glycaemic excursions (2). Glycaemic excursions are disruptive to the individual and measures of variability are associated with subsequent hypoglycaemia (3). Therefore, diabetes management in Ramadan should target glycaemic variability to empower people with diabetes to fast safely for prolonged periods (4). For this purpose, we planned to evaluate the glucose variability that might occur during the month of Ramadan by monitoring the treatments and blood glucose levels in our patients.

MATERIALS AND METHODS

This study included one hundred patients diagnosed with type 2 Diabetes Mellitus who presented to the Sakarya University, Education and Research Hospital Outpatient Diabetes Clinic. At three months follow-up, laboratory studies were conducted at least 15 days before Ramadan started. Patients with type 1 diabetes, gestational diabetes, chronic kidney and liver failure, thyroid dysfunction, severe anemia, and oncologic and hematological malignancies were excluded.

Demographic data, anthropometric characteristics, additional diseases, and diabetic complications of patients were evaluated. Patient's biochemical parameters and three-month glycated hemoglobin (HbA1c) values were scanned and recorded at pre-Ramadan (days before Ramadan start) and post-Ramadan (within o week after Ramadan fasting was completed).

The treatment they had received before Ramadan was reassessed to reduce the risk of hypoglycemia (defined as glucose level below 70 mg/dl or 3,9 mmol/L) that may occur during fasting. Blood glucose levels were evaluated at the follow-ups and a dose reduction was performed when necessary. According to their treatment, patients were divided into three groups: the metformin group, the multiple oral anti-diabetic group (OAD), and the insulin group. Group 1 consisted of patients who received metformin only.

Group 2 consisted of patients who received DPP-4 Inhibitors + Metformin, Sulphonylurea + Metformin, or meglitinide + metformin therapy. Patients were instructed to take Sulphonylurea before iftar (the breaking of fast with a meal at sunset).

Group 3 consisted of patients who received intensive insulin or premixed insulin therapy.

All patients were interviewed by their physicians, diabetes educators and nutritionists before fasting. All patients were instructed to check and keep records of their blood glucose reading meters. Capillary blood glucose was monitored five times per day (before sahur, at 11 am, 5 pm, before iftar, and two hours after iftar) and was performed once a week during Ramadan (four weeks). Patients were also screened for the presence of hypoglycemia symptoms.

Demographic data, anthropometric data, biochemical data, and pre- and post-Ramadan fasting HbA1c levels were compared between the three groups. The lowest and highest blood glucose measurements, taken over the four weeks, five times a day, were labelled as minimum/maximum values and treatment groups were compared accordingly. We also selected the minimum and maximum blood glucose measurements in each group and documented them as "total". The differences between the minimum/maximum values for each period and the totals were calculated and labelled as "delta". Groups were compared based on the "delta" values. Also, the changes in HbA1c levels before and after Ramadan were compared.

Statistical Analysis

Data analysis was performed using the SPSS 10.0 statistical program [SPSS Inc. Chicago, IL]. Normally distributed continuous data were reported as the mean and standard deviation (SD), whereas non-normally continuous data were reported as the median and interquartile range (IR). ANOVA was used for the comparison of normally distributed data, and the Kruskal-Wallis test was used for the comparison non-normally distributed data. The Chi-square test was used to determine the association between the categorical data. $P < 0.05$ was considered significant

RESULTS

A total of one hundred patients (age, mean (SD) 57 years; Female/Male (F/M) 48/52) were included in the study. There were 38 patients in the metformin group (age, mean (SD) 56 years; F/M 19/19), 44 patients in the multiple OAD group (age, mean (SD) 55 years, F/M 24/20), and 18 patients in the insulin group (age mean (SD) 60 years; F/M 9/9). Demographic data of the patients are summarized in Table 1.

There was no significant difference between the metformin group, multiple OAD group and insulin group in terms of age, gender, BMI (basal metabolic index), additional diseases, diabetic complications (except diabetic nephropathy) or hypoglycemia symptoms ($p> 0.05$). Diabetic nephropathy and duration of diabetes mellitus were statistically different between the three groups ($p < 0.05$) (Table 1). Fasting plasma glucose (FPG) levels and HbA1c levels at baseline and after fasting were also significantly different between the three groups ($p < 0.05$) (Table 2).

When blood glucose measurements and their variability were examined, Sahur maximum, 11 am minimum and maximum, 5 pm minimum and maximum, and iftar minimum and maximum

Table 1. Demographic Data

	METFORMİN	OAD	INSULIN	P
Number of person (N)	38	44	18	
Age (Y)	55,9 ± 10,1	55,2 ± 9,7	59,5 ± 8,2	0,274
Gender (Female/Male)	19 / 19	24 / 20	9 / 9	0,903
*BMI (KG/M^2)	30.1 ± 5.65	30.2 ± 7,3	33,3 ± 10,3	0,813
*DM duration (year)	6 ± 6	6 ± 7	11 ± 8	0,003
Hypertension (N/%)	20 (52,6)	25 (56,8)	15 (83,3)	0.077
Hyperlipidaemia (N/%)	22 (57,9)	34 (77,3)	14(77,8)	0.118
Coronary artery disease (N/%)	2 (5.3)	4 (9,1)	2 (11.1)	0.707
Peripheral artery disease (N/%)	0	0	0	
Cerebrovascular disease (N/%)	1 (2,6)	1 (2,3)	1 (5,6)	0.778
Diabetic neuropathy (N/%)	2 (5.3)	1 (2,3)	1 (5,6)	0.736
Diabetic retinopathy (N/%)	1 (2,6)	1 (2,3)	0	0.794
Diabetic nephropathy (N/%)	1 (2.6)	3 (6,8)	4 (22.2)	0.038
Hypoglycaemia (N/%)	1 (2,6)	1 (2,3)	0	0.794

*Abnormal distribution; BMI, body mass index; DM, diabetes mellitus; F, female; M, male

Table 2. Laboratory Data

	METFORMIN	OAD	INSULIN	P
*FPG1 (mg/dl) median (IR)	138 (34,5)	150 (48)	200 (113)	0.000
HBA1C (%) mean (SD)	6.6 (0.75)	7.4 (1.1)	8.4 (1.8)	0.000
LDL 1 (mg/dl) mean (SD)	138 (39.9)	146 (33.8)	143 (45.8)	0.645
*TG 1 (mg/dl) median (IR)	137 (86.5)	146 (124)	170 (187)	0.137
Cr (mg/dl) mean (SD)	0.74 (0.16)	0.76 (0.21)	0.80 (0.24)	0.55
ALT 1 (mg/dl) mean (SD)	22 (15.5)	20 (9)	22 (12)	0.319
*FPG 2 (mg/dl) median (IR)	134 (37)	146 (47)	164 (77)	0.042
HBA1C2 (%) mean (SD)	6.5 (0.9)	6.9 (0.9)	7.9 (1.4)	0.000
*LDL2 (mg/dl) median (IR)	125 (52)	131 (34)	144 (51)	0.624
*TG2 (mg/dl) median (IR)	162 (84)	151 (116)	155 (195)	0.699
Cr 2 (mg/dl) mean (SD)	0.72 (0.16)	0.72 (0.17)	0.79 (0.2)	0.38
*ALT 2 (mg/dl) median (IR)	20 (8.5)	21 (9)	22 (15)	0.740

1: Pre-Ramadan; 2: Post-Ramadan; FPG, fasting plasma glucose; LDL, low density lipoprotein; TG, triglyceride; HBA1C, glycated hemoglobin; ALT, alanine transaminase; AST, aspartate transaminase

blood glucose levels were significantly different ($p < 0.05$) (Table 3).

Table 4. Blood Glucose Measurement Data of the Events

	METFORMIN	OAD	INSULIN	P
*SAHUR MIN median (IR)	110 ± 19	112 ± 46	117 ± 76	0.394
SAHUR MAX mean (SD)	177 ± 51	186 ± 46	246 ± 76	0.000
11 MIN mean (SD)	129 ± 25	132 ± 27	162 ± 36	0.000
11 MAX mean (SD)	180 ± 44	193 ± 47	243 ± 62	0.000
*17 MIN median (IR)	107 ± 21	106 ± 24	135 ± 57	0.003
*17 MAX median (IR)	135 ± 49	137 ± 41	198 ± 79	0.000
*IFTAR MIN median (IR)	106 ± 26	100 ± 29	129 ± 67	0.000
*IFTAR MAX median (IR)	135 ± 50	132 ± 55	195 ± 107	0.001
*IFTAR 2 MIN median (IR)	135 ± 70	136 ± 55	178 ± 59	0.110
*IFTAR 2 MAX median (IR)	206 ± 109	215 ± 81	288 ± 147	0.128

2: 2 hours after iftar; MIN, minimum ; MAX, maximum

Table 3. Blood Glucose Variability Factors in Patients

	METFORMIN	OAD	INSULIN	P
*SAHUR MIN median (IR)	110 ± 19	112 ± 46	117 ± 76	0.394
SAHUR MAX mean (SD)	177 ± 51	186 ± 46	246 ± 76	0.000
11 MIN mean (SD)	129 ± 25	132 ± 27	162 ± 36	0.000
11 MAX mean (SD)	180 ± 44	193 ± 47	243 ± 62	0.000
*17 MIN median (IR)	107 ± 21	106 ± 24	135 ± 57	0.003
*17 MAX median (IR)	135 ± 49	137 ± 41	198 ± 79	0.000
*IFTAR MIN median (IR)	106 ± 26	100 ± 29	129 ± 67	0.000
*IFTAR MAX median (IR)	135 ± 50	132 ± 55	195 ± 107	0.001
*IFTAR 2 MIN median (IR)	135 ± 70	136 ± 55	178 ± 59	0.110
*IFTAR 2 MAX median (IR)	206 ± 109	215 ± 81	288 ± 147	0.128

2: 2 hours after iftar

There was also a significant association between before sahur, 11 am, 5 pm, and iftar blood glucose levels among the three groups ($p < 0.05$). There was no significant association between HbA1c changes ($p > 0.05$) (Table 4).

Blood glucose levels and HbA1c variability are summarized in Figure 1.

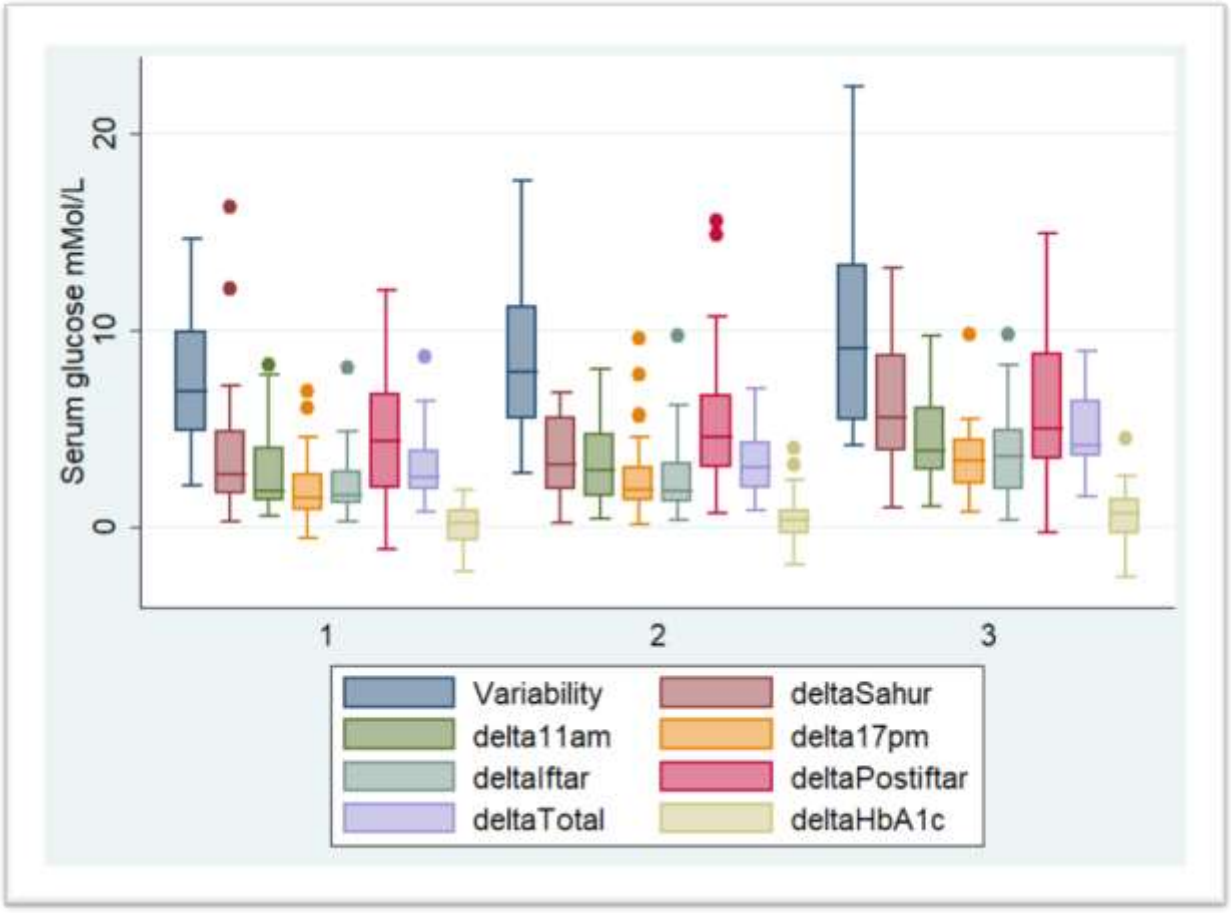

Figure 1. Blood glucose levels and HbA1c variability

DISCUSSION

It is known that there is an increasing prevalence of diabetes in Muslim countries, and people with diabetes who want to fast due to their religious beliefs frequently attend diabetes centres in our country and other Muslim countries. Numerous studies have been conducted on diabetes regulations, hypoglycaemia, and hyperglycaemia. On the contrary, in many other studies, it was found that fasting did not impair blood glucose regulations and did not increase the risk of hypoglycaemia. The studies are very different and varied in terms of design, the number of patients, and the study objectives. In our study, we aimed to investigate the effect of fasting on glycaemic regulation and variability in patients with type 2 diabetes who visited our clinic.

One of the most important complications that may occur in the summer months, due to the prolonged fasting period is hypoglycaemia (5,6). In the EPIDIAR study, severe hypoglycaemia rates were found to be high especially in the patients who used insulin (2). Expert opinions suggested that reducing the incidence of hypoglycaemia can be achieved by reducing the

total dose of insulin by 20–50% (2,7). In another study, continuous glucose monitoring recordings, during, before, and after Ramadan showed wide intra- and interindividual variability. When the mean glucose measurements were evaluated, there was a slow decline before the fasting period and a rapid increase after iftar. The results indicated a higher risk of after iftar excursions, poorer glucose control in insulin-treated patients as well as in patients taking sulphonylurea. This difference was more significant in the group receiving insulin treatment compared to the group receiving OAD (8)

In our study, there was no increase in glycaemic variability in the patient group using only metformin and using more than one OAD, whereas in the patients using mixed and basal-bolus insulin, there was a significant increase in the risk of glycaemic fluctuations and hypoglycaemia. Most patients with baseline blood glucose levels regulated by OAD and without comorbidities are able to tolerate long periods of fasting. When these results are evaluated, it should be kept in mind that hypoglycaemia and associated comorbidities may be seen more in patients receiving insulin therapy. In particular, the insulin group required more frequent warning of the acute and chronic complications of fasting.

In our study, control HbA1c values decreased in all groups, including the insulin group. Compared with BMI, LDL, and triglyceride levels, there was no significant difference between the groups using OAD and insulin. In many studies, significant decreases have been observed when comparing other periods of the year with the month of Ramadan in the lipid profile, HbA1c levels, arterial blood pressure, and uric acid levels (9). In a study involving 23 patients, a significant decrease in the body fat mass was found when there were no differences in BMI measurements, and it was thought that the decrease in HbA1c could be due to a decrease in body fat (10). Again, a study conducted in Turkish non-fasting diabetic showed that patients had higher plasma glucose levels during Ramadan and after Ramadan compared to fasting diabetic patients (11). These results suggest that fasting may be useful for some of the diabetic patients.

As a result of the EPIDIAR study, there was an increase in the risk of hypoglycaemia, hyperglycaemia, dehydration, ketoacidosis, and thrombosis in patients with type 2 diabetes (2) However, in many studies, there was no increase in risk (2,12-16). Of course, different factors such as patient group, fasting period and percentage of patients with complications may affect the results. In our study, none of the patients had acute complications such as ketoacidosis, hyperosmolar hyperglycaemic coma, or severe hypoglycaemia requiring hospitalisation. Proactive and focused nutritional advice, together with appropriate dose adjustments of anti-diabetic medications, should help keep blood glucose levels better controlled and more stable during Ramadan fasting (8,17-21).

CONCLUSION

There is no clear consensus on how to treat patients with diabetes who want to fast. In our study, patients using single or several OADs were more tolerant of fasting, whereas patients who were on insulin were found to be less tolerant. As a result, the increasing number of diabetic patients with the growing prevalence of diabetes is still a problem for physicians. The most appropriate approach is for the treatment decision to be based on the patients' characteristics and aim to provide the least harm to the patients.

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Conflict of Interest Disclosure: The authors declare that they have no conflict of interest.

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