

The Effects of Fasting during Ramadan on Glycemic Excursions Detected by Continuous Glucose Monitoring System (CGMS) in Patients with Type 2 Diabetes

Bonakdaran S H, MD, Khajeh-Dalouie M, MD

Endocrine research center, Mashhad University of Medical Sciences, Iran

SUMMARY

Objective: Safety of fasting in Ramadan for diabetic patients is not clearly known. The aim of this study was to determine the effects of fasting on glycemic excursions by continuous glucose monitoring system (CGMS).

Materials and Methods: This pilot, observational study conducted in the Endocrine Research Center, Mashhad University of Medical Sciences, Mashhad, IRAN, in Ramadan 2008. Seventeen well controlled patients with diabetes type 2 who were taking oral agents underwent 72 hour monitoring of glycemic excursions by CGMS one month before Ramadan and during Ramadan. The extent and duration of hyperglycemic and hypoglycemic events were evaluated and compared.

Results: A significant reduction in hyperglycemic events was observed during Ramadan. The extent and duration of hypoglycemic events was not significantly different between two states (Ramadan and before). A significant increase in number of hypoglycemic events in Ramadan was found in patients who take sulfonylurea compared with those who take only metformin.

Conclusion: Fasting in Ramadan can be safe for well controlled patients with type 2 diabetes.

KEY WORDS:

Ramadan- Diabetes- CGMS- Fasting

INTRODUCTION

Fasting in Ramadan is one of the five pillars of Islam. Ramadan is a lunar month and can be 29 to 30 days long. The length of days may reach to 20 hours in some seasons. Muslims are prohibited from smoking and intaking any thing including medication during Ramadan from predawn (Suhur) to sunset (Iftar). Although the Holy Quran exempts patients who are harmed by fasting from doing it¹, many patients including diabetics, insist on fasting. The EPIDIAR study in 13 Islamic countries showed that 40-50 million diabetic patients (43% of type 1 and 79% of type 2) fast during Ramadan². The definite effects of fasting on control of blood glucose in diabetic patients and its complications are mainly unknown. Some studies have shown harmful effects like increasing the number of severe hypoglycemia or hyperglycemia episodes²⁻⁴. On the other hand most of studies have reported that fasting

did not significantly change the glycemic control, and it seems safe for low risk diabetic patients if proper changes in diet, physical activities, medication dosing and timing have been made⁵⁻⁷. In 2005 The American Diabetes Association (ADA) published a recommendation for management of diabetes in Ramadan⁸. According to that study, patients with type 2 diabetes who are well controlled with only diet or metformin therapy are considered low risk and may safely fast. All of the previous published studies on the effect of fasting in diabetes, are based on symptoms of hyper and hypoglycemia, measurement of fasting blood sugar (FBS) and postprandial glucose by self monitoring blood glucose (SMBG), measurement of glycosylated hemoglobin (HbA1C) or fructosamine level. Hypoglycemia is a rare cause of mortality in patients with type 2 diabetes. Mild hypoglycemia following daytime fasting is the most prevalent complication of diabetes during Ramadan⁹. The role of postprandial hyperglycemia on the microvascular and possibly macrovascular complications have been confirmed in patients with diabetes¹⁰. Several studies have reported a manifold increase in postprandial hyperglycemia after Iftar and Suhur, which could be due to reduction in medications dosage or increase in food or sugar intake^{2,11}. As we know the majority of hypoglycemic and hyperglycemic episodes particularly mild hypoglycemia and postprandial hyperglycemia, are asymptomatic and measurement of HbA1C and SMBG would not be sufficient to detect them. SMBG gives an incomplete picture of blood glucose excursions and several glycemic excursions may occur despite an ideal HbA1C¹². The continuous glucose-monitoring system (CGMS) allows identification of glucose excursions and it is a better method for glycemic control¹³. The aim of this study was to determine the prevalence and extent of hypoglycemia and hyperglycemia in patients with type 2 diabetes in non-fasting state (one month before Ramadan) and comparing the results with fasting state in Ramadan.

MATERIALS AND METHODS

Patient's selection: Seventeen low risk patients with type 2 diabetes, who were willing to fast at least 20 consequent days in Ramadan, were selected. They were informed about the risks of hypoglycemia and hyperglycemia aggravation during Ramadan. The study protocol was approved by the research ethics committee of MUMS (Mashhad University of Medical Sciences). All patients gave informed voluntary consent. Exclusion criteria included: type 1 diabetes, type 2 diabetic

This article was accepted: 2 October 2011

Corresponding Author: Shokoufeh Bonakdaran, Mashhad University of Medical Sciences, Endocrine Research Center, Ghaem Hospital- Ahmad Abad Street, Mashhad, Khorasan Razavi 91766, Iran (Islamic Republic Of) Email: bonakdaransh@mums.ac.ir

patients taking insulin, poor control diabetes (HbA1C > 8% or 64 mmol/l), history of recent or recurrent hypoglycemia, pregnancy, lactation and presence of diabetes' complications (nephropathy, retinopathy, cardiovascular disease, uncontrolled hypertension).

The CGMS system: CGMS measures interstitial glucose every 10 seconds and stores the average every 5 minutes, with a total of 288 times of recording each day. It is estimated that the difference in plasma and interstitial fluid glucose to be less than 6%. A communicator device downloads data stored in the monitor on a personal computer.

Study protocol: this is a pilot, open-label, observational study that was conducted at autumn 2008 in Endocrine Research Center, Mashhad, Iran. Patients who met inclusion criteria received intensive training, at least one hour, for using CGMS one month before Ramadan. Then sensor was inserted subcutaneously into the anterior abdominal wall. Each subject was asked to enter 4 capillary glucose measurements which were taken daily with Accucheck Glucometer® that was provided by us. It was mandatory for all patients to record their dietary programs, time of all meals, quality and quantity of meals, and time and extent of any exercise. The time of meals, medication usage and exercise were entered into the device by patients. Each patient was asked to come back after 72 hours for sensor disconnection and downloading data with Medtronic MiniMed software. The monitoring process was repeated during Ramadan, after 15 days of consequent fasting and without any changes in medication dosage and physical activities. We defined a hypoglycemic episode as a glucose value less than 3.88 mmol/lit with or without symptoms. Hyperglycemia was defined as a value more than 10 mmol/lit. We counted the percent time of hypoglycemia and their durations as well as periods with hyperglycemia. The correlation coefficient and mean absolute difference (MAD) were calculated by Medtronic software and defined as >0.79 and <28%, respectively.

Statistical analyses

Statistical analyses performed with SPSS version 14. Normally distributed quantitative variables were demonstrated as mean \pm standard deviation. For comparison of quantitative variables, the independent t test and Mann-Whitney test were utilized. Paired t tests for parametric parameters and Wilcoxon test for non parametric parameters were used to analyze the changes in glycaemic excursions before and during Ramadan. P value less than 0.05 considered significant.

RESULTS

17 patients (10 females and 7 males) completed the study. Mean patients age was 42.4 ± 8.5 years and mean duration of diabetes was 6.9 ± 4.7 years. Their diabetes was under good control and mean HbA1C was 6.3 ± 1.8 %. 53% of patients (9 patients) were taking only metformin and 47 % (8 patients) had a combination of metformin and glibenclamide.

The mean number of glucose reading by CGMS, correlation coefficient between SMBG and CGMS and mean absolute difference before and during Ramadan were in normal range [Table I]. We found frequent episodes of asymptomatic

hyperglycemia and hypoglycemia in well controlled patients before Ramadan. During Ramadan the frequency of hyperglycemic episodes decreased. The difference between the number of hyperglycemic episodes before and during Ramadan was significant. The overall incidence of asymptomatic hypoglycemia was increased in Ramadan but the patients reported neither a major nor a minor hypoglycemic event. The differences between duration of hypoglycemia episodes in two states were not significant. Changes in percentage of hyperglycemia and hypoglycemia events in Ramadan and comparison of CGMS results before and during Ramadan are shown in table I. We compared mean fasting interstitial glucose (FBS) of non-fasting state with interstitial glucose before Suhur in fasting state. Interstitial glucose 2 hours after breakfast was compared with interstitial glucose 2 hours after Suhur. Also interstitial glucose after lunch and dinner in non-fasting state was compared with interstitial glucose after Iftar in Ramadan. The results showed an improvement in postprandial blood glucose in month of Ramadan [table II]. Regarding medication usage patients were divided into two groups: group I, those who only took metformin and group II, patients who had sulfonylurea or both metformin and sulfonylurea in their regimens. The difference of occurring glycaemic events especially hypoglycemic ones in two groups was significant in Ramadan [Table III]. We analyzed all complications related to CGMS including bleeding, pain, and local infection during the study. All patients completed the CGMS integrity and no CGMS complications were found. No diabetes related adverse events were observed during Ramadan.

DISCUSSION

The effects of fasting in Ramadan on glycaemic excursions of patients with type 2 diabetes are not clearly known. In best of our knowledge this study is the first study of assessing glycaemic excursions by CGMS in fasting state (Ramadan) and comparing the results with non fasting state (one month before Ramadan). We selected low risk diabetic patients for our study. Despite good control of diabetes in these patients, CGMS results showed frequent hyperglycemic and hypoglycemic episodes in them one month before Ramadan. Our results are consistent with the results of other studies that evaluate well controlled diabetic patients¹⁴⁻¹⁶. We found a significant reduction of hyperglycemic events during Ramadan. The prevalence of major hyperglycemia during Ramadan in our study was not as high as what was reported in many other studies. Comparable with our results, several studies have shown an improvement in glycaemic control during Ramadan⁵⁻⁷. On the contrary in the EPIDAR study, the frequency of hyperglycemia episodes was significantly higher during Ramadan². The possible causes of difference between our results and EPIDAR results may be related to several factors: 1) difference in sample size and racial variation in our patients, 2) we observed all (symptomatic and asymptomatic) events of hyperglycemia, and finally 3) we selected well controlled diabetic patients for fasting but EPIDAR study included all diabetic patients willing to fast.

We detected asymptomatic hypoglycemic events in well controlled patients during Ramadan, and it was higher in patients who received sulfonylurea. The most common cause

Table I: Change in outcome measures during Ramadan

	Before Ramadan	During Ramadan	p
Number of glucose reading by CGMS(time)	712.4±182.05	704.52±194.5	0.77
Mean absolute difference (MAD) (%)	12.9±9.3	11.22±3.9	0.29
Percent of hyperglycemia (%)	28.1±24.2	15.9±21.8	0.04
Duration of hyperglycemia(minute)	1048.76±920.9	467.15±415.04	0.003
Percent of hypoglycemia (%)	0.7±2.6	1.6±3.06	0.21
Duration of hypoglycemia(minute)	30.09±113.57	67.6±121.05	0.24

Data is expressed as mean ± SD

Differences were studied by Student's t test

Table II: Comparison of pair glycemic targets in patients

	mean± SD	95% Confidence interval	p
Fasting interstitial glucose(mg/dl) With	138.0± 31.6		
Interstitial glucose before Suhur(mg/dl)	118.8±25.3	4.2-34.06	0.01
Interstitial glucose after breakfast(mg/dl) With	192.1±60.3		
Interstitial glucose after Suhur(mg/dl)	157.7± 39.1	3.5-65.2	0.03
Interstitial glucose after lunch (mg/dl) With	177.5±41.1		
Interstitial glucose after Iftar(mg/dl)	155.8±47.7	-4.2-47.7	0.09
Interstitial glucose after dinner(mg/dl) With	170.7±50.2		
Interstitial glucose after Iftar	155.8±47.7	-14.0-43.8	0.29

Table III: Change in outcome measures during Ramadan according to type of treatment

	Metformin	Metformin+Sulfonylurea or Sulfonylurea	p
Number of patients	9	8	
Percent of hyperglycemic events before Ramadan	17.5±13.5%	40.1±28.7%	0.01
Percent of hyperglycemic events during Ramadan	15.1±22.8%	27.5±20.0%	0.71
Duration of hyperglycemia before Ramadan(minute)	656.9±631.5	1489.6±1031.0	0.15
Duration of hyperglycemia during Ramadan(minute)	276.7±301.8	681.3±436.5	0.31
Percent of hypoglycemic events before Ramadan	0.11±0.3%	1.3±3.8%	0.03
Percent of hypoglycemic events during Ramadan	0.11±0.3%	3.3±3.8%	<0.001
Duration of hypoglycemia before Ramadan (minute)	4.7±14.2	58.6±165.8	0.03
Duration of hypoglycemia during Ramadan (minute)	10.4±31.3	153.5±157.2	<0.001

Data is expressed as mean ± SD

Differences were studied by Student's t test

of hypoglycemia is medication especially in intensive glucose control regimens such as insulin therapy or sulfonylurea¹⁷. The ADA recommended caution in fasting in the case of taking insulin or insulin secreting agents⁸. In our study there was no significant difference between the duration of hypoglycemia before Ramadan and during Ramadan. Some studies have shown increased frequency of hypoglycemia in Ramadan whereas some other do not. Reported low hypoglycemic events during Ramadan in present study may be related to younger age of our patients and also selection of patients with acceptable glycemic control. A significant difference in the number of hypoglycemic events between two groups of patients (patients received only metformin versus patients who used sulfonylurea in their regimen) was observed. It seems that the addition of sulfonylurea, increases the risk of hypoglycemia and patients should be strongly advised for risk of hypoglycemia during Ramadan.

This study is the first report of glucose changes in patients with diabetes during Ramadan. The most important limiting factor in the interpretation of our results is the small sample size.

CONCLUSION

With respect to our results, it seems that in well controlled patients with type 2 diabetes who are on oral antidiabetes agents especially metformin, the risk of fasting is very low and patients may fast safely in Ramadan. However patients have to receive an appropriate education including frequent blood glucose measurement, information about sign and symptoms of hyperglycemia and hypoglycemia, changes in meal pattern, physical activity and medications.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Dr. Raof from the Parsian diabetes center for his valuable assistance in this study and Vice Chancellor for Research at Mashhad University of Medical Sciences for financial support (number:85479)

AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist.

REFERENCES

1. Surah Al-Bagarah(chapter 2) verses 183-185. The Holy Quran
2. Salti I, Benard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C *et al.* 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 Oct;27(10): 2306-11.
3. Alberti H, Boudriga N, Nabli M. Lower attendance rates and higher fasting glucose levels in the month of Ramadan in patients with diabetes in a Muslim country. *Diabet Med.* 2008 May; 25(5): 637-8.
4. Ahmadani MY, Riaz M, Fawwad A, Hydrie MZ, Hakeem R, Basit A. Glycaemic trend during Ramadan in fasting diabetic subjects: a study from Pakistan. *Pak J Biol Sci.* 2008 Aug 15; 11(16): 2044-7.
5. Yarahmadi S, Larijani B, Bastanhagh MH, Pajouhi M, Baradar Jalili R, Zahedi F *et al.* Metabolic and clinical effects of Ramadan fasting in patients with type II diabetes. *J Coll Physicians Surg Pak.* 2003 Jun; 13(6): 329-32.
6. Benaji B, Mounib N, Roky R, Aadil N, Houti IE, Moussamih S *et al.* Diabetes and Ramadan: review of the literature. *Diabetes Res Clin Pract.* 2006 Aug; 73(2): 117-25.
7. 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 Dec; 25(12): 1858-63.
8. Al-Arouj M, Bouguerra R, Buse J, Hafez S, Hassanein M, Ibrahim MA *et al.* Recommendations for management of diabetes during Ramadan. *Diabetes Care.* 2005 Sep; 28(9): 2305-11.
9. Hassanein M, Bravis V, Hui E, Devendra D. Ramadan-focused education and awareness in type 2 diabetes. *Diabetologia.* 2009 Feb; 52(2): 367-8.
10. Cavalot F, Petrelli A, Travers M, Bonomo K, Fiora E, Conti M *et al.* Postprandial blood glucose is a stronger predictor of cardiovascular events than fasting blood glucose in type 2 diabetes mellitus, particular in women. *J Endocrinol Metab* 2006; 91: 813-9.
11. M'Guil M, Ragala MA, El Guessabi L, Fellat S, Chraibi A, Chabraoui L *et al.* Is Ramadan fasting safe in type 2 diabetic patients in view of the lack of significant effect of fasting on clinical and biochemical parameters, blood pressure, and glycemic control? *Clin Exp Hypertens.* 2008 Jul; 30(5): 339-57.
12. Boland E, Mansod T, Delucia M, Brandt CA, Fernando S, Tamborlane WV. Limitation of Conventional methods of self monitoring of blood glucose. *Diabetes Care* 2001; 24: 1858-62.
13. Garg S, Zisser H, Schwartz S, Bailey T, Kaplan R, Ellis S *et al.* Improvement in glycemic excursions with a transcutaneous, real-time continuous glucose sensor: a randomized controlled trial. *Diabetes Care.* 2006 Jan; 29(1): 44-50.
14. Hay LC, Wilmshurst EG, Flucher G. Unrecognized hypo and hyperglycemia in well Controlled patients with type 2 diabetes mellitus. *Diabetes Technol Ther* 2003; 5: 19-26.
15. Bode BW, Schwartz S, Stubbs HA, Block JE. Glycemic characteristics in continuously monitored patients with type 1 and type 2 diabetes: Normative values. *Diabetes Care* 2005; 28: 2361-6.
16. Bonakdaran S, Rajabian R. Prevalence and extent of glycemic excursions in well-controlled patients with type 2 diabetes mellitus using continuous glucose-monitoring system. *Indian J Med Sci.* 2009 Feb; 63(2): 66-71.
17. Amiel SA, Dixon T, Mann R, Jameson K. Hypoglycaemia in Type 2 diabetes. *Diabet Med.* 2008 Mar; 25(3): 245-54.