Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Diabetes & Metabolism 41 (2015) 28–36

Original article

Glucose excursions and glycaemic control during Ramadan fasting in diabetic patients: Insights from continuous glucose monitoring (CGM)

N. Lessan [a,*], Z. Hannoun [a], H. Hasan [b], M.T. Barakat [a]

[a] *Imperial College London, Diabetes Centre, PO Box 48338, Abu Dhabi, United Arab Emirates*
[b] *University of Sharjah, United Arab Emirates*

Received 9 September 2014; received in revised form 5 November 2014; accepted 10 November 2014

Abstract

Aim. – Ramadan fasting represents a major shift in meal timing and content for practicing Muslims. This study used continuous glucose monitoring (CGM) to assess changes in markers of glycaemic excursions during Ramadan fasting to investigate the short-term safety of this practice in different groups of patients with diabetes.

Methods. – A total of 63 subjects (56 with diabetes, seven healthy volunteers; 39 male, 24 female) had CGM performed during, before and after Ramadan fasting. Mean CGM curves were constructed for each group for these periods that were then used to calculate indicators of glucose control and excursions. Post hoc data analyses included comparisons of different medication categories (metformin/no medication, gliptin, sulphonylurea and insulin). Medication changes during Ramadan followed American Diabetes Association guidelines.

Result. – Among patients with diabetes, there was a significant difference in mean CGM curve during Ramadan, with a slow fall during fasting hours followed by a rapid rise in glucose level after the sunset meal (*iftar*). The magnitude of this excursion was greatest in the insulin-treated group, followed by the sulphonylurea-treated group. Markers of control deteriorated in a small number ($n = 3$) of patients. Overall, whether fasting or non-fasting, subjects showed no statistically significant changes in mean interstitial glucose (IG), mean amplitude of glycaemic excursion (MAGE), high and low blood glucose indices (HBGI/LBGI), and number of glucose excursions and rate of hypoglycaemia.

Conclusion. – The main change in glycaemic control with Ramadan fasting in patients with diabetes is in the pattern of excursions. Ramadan fasting caused neither overall deterioration nor improvement in the majority of patients with good baseline glucose control.

Keywords: Diabetes mellitus; Glucose; Continuous glucose monitoring; CGM; Ramadan fasting; Muslim

1. Introduction

Fasting during the Muslim holy month of Ramadan is an obligatory duty for all healthy adult Muslims. The fast entails abstinence from eating and drinking from dawn to sunset for a whole lunar month (29 or 30 days). Between sunset and dawn, there are no restrictions on food or fluid intake.

Fasting may have certain health benefits [1–3], but it also brings challenges to certain patient groups, including those with diabetes [4,5]. Although sickness exempts the individual from this religious duty (Holy Koran, Al-Bakarah, 183–185), many patients, including those with diabetes, choose to go ahead with fasting for social, cultural and religious reasons [4,6,7], thereby often putting themselves at increased risk of dysglycaemia during the fast [4]. This is a major concern for patients taking either insulin or sulphonylurea. Furthermore, the meal at sunset often includes high-calorie, carbohydrate-rich and usually sweet food, which can lead to major glycaemic excursions in these patients.

Most patients who practise fasting appear to have no complications from it, at least in the short-term. Observational

Abbreviations: HPLC, High-performance liquid chromatography; HbA_{1c}, Glycosylated haemoglobin; CGM, Continuous glucose monitoring; IG, Interstitial glucose; DPP-IV, Dipeptidyl peptidase-IV; AUC, Area under the curve; MAGE, Mean amplitude of glycaemic excursion; HBGI, High blood glucose index; LBGI, Low blood glucose index; T1DM, Type 1 diabetes mellitus; T2DM, Type 2 diabetes mellitus.

* Corresponding author. Tel.: +9712 4040800×928; fax: +009712 4040900.
E-mail addresses: naderlessan@aol.com, nlessan@icldc.ae (N. Lessan).

http://dx.doi.org/10.1016/j.diabet.2014.11.004
1262-3636/

studies, such as the large-scale questionnaire-based Epidemiology of Diabetes and Ramadan (EPIDIAR) study [4], indicate that there is a significant group of patients who do experience more hyper- and hypoglycaemia during Ramadan. Other studies have used fasting plasma glucose, multiple-point capillary glucose, fructosamine and/or HbA_{1c} as markers of glycaemic control [8–10]. The Ramadan fast entails a major shift in timing and type of meals. As such, "snapshots" and markers of mean glucose fail to include this major aspect of the Ramadan fast. The potential changes in glucose patterns can be more adequately explored using continuous glucose monitoring (CGM), a technique available since the 1990s [11–15]. In the present study, CGM was used to investigate glucose excursions among patients with diabetes during the Ramadan fast.

2. Research and design methods

2.1. Subjects

Patients aged ≥ 16 years ($n = 56$) with diabetes were recruited from the Imperial College London Diabetes Centre (ICLDC) in Abu Dhabi. Selection was based on the patient's decision to fast, and ability and willingness to complete the study. Patients with unstable diabetes and those whose diabetes treatment was likely to alter for any reason other than Ramadan fasting were excluded. Healthy subjects without diabetes ($n = 7$) were also included for comparison (control group).

Ethics approval was obtained from the ICLDC Research Ethics Committee (IREC ref no. 004). The CGM procedure was explained to patients at recruitment, and their informed consent was obtained. Changes to treatment during Ramadan followed published guidelines [16,17], and involved changes in time of ingestion and a 20–30% dose reduction in patients using either sulphonylureas or insulin. There were no dose changes in patients taking other oral antidiabetic drugs (OADs).

2.2. CGM procedure

CGM was performed using the MiniMed CGMS® Gold system (Medtronic, Northridge, CA, USA). The system does not offer a real-time display of glucose records and, as such, patients are blinded to their results pending a computer download. Fasting CGM was performed over at least two consecutive days during Ramadan (1431 or 1432 of the Muslim calendar: 11 August to 9 September 2010 or 1–30 August 2011). Duration of the daily fast was about 14 h 20 min on average. Non-fasting CGM for the same length of time was obtained for each patient within three months either before ($n = 34$) or after ($n = 29$) Ramadan.

All participants were instructed on the use of the CGM system and the capillary blood sampling method for calibration of CGM (ACCU-CHEK Go blood glucose meter, Roche Diagnostics, Indianapolis, IN, USA). The subcutaneous CGM sensor was inserted into the anterior abdominal wall and secured with adhesives. The sensor was then connected to the measuring device. A more detailed description of the procedure has been described elsewhere [11,12,15]. Patients' height and weight were measured using conventional stadiometers and weighing scales. Glycated haemoglobin (HbA_{1c}) was measured using the high-performance liquid chromatography (HPLC) method (Variant II, Bio-Rad Laboratories, Hercules, CA, USA).

2.3. Data analysis and statistics

The CGM sensor records interstitial glucose (IG) at 5-min intervals for a total of 288 readings every 24 h. By averaging the IG readings at the same timepoints over consecutive days, a mean 24-h CGM curve can be constructed. Two such curves representing the pre-Ramadan and Ramadan periods, respectively, were obtained for each group (controls vs diabetes patients), and the IG readings at the 288 individual timepoints during these two periods were compared, with further analyses and comparisons by medication group. Also, recordings of different sensor-generated parameters from individual patients were used to calculate mean ± SD values for IG, maximum and minimum IG, area under the mean CGM curve (AUC), number of glucose excursions, and percentages of hyperglycaemic (IG ≥ 8.3 mmol/L) and hypoglycaemic (IG ≤ 3.9 mmol/L) excursions. The number of hypoglycaemic events (IG ≤ 3.9 mmol/L over a 5-min interval as recorded by CGM) and time spent in hypoglycaemia were also obtained from each individual's CGM data. Hypoglycaemia rate was defined as the total duration of hypoglycaemia divided by the total duration of CGM in each patient and expressed as a percentage. The total number of glucose excursions as well as the total number of hypoglycaemic and hyperglycaemic excursions were obtained from individual CGM data recordings. Means ± SD for these parameters were calculated from the collective data.

The mean amplitude of glycaemic excursion (MAGE) [16] and high and low blood glucose indices (HBGI and LBGI, respectively) were calculated, using methods as previously described [17,18]. MAGE is a common measure of the volatility of blood glucose levels. Higher MAGE values indicate an increased number of glucose excursions and poorer glycaemic control. HBGI and LBGI are non-negative numbers calculated to measure the frequency and extent of high and low blood glucose readings, respectively. The higher the index value, the greater the risk of hypoglycaemia (LBGI) or hyperglycaemia (HBGI).

SPSS 20.0 software was used for the statistical analyses. For comparative statistics, non-parametric tests (Wilcoxon's signed-rank test and Mann-Whitney U-test as appropriate) were performed. Ramadan and non-Ramadan parameters were compared in subjects with and without diabetes. The controls and patients in the different medication groups during fasting and non-fasting periods were also compared. Medication ranged from none ($n = 4$) to metformin alone ($n = 4$), a metformin/gliptin combination ($n = 16$), and a variety of other permutations of OADs, including sulphonylurea ($n = 19$) and glucagon-like peptide (GLP)-1 analogues ($n = 8$) with ($n = 7$) or without ($n = 1$) insulin. Post hoc analyses included comparisons of the following medication categories, regardless of diabetes type: group 1, no medication or metformin alone ($n = 8$); group 2, gliptin with/without metformin ($n = 16$); group 3, sulphonylurea (or medication including a sulphonylurea,

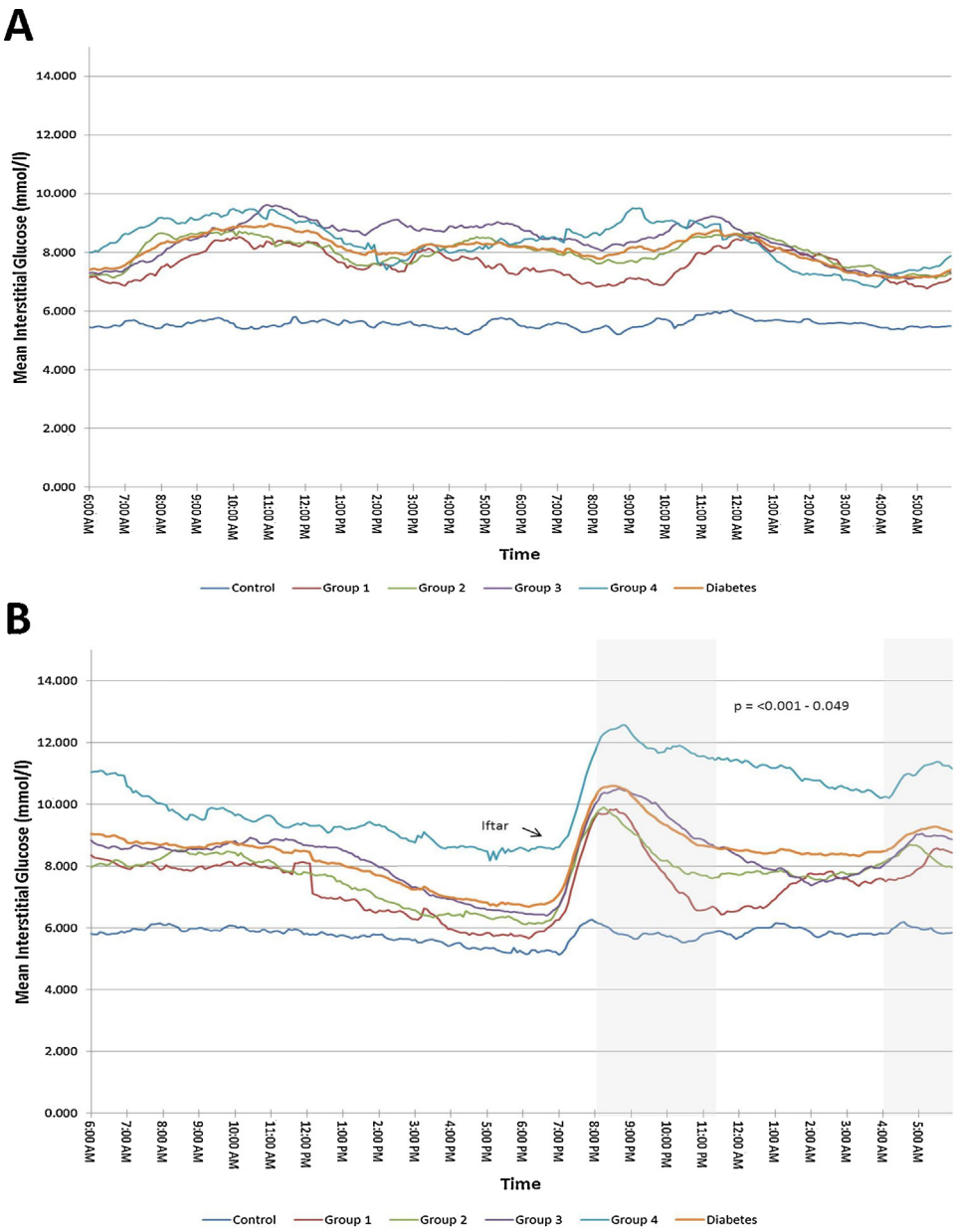

Fig. 1. Mean continuous glucose monitoring (CGM) recordings for diabetes patients and control subjects during non-fasting (A) and fasting (B) by type of treatment: group 1: diet with/without metformin; group 2: gliptin with/without metformin; group 3: sulphonylurea with/without other oral agent(s); group 4: insulin with/without other oral antidiabetic agents (OADs). The difference between patient groups and controls was highly significant ($P < 0.05$, Wilcoxon's signed-ranked test) for mean interstitial glucose during *iftar* and the predawn meal *suhoor* (shaded areas, B).

$n = 19$); and group 4, insulin with/without other agents ($n = 13$). The latter group included one patient using an insulin pump system. Data were presented as means ± SD.

3. Results

3.1. Patients with diabetes

Patients' characteristics are shown in Table 1. CGM was performed for 3.1 ± 0.8 days and 3.0 ± 0.9 days during Ramadan and non-Ramadan periods, respectively. There were 50 patients with type 2 diabetes mellitus (T2DM; age 47.3 ± 10.6 years; 34 male, 16 female) and six patients with type 1 diabetes mellitus (T1DM; age 23.3 ± 7.0 years; four male, two female). The mean non-Ramadan HbA_{1c} in diabetes patients was 7.2 ± 1.2%. CGM recordings both during and before/after Ramadan showed wide intra- and interindividual variability. During Ramadan, CGM curves showed a rapid rise in IG after *iftar* (breaking of the fast; Fig. 1B). Also, there were no statistically significant changes in mean IG, maximum IG, minimum IG, AUC and MAGE (Table 2). The amount of time spent in hypoglycaemia (2.4 ± 1.6% vs 1.1 ± 1.0%), euglycaemia (60 ± 29.1% vs 60.1 ± 26.8%) and hyperglycaemia (37.6 ± 31.2% vs 38.8 ± 27.8%) did not change with Ramadan

Table 1
Patients' characteristics during the pre-Ramadan (non-fasting) period.

Parameter	Value (mean ± SD)
n[a]	56 (39 male, 24 female)
Age (years)	44.9 ± 12.1
HbA_{1c} (%)	7.2 ± 1.2
Weight (kg)	82.2 ± 17.5
Body mass index (kg/m^2)	29.7 ± 6.5
SBP/DBP (mmHg)	119.6 ± 18.0/72.0 ± 9.9
LDL cholesterol (mmol/L)	2.8 ± 0.9
HDL cholesterol (mmol/L)	1.1 ± 0.2
Triglycerides (mmol/L)	1.9 ± 1.2

SBP/DBP: systolic/diastolic blood pressure; LDL/HDL: low-density/high-density lipoprotein.
[a] Number of patients who underwent continuous glucose monitoring during Ramadan.

fasting (Wilcoxon's signed-rank test). In addition, the number of high and low glucose excursions did not significantly differ between non-Ramadan and Ramadan periods.

Individual CGM records showed at least one hypoglycaemic (IG < 3.9 mmol/L) episode in 42.9% of patients during Ramadan and in 37.3% of patients in the non-Ramadan period. The overall hypoglycaemia rates were 1.11% during Ramadan and 2.41% during non-Ramadan periods; the difference was not statistically significant. There was, however, a significant difference in mean IG, HBGI, AUC and MAGE, but not in LBGI, between patients with diabetes and healthy, diabetes-free controls. These differences were observed during both Ramadan ($P < 0.001$) and non-Ramadan ($P < 0.001$) periods.

3.2. Analysis by medication category

All study groups demonstrated a similar glucose profile during Ramadan, with excursions at the time of *iftar* (Fig. 1 B). However, there was a hierarchy in overall glucose control and AUC of the mean CGM curve during Ramadan, with insulin-treated patients (Table 3) having the highest AUC during Ramadan fasting (146.1 ± 1.2 mmol/L.min; Table 2) and the metformin/no medication group having the lowest AUC (106.4 ± 0.9 mmol/L.min). During fasting, a significant increase in mean HBGI was seen in insulin-treated patients (8.1 ± 6.3 vs 14.0 ± 7.7; $P = 0.05$), whereas the change in other medication groups was not significant. LBGI was higher in the insulin-treated group (3.4 ± 3.9; $P < 0.05$) compared with those using no medication/metformin (1.3 ± 1.5) or gliptins (0.8 ± 0.7). Likewise, MAGE was higher in the insulin-treated patients (9.8 ± 3.4) compared with all other medication groups during the fasting period ($P < 0.05$).

3.3. Subjects without diabetes (control group)

CGM was performed for 2.6 ± 0.8 and 2.3 ± 0.3 days during Ramadan and non-Ramadan periods, respectively. In the control group [$n = 7$, age 36.2 ± 13.4 years; one male, six female; body mass index (BMI) 26.6 ± 2.6 kg/m^2], there were no significant changes in glucose profiles with Ramadan fasting. Indicators of overall glucose control (mean IG, maximum IG, minimum IG and AUC for mean CGM) did not change with fasting, although a small glucose rise with a peak of 6.6 mmol/L was seen at *iftar*. During Ramadan, there were no statistically significant changes in MAGE, HBGI, LBGI, maximum IG and minimum IG (Table 2). The amount of time spent in euglycaemia (98.0 ± 5.0% vs 99.1 ± 2.4%), hyperglycaemia (0.3 ± 0.5% vs 0.5 ± 0.8%) and hypoglycaemia (1.97% ± 2.83 vs 0.39 ± 0.7%) did not differ between non-Ramadan and Ramadan periods, respectively, in the healthy controls. The total number of excursions and number of low and high glucose excursions were also not significantly different between the two periods.

4. Discussion

The mean pre-Ramadan glycated haemoglobin level of 7.2% (55 mmol/L) in our patients with diabetes indicated good glycaemic control. This was also apparent on the patients' CGM recordings. The majority of our patients were not using either insulin or sulphonylureas, and this might explain the absence of severe hypoglycaemia in our study population during Ramadan fasting although, as already indicated, short episodes of hypoglycaemia were recorded by CGM. Yet, in spite of this, patients continued with their fasting until *iftar* time with no serious consequences.

CGM is a minimally invasive procedure well suited for the investigation of any possible changes in glucose profiles during Ramadan fasting. Yet, its use during this time was unwelcome by many patients who wished to have this time of year free of intrusions because of spiritual and cultural needs. CGM uses a subcutaneously inserted sensor to obtain a continuous record of IG, which correlates well with blood glucose levels [15]. CGM has been used both clinically and as a research tool to explore glucose patterns in different groups of patients [12,13]. Our study was open to all adult patients with diabetes who wished to fast during Ramadan. The main considerations were the patients' ability to complete the study and the stability of their glycaemic control. As such, patients whose treatment was likely to change for any reason other than the Ramadan fast were excluded. CGM measures tissue glucose rather than blood glucose and it has been shown that, on average, changes in tissue glucose lag behind those in blood glucose [19]. This means that the results of any CGM study need to be interpreted with caution. Other issues to consider are inaccuracies in CGM readings when glucose is in the hypoglycaemic range [19]. In spite of this, however, CGM remains an invaluable tool when glucose changes are under investigation. Also, this study used the Medtronic Gold CGM system rather than a "real-time" device, which therefore blinded patients of their current glucose levels and thus eliminated the possibility of their interfering with the observations.

Previous studies have shown conflicting changes in overall glycaemic control during Ramadan [8,10,20–22]. This may be, in part, a reflection of cultural differences and nutritional habits in different Muslim countries. Our present study showed no significant differences in markers of overall glycaemic control and number of high or low glucose excursions between pre-Ramadan

Table 2
Indicators of glycaemic control derived from continuous glucose monitoring in diabetes patients and controls during non-fasting (NF) and fasting (F) periods.

Group	Diabetes		Controls		Group 1		Group 2		Group 3		Group 4	
	NF	F	NF	F	NF	F	NF	F	NF	F	NF	F
Min IG (mmol/L)	4.0 ± 1.5	4.05 ± 1.1	5.2 ± 0.5	5.1 ± 0.5	6.8 ± 1.6	5.7 ± 0.8	7.1 ± 1.4	6.1 ± 1.0	7.0 ± 1.6	6.4 ± 1.1	6.8 ± 1.6	8.2 ± 1.2
Max IG (mmol/L)	13.4 ± 4.0	14.9 ± 4.1	6.1 ± 0.9	6.3 ± 0.9	8.5 ± 3.2	9.9 ± 4.5	8.7 ± 4.9	9.9 ± 3.5	9.3 ± 3.4	10.5 ± 3.9	9.5 ± 4.6	12.6 ± 4.0
Mean IG (mmol/L)	8.0 ± 2.1	10.1 ± 2.0	5.6 ± 0.2	5.8 ± 0.2	7.6 ± 0.5	7.4 ± 1.0	8.0 ± 0.5	7.8 ± 0.8	8.1 ± 0.6	8.3 ± 1.0	8.4 ± 0.7	10.2 ± 1.2
AUC (mmol/L.min)	116.0 ± 29.0	121.5 ± 28.4	80.3 ± 0.2	83.3 ± 0.3	109.6 ± 0.5	106.3 ± 1.0	115.6 ± 0.5	111.6 ± 0.8	116.7 ± 0.6	119.2 ± 1.0	120.3 ± 0.7	146.1 ± 1.2
MAGE[a] (mmol/L)	5.8 ± 2.5	6.7 ± 3.4	2.5 ± 0.4	2.41 ± 0.3	4.5 ± 1.9	6.8 ± 4.1	5.6 ± 2.3	4.8 ± 2.0	5.8 ± 2.0	6.2 ± 2.0	7.4 ± 4.0	9.8 ± 3.4
HBGI[a]	5.5 ± 5.4	6.8 ± 6.4	0.5 ± 0.2	0.3 ± 0.3	1.5 ± 0.9	1.5 ± 1.6	2.3 ± 1.0	20 ± 1.5	2.5 ± 1.3	3.1 ± 2.3	8.1 ± 6.3	13.9 ± 7.7
LGBI[a]	2.2 ± 3.7	1.8 ± 2.4	1.8 ± 0.8	1.2 ± 0.6	0.8 ± 0.9	1.3 ± 1.5	2.7 ± 5.7	0.8 ± 0.7	1.9 ± 2.2	1.6 ± 1.6	3.3 ± 3.0	3.4 ± 3.9

Group 1: diet with/without metformin; Group 2: gliptin with/without metformin; Group 3: sulphonylurea with/without other oral agent(s); Group 4: insulin with/without other oral agents; except for Group 4 ($P < 0.04$ for HBGI, $P < 0.02$ for AUC and mean IG), within-group differences during F and NF periods were not significant (Wilcoxon's signed-rank test); IG: interstitial glucose; AUC: area under the mean CGM curve; MAGE: mean amplitude of glycaemic excursion; HBGI/LBGI: high blood/low blood glucose index.

[a] Absolute numbers; MAGE indicates blood glucose volatility; HBGI and LBGI indicate hyperglycaemia and hypoglycaemia risk, respectively.

Table 3
Insulin-treated patients, their dosages and other medications during fasting (Ramadan) and non-fasting (pre-Ramadan).

Patient no.	Type of diabetes	Type of insulin	Non-fasting	Fasting	Antidiabetic drug	Fasting	Non-fasting
1	Type 1	Detemir Aspart	8 + 0 + 8 units 5 + 5 + 5 units	12 + 0 + 4 units 3 + 0 + 2 + 3 + 3 + 3 units	– –	– –	– –
2	Type 1	Glargine Aspart	14 units QD 6 + 6 + 6 units	14 units QD 6 + 0 + 8 units	– –	– –	– –
3	Type 1	Glargine Lispro	16 units QD 8 + 10 + 6 units	16 units QD 6 + 0 + 8 units	– –	– –	– –
4	Type 1	Biphasic aspart 30	40 + 0 + 30 units	30 + 0 + 40 units	–	–	–
5	Type 1	Glargine Aspart	40 units QD 25 + 25 + 25 units	35 units QD 18 + 0 + 30 units	– –	– –	– –
6	Type 1	Lispro	40–50 units daily	40–50 units daily	–	–	–
7	Type 2	Biphasic aspart 30 –	50 + 0 + 50 units –	35 + 0 + 55 units –	Glibenclamide/metformin 5/500 mg Liraglutide	1 + 1 + 1 tablet 0.6 mg QD	1 + 0 + 1 tablet 0.6 mg QD
8	Type 2	Glargine Aspart	40 units QD 18 + 18 + 18 units	40 units QD 15 + 0 + 18 units	Metformin –	1000 mg BID –	1000 mg BID –
9	Type 2	Glargine Glulisine	46 units QD 12 + 12 + 16 units	46 units QD 10 + 0 + 16 units	Glibenclamide/metformin 5/500 mg Liraglutide	1 + 0 + 1 tablet 1.8 mg QD	1 + 0 + 1 tablet 1.8 mg QD
10	Type 2	Glargine Aspart	60 units QD 30 + 30 + 30 units	60 units QD 25 + 0 + 35 units	Metformin –	1000 mg BID –	1000 mg BID –
11	Type 2	Glargine Liraglutide	60 units QD 1.8 mg QD AM	56 units QD 1.8 mg QD PM	Glimepiride –	1 mg QD at *iftar* –	1 mg QD at breakfast –
12	Type 2	Glargine Aspart	60 units QD 2–3 units as needed	50 units QD 2–3 units as needed	Glibencamide/metformin 5/500 mg Sitagliptin/metformin 50/1000 mg	1 tablet QD at *iftar* 1 tablet BID	1 tablet QD at breakfast 1 tablet BID
13	Type 2	Glargine Aspart	50 units QD 30-20-30 units	40 units QD 22-0-35 units	– –	– –	– –

Doses of other oral hypoglycaemic agents were changed to allow safer Ramadan fasting on the basis of doctors' advice, clinical guidelines and sometimes by patients themselves (to a dose they were more comfortable with); twice daily: BID; once daily: QD.

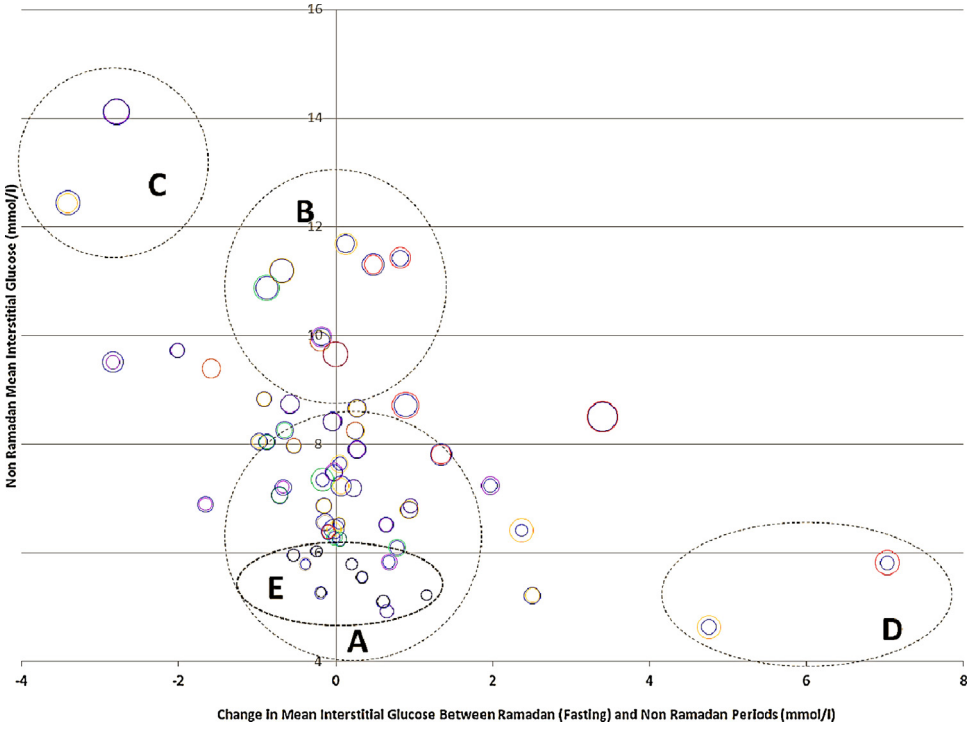

Fig. 2. Mean interstitial glucose (IG) levels during non-Ramadan (blue circles) and Ramadan fasting derived from continuous glucose monitoring (CGM) data from the same patients (concentric circles). Circle size corresponds to standard deviation (SD). Red: insulin-treated; orange: sulphonylurea (SU)-treated; purple: gliptins with/without metformin; green: no medication/metformin; and black: controls (no diabetes). Different trends are identified: A: good initial control with no significant change on fasting; B: poor initial control with no significant change on fasting; C: poor initial control with improvement on fasting; and D: good initial control with further improvement on fasting. In general, no significant SD changes were seen between non-Ramadan and Ramadan, indicating similar trends in overall glucose excursions during the two periods. The main outliers (D) were patients taking insulin and SU.

and Ramadan periods. Although the lack of statistical significance may be partly explained by our relatively small sample size, it is worth pointing out that the absolute differences in these parameters during the pre-Ramadan and Ramadan periods were also very small. In spite of this, there was wide intra- and interindividual variability in CGM profiles during fasting (Fig. 2). This variability can be explained by personal, nutritional, medical, cultural and social as well as religious factors. This further highlights the importance of individualized advice focusing on the type and timing of meals, as well as making appropriate changes to medication and dosages (Fig. 3).

An interesting observation from the mean CGM curve during Ramadan fasting is the rapid rise in glucose at *iftar* (Fig. 1). Although the likely explanation for this is the type of meal consumed at this time, other factors could also contribute to the rapid rise. A common practice among fasting Muslims is to eat food with a high glucose content – often dates – followed by the main meal. The dietary composition of a typical Emirati *iftar* meal is 156 g of carbohydrates (46 g of simple sugars), 32 g of protein, 71 g of fat and 4 g of fibre, adding up to 1391 calories. Antidiabetic medication is usually taken just before or sometimes after the main meal, and may be one of the factors contributing to *iftar* glucose excursions. Hormonal changes on prolonged fasting may be another factor to consider. In some cultures, *iftar* constitutes a small snack, followed by a gap during which evening prayers are made, so the main evening meal is taken later. Based on our present findings, we believe this latter practice may be more appropriate for patients with diabetes and that medication should be taken when the fast is broken.

Changes in glucose profiles during Ramadan fasting have previously been reported in T2DM patients [21]. Our present study intended to expand our previous findings by using a larger number of patients. In the present study, Ramadan glucose excursions were examined according to different medication categories, and indicated a higher risk of post-*iftar* excursions and poorer glucose control in insulin-treated patients as well as in patients taking sulphonylurea, thus providing additional support for the current evidence-based guidelines for Ramadan fasting. Our present findings show that insulin- and sulphonylurea-treated patients behave differently from those treated with diet alone, metformin or dipeptidyl peptidase (DPP)-4 inhibitors. The exaggerated hyperglycaemic excursions at *iftar* time in the former patients may be due in part to the timing of medication administration, which may be after rather than some time before the *iftar* meal. Nevertheless, the differences across treatment groups suggest that a change from sulphonylureas to DPP-4 inhibitors may be an appropriate strategy in some patients and could be done at the pre-Ramadan consultation. Also, it seems clear that the glucose excursions accompanying Ramadan fasting pose short-term risks in some diabetic patients who fast during Ramadan [4]. Nevertheless, it is worth noting there are no current data

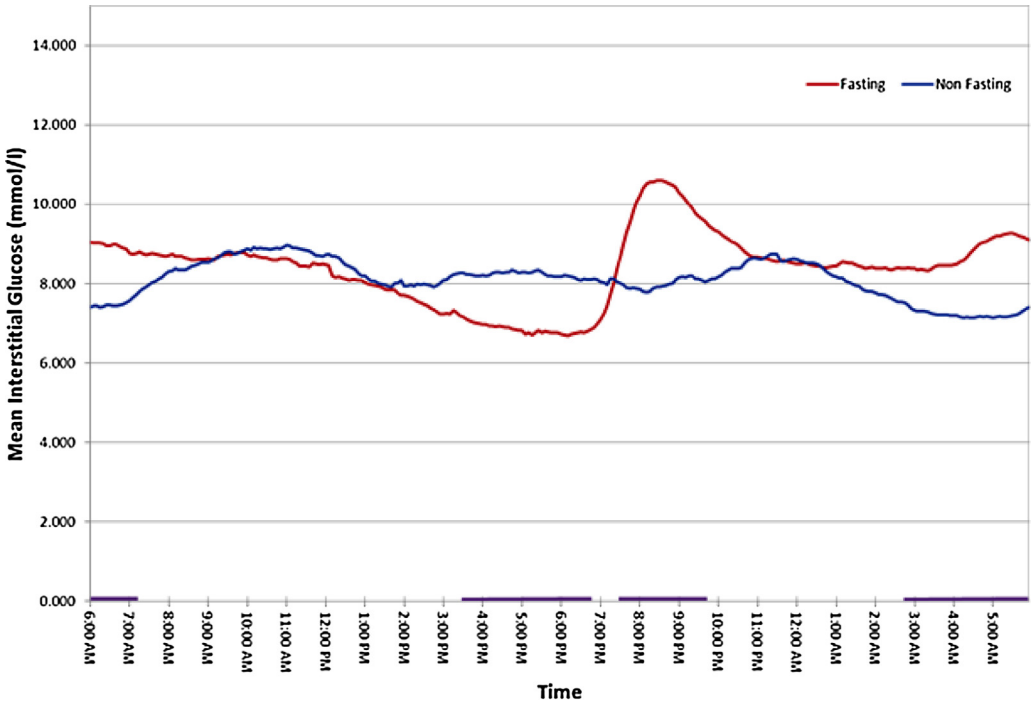

Fig. 3. Mean 24-h continuous glucose monitoring (CGM) profiles derived from all patients with diabetes ($n = 56$) during Ramadan (Fasting) and non-Ramadan (Non-fasting) periods. The purple bars along the *x*-axis depict periods when the difference between the two CGM recordings were statistically significant.

on the long-term effects of Ramadan fasting on patients with diabetes.

5. Conclusion

Our present findings add further evidence to the currently available recommendations [23,24], and emphasize the importance of nutritional advice and the timing of antidiabetic medications. Also, this study has shown for the first time the changes of glucose profiles in patients with diabetes who fast during Ramadan. Our CGM data highlight the surge in interstitial and, thus, blood glucose at the time of *iftar*, which was apparent even in this group of well-controlled patients. It is likely that, in many patients with diabetes, this effect may be even more pronounced and may thus constitute risks in both the short and longer term. Contrary to our expectations, hypoglycaemia was not a major problem, although short episodes of low IG were recorded in a significant number of patients.

In addition, our study underlines the importance of appropriate pre-Ramadan counselling for patients with diabetes who intend to fast during Ramadan. Proactive and focused nutritional advice, together with appropriate dose adjustments to antidiabetic medications, should help to keep blood glucose levels better controlled and more stable during Ramadan fasting. Indeed, further research aimed at identifying what these dose changes should be is currently being planned.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgements and funding

Funding for this study was through a research grant from the Sheikh Hamdan Award for Medical Sciences (grant number MRG 09/2007-8). The authors wish to thank ICLDC Doctors and other staff for their help in patient recruitment. NL designed and conducted the study and wrote the manuscript. ZH analysed the data, and contributed to conducting the study and the manuscript. HH analysed the data and contributed to the discussion. MTB reviewed the manuscript and contributed to the discussion. All co-authors have read and approved the final version of the manuscript.

References

[1] Adlouni A, Ghalim N, Benslimane A, Lecerf JM, Saile R. Fasting during Ramadan induces a marked increase in high-density lipoprotein cholesterol and decrease in low-density lipoprotein cholesterol. Ann Nutr Metab 1997;41:242–9.
[2] Adlouni A, Ghalim N, Saile R, Hda N, Parra HJ, Benslimane A. Beneficial effect on serum apo AI, apo B and Lp AI levels of Ramadan fasting. Clin Chim Acta 1998;271:179–89.
[3] Azizi F. Islamic fasting and health. Ann Nutr Metab 2010;56:273–82.
[4] 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;27:2306–11.
[5] 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;25:637–8.
[6] Bravis V, Hui E, Salih S, Mehar S, Hassanein M, Devendra D. Ramadan education and awareness in diabetes (READ) programme for Muslims with Type 2 diabetes who fast during Ramadan. Diabet Med 2010;27:327–31.
[7] Hassanein M, Bravis V, Hui E, Devendra D. Ramadan-focused education and awareness in type 2 diabetes. Diabetologia 2009;52:367–8.

[8] 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;25:1858–63.
[9] 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;29:709–15.
[10] 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;13:329–32.
[11] Mastrototaro J. The MiniMed Continuous Glucose Monitoring System (CGMS). J Pediatr Endocrinol Metab 1999;12(Suppl 3):751–8.
[12] Mastrototaro JJ. The MiniMed continuous glucose monitoring system. Diabetes Technol Ther 2000;2(Suppl 1):S13–8.
[13] Mastrototaro JJ, Gross TM. Reproducibility of the continuous glucose monitoring system matches previous reports and the intended use of the product. Diabetes Care 2003;26:256 [author reply -7].
[14] Lessan NG, Abdullah A, Hassan H, Nasir Q, Athamneh S. Glycaemic patterns detected by CGMS in patients with diabetes mellitus in the United Arab Emirates. Diabetes Technol Ther 2006;8:513–5.
[15] Gross TM, Bode BW, Einhorn D, Kayne DM, Reed JH, White NH, et al. Performance evaluation of the MiniMed continuous glucose monitoring system during patient home use. Diabetes Technol Ther 2000;2:49–56.
[16] Service FJ, Molnar GD, Rosevear JW, Ackerman E, Gatewood LC, Taylor WF. Mean amplitude of glycaemic excursions, a measure of diabetic instability. Diabetes 1970;19:644–55.
[17] McCall AL, Cox DJ, Crean J, Gloster M, Kovatchev BP. A novel analytical method for assessing glucose variability: using CGMS in type 1 diabetes mellitus. Diabetes Technol Ther 2006;8:644–53.
[18] Hermanides J, Phillip M, DeVries JH. Current application of continuous glucose monitoring in the treatment of diabetes: pros and cons. Diabetes Care 2011;34(Suppl 2):S197–201.
[19] Boyne MS, Silver DM, Kaplan J, Saudek CD. Timing of changes in interstitial and venous blood glucose measured with a continuous subcutaneous glucose sensor. Diabetes 2003;52:2790–4.
[20] Ziaee V, Razaei M, Ahmadinejad Z, Shaikh H, Yousefi R, Yarmohammadi L, et al. The changes of metabolic profile and weight during Ramadan fasting. Singapore Med J 2006;47:409–14.
[21] Lessan N, Hasan H, Barakat MT. Ramadan fasting: a study of changes in glucose profiles among patients with diabetes using continuous glucose monitoring. Diabetes Care 2012;35:e37.
[22] Ahmadani MY, Riaz M, Gul A, Waheed MI, Hydrie MZ, Hakeem R, et al. Clinical profile of fasting diabetic subjects during Ramadan. J Coll Physicians Surg Pak 2007;17:446–7.
[23] Al-Arouj M, Assaad-Khalil S, Buse J, Fahdil I, Fahmy M, Hafez S, et al. Recommendations for management of diabetes during Ramadan: update 2010. Diabetes Care 2010;33:1895–902.
[24] 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;28:2305–11.