

Rate, Timing, and Severity of Hypoglycemia in Adolescents with Type 1 Diabetes during Ramadan Fasting: A Study with Freestyle Libre Flash Glucose Monitoring System

Bachar Afandi¹, Walid Kaplan¹, Lina Majd¹, Sana Roubi¹

¹Tawam Endocrine and Diabetes Center, Tawam Hospital, Al Ain, UAE

Abstract

Objectives: The objective of this study is to assess the frequency, timing, and severity of hypoglycemia in adolescents with type 1 diabetes mellitus (T1DM) during fasting the month of Ramadan. **Patients and Methods:** Twenty-five adolescents with T1DM who fasted Ramadan were monitored using the FreeStyle Libre[®] flash glucose monitoring (FGM) system. Percentage and total duration of hypoglycemia were extracted from the FGM downloads, and the differences were compared between different times of the day and night according to the eating pattern in Ramadan. **Results:** Mean age was 16 ± 3 years and mean glycosylated hemoglobin was $8.6 \pm 1.2\%$, mean glucose level was 200 ± 84 mg/dl (11.1 ± 4.7 mmol/L), and the overall time spent in hypoglycemia was $5.7\% \pm 3.0\%$. The average daily time spent in hypoglycemia was 1.39 h per patient. The incidence of hypoglycemia was 0% from 19:00 to 23:00 pm and 69% from 11:00 to 19:00. Analysis of hypoglycemia revealed that 65% were between 61 and 70 mg/dl and 8% lower than 50 mg/dl. **Conclusions:** Hypoglycemia is typically encountered during the hours preceding Iftar time indicating an over-effect of basal insulin. Basal insulin reduction is necessary to minimize the risk of hypoglycemia

Keywords: Adolescent diabetes, flash glucose monitoring, hypoglycemia, Ramadan fasting

INTRODUCTION

Previous studies have indicated an increased risk of hypoglycemia, hyperglycemia, diabetic ketoacidosis (DKA),^[1] dehydration, and thrombosis^[2] during fasting Ramadan in patients with type 1 diabetes (T1DM). Such findings have led to listing T1DM as a high-risk factor for fasting by the IDF-DAR Practical Guidelines^[3] and the American Diabetes Association Consensus Statement.^[4] However, many patients with T1DM take the potential risks and insist on fasting against medical advice.

Due to the lack of well-controlled clinical studies, there have been limited and inconsistent data regarding basal insulin dose adjustment during Ramadan fasting in adolescents with T1DM; hence, health-care providers have been giving conflicting recommendations in this regard. Indeed, current practices are supported by very limited literature and indicate the need to reduce the basal insulin dose during the day and to increase preprandial boluses during eating hours.^[5-11]

In this study, we examined the rate, timing, and severity of hypoglycemia using the data generated from the flash glucose

monitoring (FGM) in a group of adolescents with T1DM who fasted the month of Ramadan.

PATIENTS AND METHODS

The study was approved by Al Ain Human Research Ethical Committee. A total of 25 adolescents with T1DM on multiple daily injection (MDI) regimens who intended to fast the month of Ramadan 2016 were recruited. All patients were evaluated at Tawam Diabetes and Endocrine Center by their physicians, nutritionists, and diabetes educators before fasting. Only patients treated with insulin glargine 100 as their basal insulin were recruited. Basal insulin treatment was modified according to available guidelines,^[3] where insulin glargine dose was reduced by 25%–30% of pre-Ramadan dose and administered between

Address for correspondence: Dr. Bachar Afandi,
Tawam Endocrine and Diabetes Center, Tawam Hospital, Al Ain, UAE.
E-mail: bafandi@seha.ae

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07:00 and 08:00 pm, which is the time of the fast-breaking meal (Iftar). Glucose was monitored using the FGM (FreeStyle® Libre™, Abbott Diabetes Care, Alameda, CA) for 14 days, and only the past 7 days were considered in the analysis.^[12,13] Patients were new to the technology and were trained by diabetes educators competent with its use. Hypoglycemia was identified as glucose <70 mg/dL (3.9 mmol/L), and its percentage was calculated by dividing the minutes of the reported hypoglycemia over the total period of monitoring (converted into minutes). To assess the relationship between hypoglycemia and fasting, the day was divided into four intervals in relation to food intake in Ramadan as follows: Block A: The peak eating time (19:00–23:00), Block B: Variable eating (23:00–03:00), Block C: Last prefasting meal (03:00 am–07:00), and Block D: The fasting hours (07:00–19:00). The severity of hypoglycemia was assessed by calculating the proportion of mild and severe hypoglycemia (60–69 mg/dL and <50 mg/dL, respectively) of the total flashed episodes of hypoglycemia. Data analysis was done using Microsoft Office Excel (version 2010; Microsoft, Redmond, Washington, USA). Descriptive statistics was conducted on the variables. $P < 0.05$ considered statistically significant.

RESULTS

The month of Ramadan in 2016 started on June 6 and ended in the evening of July 5, and fasting hours started from around 04:00 am and ended around 07:00 pm. A total of 25 patients were enrolled (18 females). Mean age was 16 ± 3 years, duration of diabetes was 6 ± 3 years, and mean glycated hemoglobin was $8.6\% \pm 1.2\%$ (70.5 mmol/L). All patients fasted safely with no reports of DKA or hospital admissions. The mean \pm standard deviation glucose was 200 ± 84 mg/dl (11.1 ± 4.7 mmol/L), and the overall incidence of hypoglycemia was $5.7\% \pm 3.0\%$ of the total monitoring period. The average daily flashes to check glucose were 16 per patient (range 3–50). The average daily time spent in hypoglycemia was 1.39 h per patient. The rate of hypoglycemia according to time intervals for all patients was 0%, 4%, 27%, and 69% in Blocks A, B, C, and D, respectively [Figure 1]. Out of the 333 hypoglycemic flashes for all patients, 65% were between 60 and 69 mg/dl, 27% between 50 and 59 mg/dl, and 8% below 50 mg/dl [Figure 2].

DISCUSSION

To the best of our knowledge, this is the first study that assesses the pattern and severity of hypoglycemia in adolescents with T1DM during fasting in Ramadan when standardized basal insulin reduction was implemented. The prevalence increases sharply toward the end of the fasting hours, which reflects the action time of the basal insulin.

Adolescents with T1DM are classified as high and very high risk for fasting during the month of Ramadan.^[3] We have previously reported that better glycemic control before Ramadan correlates with less glucose fluctuation during fasting.^[14] However, to reduce the risk during prolonged

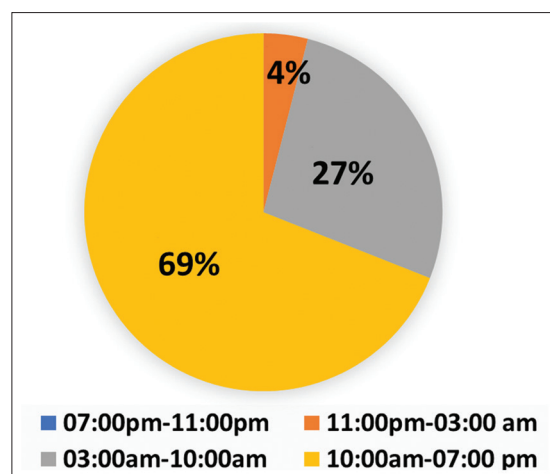


Figure 1: Rate and timing of hypoglycemia in adolescents with T1DM during Ramadan fasting

fasting, it is prudent to monitor blood glucose very closely and to individualize the dose adjustment of both basal and prandial insulins to match eating habits. A recent study by Alamoudi *et al.* evaluated the risk of hypoglycemia in patient with T1DM treated with insulin pump, and MDIs revealed that the rate and severity of hypoglycemia were similar in both groups; however, insulin dose modification was not standardized and the study did not look into the details of hypoglycemia timing.^[15]

Continuous glucose monitoring (CGM) devices have the advantage of providing glucose values every 5–15 min, and they can predict and detect hypoglycemia during fasting. Only few studies reviewed glucose level fluctuation using CGM.^[16-21] The use of CGM in our population uncovered the incidence of unrecognized hypoglycemia during fasting in adolescents with T1DM.^[16] Al-Agha *et al.* reported on the use of FGM system in children and adolescents with T1DM. They reported hypoglycemia by quantifying the number of episodes of hypoglycemia rather than the percent of time spent in hypoglycemia. Mild hypoglycemia in this study was significantly higher during fasting hours with no reports of severe hypoglycemia; the report did not discuss insulin dose modification during fasting.^[21] Differences in the rate, timing, and severity of hypoglycemia between this study and ours could be related to the length of fasting hours (15 in our study vs. 14 in the Saudi study), insulin dose modification, or other individual factors. While few studies recommend reducing the dose of basal insulin during Ramadan,^[5-11] Deeb *et al.* reported no difference in the frequency of hypoglycemia between T1DM patients who reduced or did not reduce the dose of basal insulin.^[22] The study, however, used patient blood glucose monitoring diary and did not look into the pattern of hypoglycemia.

In the present study, while the overall glycemic control was elevated, in spite of reducing the dose of the basal insulin in all participants by 25% during Ramadan, the frequency of hypoglycemia increased sharply in the late hours of the fasting,

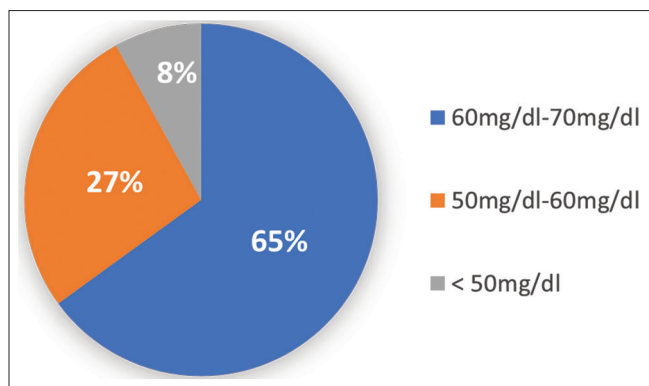


Figure 2: Severity of hypoglycemia in adolescents with T1DM during Ramadan fasting

which represents the period of time under the main effect of the basal insulin. Patients spent an average of 1.39 h per fasting day in hypoglycemia and 8% was documented to be severe yet asymptomatic, which might have grave clinical implications.

CONCLUSIONS

Hypoglycemia during fasting in adolescents with T1DM is encountered extensively in the last few hours of fasting. The current recommendations of reducing the dose of basal insulin during Ramadan should be aimed at reducing the severity and duration of hypoglycemia. CGM is of great value in detecting hypoglycemia in adolescents with T1DM.

Author's contribution

All authors contributed to the published work. They all had full access to the data, and they together drafted, revised, and approved the final version of the manuscript.

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Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

The study was approved by the Al Ain District Ethical Review Board and all participants/parents provided an informed consent before the study commencement.

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Reviewers:

Abdulwahab El Barsha (Benghazi, Libya)
Khadija Hafidh (Dubai, UAE)

Editors:

Salem A Beshyah (Abu Dhabi, UAE)
Elmahdi Elkhammas (Columbus, Ohio, USA)