

SPOTLIGHT ARTICLE*Diabetic Hypoglycemia June 2014, Volume 7, Issue 1: page 15-19*

Religious fasting, Ramadan and hypoglycemia in people with diabetes

Alia Gilani¹, Melanie Davies², Kamlesh Khunti²¹ NHS Glasgow, United Kingdom² Leicester Diabetes Centre, Leicester General Hospital, Leicester, United Kingdom

Abstract

Most Muslims with diabetes will take part in Ramadan even though they may be exempt from doing so. In some countries a religious fast can last between 10 and 21 hours. The main risk of fasting to people with diabetes is hypoglycemia. People with diabetes who fast may have to alter the dose of their medications or modify their therapeutic regimen to avoid hypoglycemia, which can have adverse effects on glycemetic control. Therapies which pose a high risk of hypoglycemia when used during fasting are sulfonylureas and insulin therapy. Metformin, incretin therapies and the newer sodium glucose co-transporter 2 inhibitor class have a low risk of hypoglycemia. The practice of fasting during Ramadan is advocated for all healthy individuals. If deemed detrimental to health then a person can be considered exempt from fasting; this includes frail and elderly people, pregnant and breast feeding women, children and people with multi-morbidities.

Keywords: *diabetes, hypoglycemia, Ramadan, religious fasting*

Introduction

Living in a diverse society, it is important that healthcare professionals are kept informed about cultural and religious practices, which can affect the control of diabetes. The practice of fasting by Muslims has implications for Muslim people with diabetes, in particular an increased risk of hypoglycemia during the period of Ramadan and at other times of fasting throughout the year. Hypoglycemia is also a risk for individuals of other religions in which fasting is advocated, such as Hinduism and Judaism. The present article will focus principally on the prolonged religious fasting associated with Ramadan.

Islam is the faith followed by Muslims and is the second largest religion in the world.¹ Approximately 40–50 million individuals with diabetes across the world partake in Ramadan annually.² Ramadan, which lasts for 29–30 days, is one of the five pillars of Islam and one of the most important periods for a practicing Muslim. Fasting occurs in the ninth month of the Islamic calendar (Hijri), which is a lunar calendar. Since the Islamic calendar is 354 days long, each year Ramadan falls 10–11 days earlier in the Gregorian calendar.

Over the next decade in countries that are far from the equator, such as the UK, Ramadan will occur during the summer months, which will significantly extend the duration of fasting. This could potentially increase the risk of hypoglycemia among patients with diabetes. Healthcare professionals need to be aware of when Ramadan falls in

the Islamic calendar, the risks associated with prolonged fasting and how it should be managed.

Fasting during Ramadan

What does fasting entail?

Ramadan in Arabic is translated as “*sawm*”, literally meaning “abstention from”. Between dawn and dusk, an individual must refrain from eating, drinking, smoking and consuming oral medications during Ramadan. Outside this period the restrictions are withdrawn. The meals consumed at dawn and dusk are known in Arabic as *sahur* and *iftar*, respectively.

Who should fast?

Ramadan should be practised by all healthy and responsible Muslims. If fasting is deemed detrimental to an individual's health then the Koran allows for an exemption. This includes frail and elderly people, pregnant and breast-feeding women, children, and people with multiple morbidities for whom prolonged fasting could have an adverse effect on their health. Other categories are temporarily exempt; this would include those with an acute illness and individuals who are travelling a distance of greater than 50 miles. This group can undertake their missed fasts at a later date. While Muslim people with diabetes can therefore observe their faith and not fast during Ramadan, they may feel guilty for not fasting. Healthcare professionals should be aware that their patient may have feelings of guilt if they do not fast and they should reassure their patients and advise them

to instead give *fidyah*. This is a means of compensating for not fasting by giving alms to the poor. The current UK amount for *fidyah* is considered to be £4 per day.³ The EPIDIAR study, which is the largest Ramadan study, found that 79% of people with type 2 diabetes and 43% with type 1 diabetes fast for at least 15 days during the month of Ramadan.⁴

Impact of fasting

Participating in fasting entails more than just abstinence from food and water. Ramadan is an important spiritual period for a practising Muslim whereby Koran recitation and prayer are increased and charitable offerings are made. The beneficial effect of Ramadan on an individual's wellbeing allows a greater feeling of spiritual inner peace. Ramadan may also have an impact on several biochemical markers. For example some studies have found Ramadan to improve the lipid profile.^{5,6} This benefit may be maintained for up to 4 weeks after Ramadan⁴ or may rapidly revert back to the pre-Ramadan levels.^{7,8} Weight and blood pressure have been shown to improve during Ramadan in some studies,^{4,8} but in others did not change.^{5,6,9,10}

Blood glucose levels can be affected by prolonged fasting during Ramadan, leading to either hyperglycemia or hypoglycemia. The latter is of greater risk to participants and can occur because of the abstinence from food for many hours, the effect of medications that increase the propensity for hypoglycemia, and the participation in physical activity, for example, extended praying during the fasting period (*taraweeh*). The effect of fasting during Ramadan on glycated hemoglobin (HbA1c) has not been investigated in detail previously. HbA1c levels can be influenced by multiple factors during Ramadan, such as the dose of medication, pre-Ramadan HbA1c concentration, the timing of food consumption, the nature of the food itself, and the level of physical activity. The results of observational studies have been very variable, reporting HbA1c either to remain unchanged,^{11,12} decrease,¹³⁻¹⁵ or increase^{16,17} during Ramadan.

The relative risk of hypoglycemia is thought to increase by 1.6-fold during fasting.¹⁸ The EPIDIAR study found that the risk of severe hypoglycemia was increased by 4.7-fold (3.0–14.0 events/100 persons/month) in type 1 diabetes and 7.5-fold (0.4–3.0 events/100 persons/month) in type 2 diabetes.⁴ The risk of severe hyperglycemia was increased three-fold (5–17 events/100 persons/month) in type 1 diabetes and five-fold (1–5 events/100 persons/month) in type 2 diabetes.⁴ These were considered to be underestimates as only individuals requiring external assistance were counted.

Medication

Medication may have to be adjusted during Ramadan, and the following should be considered as risk factors in individuals with diabetes for potential complications (hypoglycemia, hyperglycemia, dehydration and ketoacidosis) associated with fasting:

- Presence of co-morbidities and diabetic complications
- Advanced age and frailty
- Risk of hypoglycemia or a history of impaired hypoglycemia awareness
- Living alone
- Type 1 diabetes
- Pregnancy

Studies have been performed on the use of diabetes medications in Ramadan in order to develop expert advice and recommendations. Certain classes of glucose-lowering drugs are associated with an increased risk of hypoglycemia, ie, sulfonylureas and insulin. As such, the largest dose of these medications should be taken in the evening along with the large meal that will usually be consumed at that time (*iftar*).

Metformin

If a patient is taking metformin three times daily, the midday dose should be omitted and a larger dose taken in the evening.^{19,20} Those on a twice-daily regimen do not need to change the times of administration. Those who experience gastrointestinal side effects or symptoms of hypoglycemia should have their dose reduced. Overall, metformin has a low (but not negligible) risk of promoting hypoglycemia.

Sulfonylureas

Long-acting agents such as glibenclamide (glyburide) should be avoided. The morning dose of a shorter-acting preparation, such as glipizide or gliclazide, can be halved and the evening dose kept the same.^{19,21} One study tried switching the timing of administration of the sulfonylurea from morning to evening and found no effect on the rate of hypoglycemia.²¹ A five-country observational study on treatment with sulfonylureas during Ramadan reported a 20% prevalence of hypoglycemia.²² Sulfonylureas have a moderate to high risk of promoting hypoglycemia as they promote insulin secretion that is not glucose-dependent.

Thiazolidinediones

One study of the use of pioglitazone during Ramadan showed no increase in the frequency of hypoglycemia when added to an individual's anti-diabetes treatment regimen, as compared with placebo.²³

Incretin-based therapies

Studies of drugs in the dipeptidyl peptidase 4 (DPP-4) inhibitor class have found them to be well tolerated during Ramadan with a low rate of hypoglycemia as insulin

secretion is glucose-dependent.²⁴ Although the trial data included two gliptins, it is thought that all gliptin drugs may be suitable for use during Ramadan as they have a low risk of hypoglycemia and are well tolerated.

Two studies of glucagon-like peptide 1 (GLP-1) agonists reported fewer episodes of hypoglycemia with exenatide or liraglutide compared with a sulfonylurea as add-on to metformin.^{14,25} Overall, incretin enhancers (DPP-4 inhibitors) and mimetics (GLP-1 agonists) when not combined with a sulfonylurea have a low propensity to cause hypoglycemia.

Sodium-glucose co-transporter 2 inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors form the latest class of oral anti-diabetes medication available for type 2 diabetes. To date, no studies have been reported of their use during Ramadan. These drugs competitively inhibit the SGLT2 co-transporter in the kidney and block the reabsorption of glucose; thus the risk of inducing hypoglycemia is low because of their insulin-independent action.

Insulin

People with type 1 diabetes are considered to be at very high risk of experiencing metabolic upset during prolonged fasting and it is not recommended that they fast for protracted periods, in particular those at risk of hypoglycemia or who have either very strict or poor glycaemic control.^{19,21} People with type 2 diabetes who are taking insulin, particularly if on a single dose of long-acting basal insulin at bedtime, are less at risk of hypoglycemia but if they wish to fast they will need to have their dosage regimen adjusted and monitor their blood glucose with care.

The risk of hypoglycemia will increase with duration of diabetes and the use of combinations of glucose-lowering therapies.

Avoiding hypoglycemia during Ramadan

Individuals who wish to undertake religious fasting should undergo a pre-Ramadan assessment with their healthcare professional. People with diabetes participating in Ramadan should be encouraged to measure their blood glucose frequently, particularly if they are on medication that increases the risk of hypoglycemia. Finger prick sampling and capillary blood glucose measurement does not constitute breaking the fast.²⁶ The history of an individual's experience of fasting during Ramadan should also be ascertained, although an individual's health status may differ considerably from the previous year. It may be prudent to allow the person with diabetes to experience a test day of fasting in the few weeks before Ramadan to assess their potential risk for hypoglycemia, especially if medications will need to be adjusted during Ramadan.

An individual may need to break their fast. The recommendations for breaking a fast are if blood glucose levels are <3.9 mmol/l (70 mg/dl) or >16.7 mmol/l (300 mg/dl).² During a fast if an individual's health deteriorates they must be advised to break the fast; failing to do so is contrary to the Islamic spirit of fasting without harming oneself. Furthermore, structured education interventions should be considered and have been found to be beneficial in terms of reducing the risk of hypoglycemia and preventing weight gain.¹⁵

Summary

Ramadan is one of the most important periods for a practising Muslim. Those who wish to partake in prolonged fasting during Ramadan should make the decision to do so based on a mutual agreement between themselves and their healthcare provider. The healthcare provider should not focus on encouraging the person with diabetes to desist from fasting, but should explore the risks and benefits with their patient. The well-informed person with diabetes will then be able to fast safely.

Comment by Professor Simon Heller of the Editorial Board

In the accompanying Spotlight Article, Gilani and colleagues highlight many of the issues that are relevant to diabetes management during the feast of Ramadan. They point out the increased likelihood of disrupted glycaemic control, particularly the high risk of hypoglycemia. They also emphasize that adults with diabetes are not obliged to fast, but that advice to refrain from fasting is often resisted by people with diabetes. Although Gilani et al appear to conclude that the challenges of fasting in people with type 1 diabetes are probably too demanding for most, it is likely that many patients will ignore professional advice and fast anyway. It is therefore incumbent on professional carers both to appreciate the importance of Ramadan to their patients and to be able to give practical advice to those who are determined to fast.

This review demonstrates the increasing focus on the management challenges associated with hypoglycemia, and cites a number of published and updated guidelines. These provide a useful reference for professionals and can be used to assist patients and their families to fast safely without major disruptions in metabolic control. Nevertheless it is striking that the data used to formulate published guidance has generally been obtained from observational studies rather than from randomized controlled trials. The few randomized controlled trials that have been published predominantly test the superiority of a specific medication to prevent hypoglycemia and maintain glycaemic control rather than comparing an overall plan of management during Ramadan. Guidance is therefore based largely on consensus developed by experienced clinicians as opposed to high-level evidence (data from randomized controlled trials and meta-analyses).

The lack of an extensive evidence base reflects the difficulty in designing and conducting robust trials in this field. Since Ramadan occupies only one lunar month every year, it is obviously a challenge to recruit sufficient participants to provide meaningful data, particularly if participants are to be randomized to different management plans. While it is theoretically possible to undertake the pilot/feasibility work at other times of the year, it is likely to be extremely difficult to recruit participants and ensure that those participating are truly fasting in the appropriate manner. Thus any trial will probably have to include a large number of centers to ensure that there is sufficient patient exposure to provide meaningful data. The degree of coordination, the number of centers required and the appropriate experimental design will challenge even those who are experienced in designing clinical trials.

Gilani et al provide important recommendations regarding the choice of oral medication, particularly the use of incretin-based therapies, which can help to avoid the significant risk of hypoglycemia during fasting. For those with type 1 diabetes, frequent blood glucose monitoring and judicious use of insulin analogs may also enable fasting to be carried out. Thus the use of insulin degludec, which provides stable low concentrations of basal insulin, may control blood glucose safely. The use of insulin degludec combined with judicious use of rapid-acting insulin analogs to cover the sahur – and particularly the iftar – meals seems an approach worth testing in a new randomized controlled trial.

In summary, the Spotlight Article emphasizes the barriers that Muslim people with diabetes face if they wish to observe the Ramadan fast, particularly when using medication, such as sulfonylureas or insulin. However, the use of new oral agents that do not increase the risk of hypoglycemia, and the latest long-acting insulin analogs, when combined with high-quality education and expert clinical input may enable individuals with type 2 or type 1 diabetes to fast safely if they are determined to do so.

References

1. Pew Research Center. The global religious landscape. *The Pew Forum on Religion and Public Life* 2012;**December**:1-82.
2. Al-Arouj M, Bouguerra R, Buse J, et al. Recommendations for management of diabetes during Ramadan. *Diabetes Care* 2005;**28**:2305-11.
3. Islamic Relief UK. Pay Fidyah and Kaffarah. Available at www.islamic-relief.org.uk/about-us/what-we-do/ramadan/fidyah-and-kaffarah/. Accessed 12 May 2014.
4. Salti I, Benard E, Detournay B, 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. Nematy M, Alinezhad-Namaghi M, Rashed MM, et al. Effects of Ramadan fasting on cardiovascular risk factors: a prospective observational study. *Nutr J* 2012;**11**:69.
6. Shehab A, Abdulle A, El Issa A, et al. Favorable changes in lipid profile: the effects of fasting after Ramadan. *PLoS One* 2012;**7**:e47615.
7. El-Hazmi MA, Al-Faleh FZ, Al-Mofleh IB. Effect of Ramadan fasting on the values of haematological and biochemical parameters. *Saudi Med J* 1987;**8**:171-6.
8. Mafauzy M, Mohammed WB, Anum MY, et al. A study of the fasting diabetic patients during the month of Ramadan. *Med J Malaysia* 1990;**45**:14-7.
9. Azizi F. Islamic fasting and health. *Ann Nutr Metab* 2010;**56**:273-82.
10. Fakhrazadeh H, Larijani B, Sanjari M, et al. Effect of Ramadan fasting on clinical and biochemical parameters in healthy adults. *Ann Saudi Med* 2003;**23**:223-6.
11. Sari R, Balci MK, Akbas SH, et al. The effects of diet, sulfonylurea, and repaglinide therapy on clinical and metabolic parameters in type 2 diabetic patients during Ramadan. *Endocr Res* 2004;**30**:169-77.
12. Yarahmadi S, Larijani B, Bastanhagh MH, et al. Metabolic and clinical effects of Ramadan fasting in patients with type II diabetes. *J Coll Physicians Surg Pak* 2003;**13**:329-32.
13. Ahmedani MY, Haque MS, Basit A, et al. Ramadan Prospective Diabetes Study: the role of drug dosage and timing alteration, active glucose monitoring and patient education. *Diabet Med* 2012;**29**:709-15.
14. Brady EM, Davies MJ, Gray LJ, et al. A randomized controlled trial comparing the GLP-1 receptor agonist liraglutide to a sulphonylurea as add on to metformin in patients with established type 2 diabetes during Ramadan: the Treat 4 Ramadan Trial. *Diabetes Obes Metab* 2014;**16**:527-36.
15. Bravis V, Hui E, Salih S, et al. Ramadan Education and Awareness in Diabetes (READ) programme for Muslims with type 2 diabetes who fast during Ramadan. *Diabet Med* 2010;**27**:327-31.
16. Belkhadir J, el Ghomari H, Klocker N, et al. Muslims with non-insulin dependent diabetes fasting during Ramadan: treatment with glibenclamide. *BMJ* 1993;**307**:292-5.
17. Uysal A, Erdogan M, Shanin G, et al. The clinical, metabolic and hormonal effects of fasting on 41 NIDDM patients, during Ramadan 1997. Paper presented at: 2nd International Congress on Health and Ramadan. 1-3 December 1997; Istanbul, Turkey.
18. Loke SC, Rahim KF, Kanesvaran R, et al. A prospective cohort study on the effect of various risk factors on hypoglycaemia in diabetics who fast during Ramadan. *Med J Malaysia* 2010;**65**:3-6.
19. Al-Arouj M, Assaad-Khalil S, Buse J, et al. Recommendations for management of diabetes during Ramadan: update 2010. *Diabetes Care* 2010;**33**:1895-902.
20. Hui E, Bravis V, Hassanein M, et al. Management of people with diabetes wanting to fast during Ramadan. *BMJ* 2010;**340**:c3053.
21. Glimpeiride in Ramadan (GLIRA) Study Group. The efficacy and safety of glimepiride in the management of type 2 diabetes in Muslim patients during Ramadan. *Diabetes Care* 2005;**28**:421-2.
22. Aravind SR, Al Tayeb K, Ismail SB, et al. Hypoglycaemia in sulphonylurea-treated subjects with type 2 diabetes undergoing Ramadan fasting: a five-country observational study. *Curr Med Res Opin* 2011;**27**:1237-42.
23. Vasan S, Thomas N, Bharani MD, et al. A double blind, randomized, multicenter study evaluating the effects of pioglitazone in fasting Muslim subjects during Ramadan. *Int J Diab Dev Ctries* 2006;**26**:70-6.
24. Schweizer A, Halimi S, Dejager S. Experience with DPP-4 inhibitors in the management of patients with type 2 diabetes fasting during Ramadan. *Vasc Health Risk Manag* 2014;**10**:15-24.
25. Bravis V, Hui E, Salih S, et al. A comparative analysis of exenatide and gliclazide during the month of Ramadan. *Diabetic Med* 2010;**27**:130.
26. Muslim Spiritual Care Provision in the NHS. Ramadan health factsheet 2009. Available at www.bcf.nhs.uk/dl/9109_8575754813.pdf/as/ramadanfactsheet2009.pdf?_ts=1&_ts=1. Accessed 12 May 2014.

Address for correspondence:

Alia Gilani
Health Inequalities Pharmacist
7 Carberry Road
Glasgow
G41 4DT
United Kingdom
E-mail: alia.gilani@nhs.net
Tel: +44 (0)797 182 5617

Conflict of interest

AG has acted as a consultant for advisory boards, received travel grants for attending conferences and received speaker fees from the following companies: Takeda, Novo Nordisk, Sanofi-Aventis, Boehringer Ingelheim, Lilly and Merck Sharp & Dohme; she is also a member of the Primary Care Diabetes Society and South Asian Health Foundation. MD has acted as consultant, advisory board member and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim and Roche; she has received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Pfizer, Merck Sharp & Dohme and GlaxoSmithKline. KK has acted as a consultant and speaker for Novartis, Novo Nordisk, Sanofi-Aventis, Lilly and Merck Sharp & Dohme; he has also received grants in support of investigator and investigator-initiated trials from Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Pfizer, Boehringer Ingelheim and Merck Sharp & Dohme.