

## Management of people with diabetes wanting to fast during Ramadan

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The holy month of Ramadan is one of five main pillars of being a Muslim. Most Muslims are passionate about fasting during this month. Although the Koran exempts sick people from the duty of fasting,<sup>1,2</sup> many Muslims with diabetes may not perceive themselves as sick and are keen to fast. A large epidemiological study of Muslims with diabetes in 13 Muslim countries (n=12 914)—the EPIDIAR study—showed that 43% of patients with type 1 and 79% of those with type 2 diabetes fasted during Ramadan.<sup>3</sup>

As the month of Ramadan follows the lunar calendar, the fasting month is brought forward by about 10 days each year, which means that over time the season in which Ramadan falls changes. For the next decade Ramadan will fall in the summer in the northern hemisphere. As daylight hours vary considerably between summer and winter months in non-equatorial countries, the length of the fast (which lasts from dawn to sunset) increases in the summer (to about 16-20 hours). People with diabetes who fast are at risk of adverse events, and the risks may increase with longer fasting periods. We review the evidence for optimum management of diabetic patients who wish to fast during Ramadan, drawing on a small evidence base comprising randomised trials, non-randomised comparison studies, and observational studies. We combine this with recommendations based on expert consensus. To reduce complications experienced by diabetic patients who fast during Ramadan, health professionals should aim to educate Muslim patients about safe fasting, not only before Ramadan but also at their annual diabetic review and at diagnosis.

### What does fasting during Ramadan involve?

Fasting during Ramadan involves abstaining from food and drink from dawn to sunset for about 30 days. Most people

### SOURCES AND SELECTION CRITERIA

We searched Embase, Medline, and the Cochrane Library from January 1970 to May 2010 for systematic reviews, randomised trials, large population based studies, case-control studies, observational studies, and published consensus statements. We used the search terms “Ramadan”, “fasting”, and “diabetes mellitus”.

take two meals a day during Ramadan—suhur (the meal before dawn and iftar (the meal after sunset).

### What are the risks of fasting for people with diabetes?

Most Muslim religious authorities accept that if a person is advised by a trusted health professional (such as a doctor or nurse) that fasting is harmful to his or her health, then that person is exempted from fasting.<sup>4</sup> The risks of fasting include hypoglycaemia, hyperglycaemia, and dehydration. The EPIDIAR study found that the change in eating patterns during Ramadan increased the risk of severe hypoglycaemia 4.7-fold (from 3 to 14 events per 100 people per month) in type 1 diabetes and 7.5-fold (from 0.4 to 3 events per 100 people per month) in type 2 diabetes. It also found a five-fold increase in the incidence of severe hyperglycaemia in patients with type 2 diabetes during Ramadan. A small observational study (n=41) conducted in 1998 found an increase in symptomatic hypoglycaemia,<sup>5</sup> but other studies have not found a significant increase in the risk of hypoglycaemia during Ramadan in patients treated with oral hypoglycaemic medications or insulin.<sup>6,7</sup> One explanation for different findings among studies is that because Ramadan occurs in a different season every nine years, and the duration and temperature of fasting days change, rates of hypoglycaemia may vary according to the year in which the study was performed. The differences in methods and the small number of patients included in these studies would also explain the disparity of the results.

Over the coming decade, the number of fasting hours will progressively increase in the northern hemisphere as Ramadan falls in the summer months. This will have important implications for Muslims with diabetes who wish to fast.

### How should patients with diabetes who fast for Ramadan be managed?

#### Assessment before Ramadan

Expert opinion recommends that if a patient has made it

### SUMMARY POINTS

Ramadan is one of the five main pillars of Islam  
Muslims are obliged to abstain from food and drink from dawn to sunset during the month of Ramadan  
Muslims with diabetes may be exempted from fasting during Ramadan, although a high proportion fast  
Patients with diabetes who fast risk hypoglycaemia, hyperglycaemia, and dehydration  
Guidelines from the National Institute for Health and Clinical Excellence emphasise the importance of individualising care on the basis of patients' social, cultural, and religious needs  
Diabetic patients who want to fast need an assessment before Ramadan and education to increase their awareness of the risks of fasting

clear that they wish to fast during Ramadan their primary physicians and/or diabetes care specialists should assess whether they increase their health risk by doing so.<sup>8</sup> Box 1 outlines how patients planning to fast during Ramadan may be categorised as either high, moderate, or low risk of adverse events. Patients classed as high risk are advised not to fast as it can lead to worsening diabetes control, result-

ing in, for example, severe hypoglycaemia and diabetes ketoacidosis. Patients at moderate risk can reduce their level of risk if they see a healthcare professional several months before Ramadan and make necessary changes to their diabetes treatment. Those at low risk can fast without healthcare advice. Patients who choose to fast despite advice not to do so need support to help them fast as safely as possible.

In case patients miss the opportunity for assessment before Ramadan, discussion with patients and provision of information packs (see the “Additional educational resources” box) that include advice on Ramadan fasting can be made available at diagnosis and also at annual diabetic review.

### Ramadan focused education

Structured education interventions have been endorsed by the National Institute for Health and Clinical Excellence as important in empowering patients to improve their journey with diabetes. In a large observational study, patients who fasted during Ramadan without attending a structured education session had a fourfold increase in hypoglycaemic events, whereas those who attended an education programme focusing on Ramadan had a significant decrease in hypoglycaemic events.<sup>9</sup> We therefore recommend that Muslim patients with diabetes attend some form of structured education intervention to increase their chance of being well when fasting during Ramadan. Patients at high risk who plan to fast despite medical advice not to are also invited to attend structured education to support their self management and decision to fast. Box 2 outlines suggested content of Ramadan focused education.

### How should fasting patients with type 2 diabetes be managed?

#### Patients taking oral hypoglycaemic agents

##### *Metformin*

Hypoglycaemia occurs in patients with type 2 diabetes taking metformin who are not fasting.<sup>14</sup> A systematic review reported that levels of risk for hypoglycaemia among people taking metformin who are not fasting range from 0% to 21%.<sup>15</sup> No data exist for the incidence of hypoglycaemia in people who fast for prolonged periods and take only metformin.

As iftar is usually the largest meal during Ramadan, expert consensus suggests that the metformin dose should be split such that two thirds of the dose is taken at iftar and one third at suhur (as the lunchtime dose during the daytime fast is not allowed). So for a regimen of, for example, metformin 500 mg three times a day, we recommend 500 mg at suhur and 1000 mg at iftar.

##### *Acarbose*

Acarbose inhibits the action of intestinal brush border alpha-glucosidases, which retards glucose absorption and modifies the secretion of insulin.<sup>16</sup> A randomised double blind study showed that the risk of hypoglycaemia is low with this class of drugs,<sup>17</sup> although we could not find any evidence that this is so during Ramadan. We suggest that it is acceptable to continue with the prescribed dose(s) of acarbose taken only with meals during fasting.

### Box 1 | Expert recommendations for risk stratification in patients with type 1 or type 2 diabetes who fast during Ramadan<sup>8</sup>

#### Patients at high risk

- Those with severe and recurrent episodes of hypoglycaemia and unawareness
- Those with poor glycaemic control
- Those with ketoacidosis in the three months before Ramadan
- Those who experience hyperosmolar hyperglycaemic coma within the three months before Ramadan
- Those with acute illness
- Those who perform intense physical labour
- Pregnant women
- Those with comorbidities such as advanced macrovascular complications, renal disease on dialysis, cognitive dysfunction, uncontrolled epilepsy (particularly precipitated by hypoglycaemia)

#### Moderate risk

- Well controlled patients treated with short acting insulin secretagogue, sulphonylurea, insulin, or taking combination oral or oral plus insulin treatment

#### Low risk

- Well controlled patients treated with diet alone, monotherapy with metformin, dipeptidyl peptidase-4 inhibitors, or thiazolidinediones who are otherwise healthy

### Box 2 | Four key areas in Ramadan focused education<sup>9</sup>

#### Meal planning and dietary advice

- The diet during Ramadan should be a healthy balanced diet
- Slow energy release foods (such as wheat, semolina, beans, rice) should be taken before and after fasting, whereas foods high in saturated fat (such as ghee, samosas, and pakoras) should be minimised<sup>10</sup>
- Advise patients to use only a small amount of monounsaturated oils (such as rapeseed or olive oil) in cooking
- Before and after fasting include high fibre foods such as wholegrain cereals, granary bread, brown rice; beans and pulses; fruit, vegetables, and salads

#### Exercise

- Regular light and moderate exercise is safe in type 2 diabetes patients<sup>11</sup>
- Rigorous exercise is not recommended as the risk of hypoglycaemia may be increased, particularly in patients taking sulphonylureas or insulin
- Encourage patients to continue their usual physical activity, especially during non-fasting periods
- Tarawih prayers (a series of prayers after the sunset meal) should be considered as part of the daily exercise regimen as they involve standing, bowing, prostrating, and sitting

#### Blood glucose monitoring

- Blood glucose monitoring does not constitute the break of fast<sup>12</sup>
- All patients who fast should be provided with the means to monitor their blood glucose<sup>13</sup>
- Capillary blood glucose testing should be done when:
  - The patient suspects they have symptoms of hypoglycaemia (subjective to the individual). Patients should be advised to break their fast if hypoglycaemia is confirmed on blood glucose testing
  - The patient is unwell (eg, has a fever)
- Testing at other times may be useful only if patients are able and willing to adjust their diabetes treatment regimens, such as insulin dosage titration

#### Recognising and managing complications

- Patients should be aware of the warning symptoms of dehydration, hypoglycaemia, and hyperglycaemia and should stop the fast as soon as any complications or acute illness occur

## ADDITIONAL EDUCATIONAL RESOURCES

## For healthcare professionals

- Al-Arouj M, Bouguerra R, Buse J, Hafez S, Hassanein M, Ibrahim MA, et al. American Diabetes Association recommendations for management of diabetes during Ramadan. *Diabetes Care* 2005;28:2305-11
- Karamat MA, Syed A, Hanif W. Review of diabetes management and guidelines during Ramadan. *JR Soc Med* 2010;103:139-47.
- 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;73:117-25.
- Ramadan health factsheet 2009 (from Muslim Spiritual Care Provision in the NHS, PO box 57330, London E1 2WJ; nhsspiritualcare@mcb.org.uk)—Provides a brief summary of issues for doctors, healthcare staff, and patients

## For patients

- Leicestershire Diabetes (www.leicestershirediabetes.org.uk)—Website with information on fasting and insulin treatment during Ramadan
- United Kingdom Ramadan Diabetes Network (www.ukRamadandiabetes.net)—Has a useful publication on diabetes and fasting
- Ramadan health guide: a guide to healthy fasting. 2007. www.ramadan.co.uk/RamadhanHealth\_Guide.pdf. (Useful Department of Health document on healthy fasting, but not specifically about diabetes)

*Rapid acting insulin secretagogues*

An open label, multicentre, randomised study showed that repaglinide, a rapid acting insulin secretagogue, contributed to improved glycaemic control, with a lower number of hypoglycaemic events among fasting patients during Ramadan when compared with glibenclamide. Patients taking repaglinide lowered their fructosamine levels from baseline, and there were 0.03 hypoglycaemic events per patient per month in this group versus 0.05 events per patient per month in the glibenclamide group.<sup>18</sup>

A small study compared repaglinide (n=27) with a group of patients taking a sulphonylurea (glimepiride (n=23) or gliclazide (n=17)). Fructosamine, HbA<sub>1c</sub>, and body weight did not change significantly in either group from before to after Ramadan. Hypoglycaemia was documented in only one patient who took glimepiride during Ramadan.<sup>19</sup> The evidence cited suggests that rapid acting insulin secretagogues taken at suhur and iftar are a safer alternative than glibenclamide for patients who fast.

*Sulphonylureas*

Early studies examined the use of glibenclamide or glimepiride during Ramadan.<sup>20</sup> A more recent, large prospective observational study (n=332) showed that changing once daily glimepiride from a morning dose taken with breakfast before Ramadan to an evening dose taken at iftar during Ramadan did not alter rates of hypoglycaemia or glycaemic control.<sup>21</sup> However, the rate of hypoglycaemia in patients taking glimepiride in the mornings during Ramadan was not studied, so whether that rate is higher than the rate in those taking glimepiride in the evenings is unknown. The incidence of hypoglycaemic events did not differ between a group of patients taking once daily glimepiride (n=21) and a group taking twice daily repaglinide (n=20) (taken at suhur and iftar).<sup>22</sup> More recently, gliclazide has been compared with newer agents, such as dipeptidyl peptidase-4 inhibitors.<sup>23</sup>

On the basis of the prospective study by the GLIRA study group<sup>21</sup> we recommend that during Ramadan clinicians

change the timing of the once daily dose of sulphonylurea (such as glimepiride) from the usual morning dose to the evening (at iftar). With regard to gliclazide, we recommend that patients take a larger dose at iftar than at suhur and that clinicians consider reducing the prescribed dose for suhur if the patient's glycaemic control before Ramadan is stable (for example, change gliclazide 160 mg twice daily to 80 mg in the morning and 160 mg in the evening).

*Thiazolidenediones*

A randomised controlled trial that compared pioglitazone 30 mg once daily with placebo in patients already taking other oral hypoglycaemic agents or alone, found no increase in hypoglycaemia during Ramadan fasting.<sup>24</sup> No studies have been reported on the use of rosiglitazone use during Ramadan. Continuing with thiazolidenediones during fasting is considered safe.

*Dipeptidyl peptidase-4 inhibitors*

A retrospective audit of Muslim patients with type 2 diabetes showed that adding vildagliptin to metformin treatment was associated with a reduced incidence of hypoglycaemic events and improved glucose control compared with patients treated with gliclazide and metformin during Ramadan.<sup>23</sup> This low grade evidence suggests that it may be safer to combine dipeptidyl peptidase-4 inhibitors, rather than sulphonylureas, with metformin in patients who are not well controlled when taking metformin alone and are planning to fast during Ramadan.

*Glucagon-like peptide-1 mimetics*

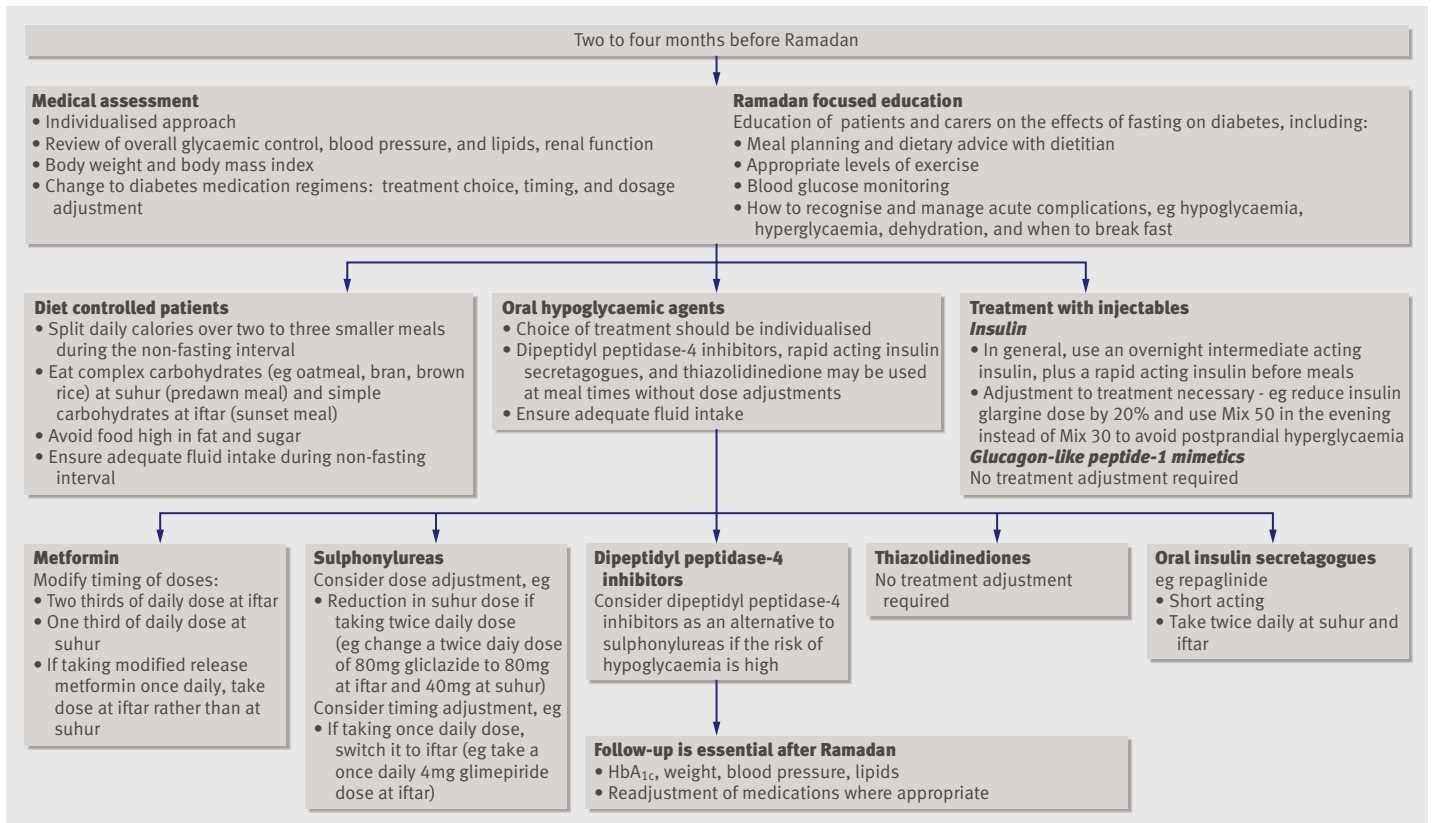
Glucagon-like peptide-1 mimetics are currently used in combination with other oral hypoglycaemic agents. In non-Ramadan studies, hypoglycaemic events associated with glucagon-like peptide-1 mimetics occurred primarily in patients taking a sulphonylurea.<sup>25</sup> The findings of an audit suggested that its dosage does not need to be adjusted during Ramadan but that other agents, such as sulphonylureas, may need dose reductions when used as a combination treatment.<sup>26</sup>

## Patients taking insulin

*Single basal insulin and oral combined treatment*

A multicentre, prospective, observational study compared fasting patients taking metformin combined with glimepiride (n=21), repaglinide (n=18), or glargine (n=10).<sup>7</sup> Although the rate of hypoglycaemia was higher in the glimepiride group (14.3%) than in the repaglinide (11%) and glargine (10%) groups, the increased rate was not significant. Glimepiride was given before iftar; repaglinide was given with both meals; and glargine at 10.00 pm. No studies have compared the incidence of hypoglycaemic events in patients taking insulin detemir or isophane insulin (NPH) (such as Insulatard, Novo Nordisk; or Humulin I, Lilly).

In a small prospective non-randomised study of 19 patients who had type 2 diabetes, were at low risk of diabetic complications, and had a pre-Ramadan HbA<sub>1c</sub> concentration of <8%, neither fasting (n=11) nor non-fasting (n=8) patients who were taking repaglinide three times a day and glargine experienced hypoglycaemic events,



An approach to oral treatment of type 2 diabetes during Ramadan for patients planning to fast

and both groups maintained stable glycaemic control.<sup>6</sup> Those who fasted took repaglinide at iftar, at midnight, and at suhur, and the doses of repaglinide and glargine remained unchanged throughout Ramadan. We advise patients who take long acting basal insulin, such as glargine, to reduce the dose by 20% to avoid hypoglycaemia. Patients taking repaglinide and single dose glargine may continue taking the same doses of repaglinide but to be safer should consider reducing glargine by 20%. The timing of repaglinide can be rearranged to coincide with suhur and iftar.

*Premixed insulins*

A randomised, open labelled, crossover study comparing Humalog Mix25 (Lilly) (25% short acting insulin lispro and 75% intermediate acting neutral lispro protamine) and Humulin M3 (Lilly) (human insulin 30% soluble, 70% isophane) given in identical doses showed that the former offered better control of postprandial blood glucose after iftar and a lower occurrence of hypoglycaemic events.<sup>27</sup> However, the findings of an observational study suggested that using Humalog Mix50 (Lilly) at ifta instead of Mix30 reduced postprandial glucose excursions and reduced hypoglycaemia.<sup>28</sup> We suggest that patients taking twice daily insulin should reduce the suhur dose by 30% if they are well controlled, and consider switching to a Mix 50 preparation if their postprandial glucose remains raised.

**Is fasting safe for pregnant women with diabetes?**  
Pregnant women with diabetes, including gestational

diabetes, are exempted from fasting and are strongly cautioned against fasting because clear maternal and fetal risks are associated with poor glycaemic control in pregnancy.<sup>29</sup> However, no outcome study of women with diabetes specifically related to Ramadan fasting has been conducted. Preconception counselling for diabetic Muslim women must include education about the substantial risks associated with poor glycaemic control to help to dissuade them from trying to fast.

**How should fasting patients with type 1 diabetes be managed?**

A small study examined the use of glargine and insulin lispro or aspart, divided in a 6:4 ratio of the total 24 hour insulin dose in nine patients with type 1 diabetes.<sup>30</sup> Of seven patients who started to fast, five continued for the whole month, and two broke the fast owing to hypoglycaemia. None of the patients had any episodes of severe hypoglycaemia or diabetic ketoacidosis requiring admission to hospital, and the patients' HbA<sub>1c</sub> concentrations remained stable at the end of Ramadan. As the insulin requirement in this study group decreased by 28% from baseline (P=0.002), the authors suggested a reduced dose (70% of a patient's usual dose) during the fast.

An open label, comparative, crossover study of 64 patients with type 1 diabetes found significantly lower (P=0.026) two hour, postprandial glucose concentrations after iftar and fewer hypoglycaemic events with insulin lispro than with regular human insulin.<sup>31</sup> In both arms isophane insulin (Humulin I) was given as the basal insulin.

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Most studies of patients with type 1 diabetes have comprised small numbers of patients and some have excluded adolescents, elderly patients, or patients with comorbidities such as renal impairment. Suggested treatments, therefore, may not be generalised to all fasting patients with type 1 diabetes, and no good evidence exists to allow us to give clear guidance for those who are not on a basal bolus regimen (basal insulins are intermediate or long acting insulins; bolus is rapid acting insulin taken with meals).

We suggest that patients with type 1 diabetes who are on a basal bolus regimen four times daily should be discouraged from fasting owing to the risks of poor glycaemic control. If patients choose to fast despite medical advice, it will help if they are familiar with carbohydrate counting. We suggest they reduce their background insulin by 20% and omit the midday rapid acting insulin if their capillary blood glucose concentration is  $\leq 7$  mmol/l. If their blood glucose concentration is  $> 7$  mmol/l, patients will need to calculate their insulin correction dose as determined by their specialists.

### Conclusion

The figure summarises the recommendations given in this article, based on the best available and most current evidence and on our collective experience in managing patients who fast during Ramadan. Overall, the evidence available for guiding management of patients with diabetes who wish to fast during Ramadan is poor, and well designed studies are lacking. An assessment of a patient's individual risk and a tailored approach to treatment seems to be the best management strategy. Offering structured education to enable patients to manage their condition better themselves during Ramadan is essential.

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