RAVEENDRAN A. V., MBBS, MD

Specialist in Internal Medicine, Badr Al Samaa, Barka, Sultanate of Oman; Former Assistant Professor of Medicine, Department of Internal Medicine, Govt. Medical College, Manjeri, Malappuram (DT), Kerala, India

ABDUL HAMID ZARGAR, MBBS, MD, DM

Member, Medical Council of India; Member Institute Body, AIIMS, New Delhi, India; Chairman, Independent Ethics Committee Fortis-Escorts Hospital & Research Centre, New Delhi, India; Past-President, Endocrine Society of India; Senior Endocrinologist, Advanced Center for Diabetes and Endocrine Care, National Highway, Gulshan Nagar, Chanapora, Srinigar, India

Diabetes control during Ramadan fasting

ABSTRACT

For diabetic patients, fasting during Ramadan, the ninth month of the Islamic calendar, can cause wide fluctuations in blood sugar levels, posing a medical challenge for patients and physicians and increasing the risk of acute metabolic complications including hypoglycemia, hyperglycemia, diabetic ketoacidosis, dehydration, and thrombosis. Proper patient education, risk stratification, and modification of antidiabetic medications can reduce the risk of complications.

KEY POINTS

A diabetic patient who develops signs or symptoms of hypoglycemia during Ramadan fasting should break the fast to avoid serious complications.

Management of complications in diabetic patients during Ramadan is similar to that for nonfasting diabetic patients. Complications include hypo- and hyperglycemia, diabetic ketoacidosis, and dehydration.

A common misconception among patients is that pricking the finger for blood sugar testing during fasting hours breaks the fast; this should be addressed during Ramadan-focused diabetes education. A N ESTIMATED 50 MILLION patients with diabetes worldwide practice daily fasting during Ramadan, the ninth month of the Islamic calendar, which lasts 29 or 30 days. In the United States, Ramadan begins this year at sundown on Friday, May 26, and ends at sundown on Sunday, June 25.

See related editorial, page 357

According to the Multi-Country Retrospective Observational Study of the Management and Outcomes of Patients With Diabetes During Ramadan, conducted in 13 countries, 94.2% of Muslim diabetic patients fasted at least 15 days, and 67.6% of these fasted every day.¹

The daily fasting period, which may extend from 14 to 18 hours, starts before sunrise and ends after sunset. The meal taken before sunrise is called *Suhur*, and the meal after sunset is called *Iftar*. The fast requires abstaining from eating, drinking, sexual activity, medications, and smoking. For diabetic patients, this poses medical challenges, increasing the risk of acute metabolic complications.

The goal of caring for diabetic patients during Ramadan fasting is to help them to fast without major complications and to empower them to modify their lifestyle in order to achieve this goal.

POSSIBLE METABOLIC COMPLICATIONS

Metabolic complications during Ramadan fasting include hypoglycemia, hyperglycemia, diabetic ketoacidosis, dehydration, and thrombosis.

Hypoglycemia

For patients with type 1 diabetes, fasting increases the risk of hypoglycemia 4.7 times, and the risk is 7.5 times higher for patients with

type 2 diabetes.² However, this is often underreported, as mild to moderate hypoglycemia

does not usually require medical assistance. Precipitating factors include long fasting hours, missing the Suhur meal, and failure to modify drug dosage and timing.

Hyperglycemia

The risk of severe hyperglycemia during fasting is 3.2 times higher in patients with type 1 diabetes and 5 times higher in those with type 2 diabetes.² Precipitating factors include lack of diet control during the Iftar meal and excessive reduction in the dosage of diabetes medications due to fear of hypoglycemia.

Diabetic ketoacidosis

Ketoacidosis can be precipitated by a lack of diet control during the Iftar meal, excessive reduction in the dosage of insulin due to fear of hypoglycemia, acute stress, and illness or infection.

Dehydration and thrombosis

Patients can become dehydrated during long fasting hours in especially hot weather, by sweating during physical activity, and by osmotic diuresis in poorly controlled diabetes.

Diabetes is a procoagulant condition, and dehydration increases the risk of thrombosis.

OVERALL MANAGEMENT GOALS **DURING RAMADAN FASTING**

Important aspects of managing diabetes during Ramadan fasting are:

- The pre-Ramadan evaluation and risk • stratification
- Promoting patient awareness with Rama-٠ dan-focused diabetes education
- Providing instruction on dietary modifica-٠ tion
- Modification of the dosage and timing of diabetes medication
- Encouraging frequent monitoring of blood glucose levels
- Advising the patient when to break the fast
- Managing complications. •

PRE-RAMADAN MEDICAL EVALUATION AND RISK STRATIFICATION

All diabetic patients who fast during Ramadan should undergo an evaluation 1 or 2 months

TABLE 1

Risk of complications during Ramadan fasting: International Diabetes Federation categories

Category 1: very high risk

One or more of the following:

- Severe hypoglycemia within the 3 months before Ramadan
- Diabetic ketoacidosis within the 3 months before Ramadan
- Hyperosmolar hyperglycemic coma within the 3 months before Ramadan
- History of recurrent hypoglycemia
- History of hypoglycemia unawareness
- Poorly controlled type 1 diabetes
- Acute illness
- Pregnancy with preexisting diabetes, or gestational diabetes treated with insulin or a sulfonylurea
- Chronic dialysis or stage 4 or 5 chronic kidney disease
- Advanced macrovascular complications
- Old age with ill health

Category 2: high risk

One or more of the following:

- Type 2 diabetes with sustained poor glycemic control
- Well-controlled type 1 diabetes
- Well-controlled type 2 diabetes on multiple-dose insulin or mixed insulin
- Pregnancy with type 2 diabetes or gestational diabetes controlled with diet only or with metformin
- Stage 3 chronic kidney disease
- Stable macrovascular complications
- Comorbid conditions that present additional risk factors
- Diabetes and intense physical activity
- Treatment with drugs that may affect cognitive function

Category 3: moderate/low risk

Well-controlled type 2 diabetes treated with one or more of the following:

- Lifestyle therapy
- Metformin
- Acarbose
- Thiazolidinediones
- Second-generation sulfonylurea
- Incretin-based therapy
- Sodium-glucose cotransporter 2 inhibitor
- Basal insulin

Adapted with permission from International Diabetes Federation and the DAR Interna-tional Alliance. Diabetes and Ramadan: Practical Guidelines. Brussels, Belgium: Interna-tional Diabetes Federation, 2016. www.idf.org/guidelines/diabetes-in-ramadan and www.daralliance.org.

before the start of Ramadan to determine their level of diabetes control and the presence of acute and chronic complications of diabetes and other comorbid conditions. Also important is to determine the patient's social circumstances, ie, knowledge about diabetes, socioeconomic factors, religious beliefs, educational status,

TABLE 2

Exemption from fasting during Ramadan

Generally exempted from fasting:

Children Elderly people People with acute illness Pregnant women Developmentally disabled people (with serious physical handicaps, intellectual disability) People with chronic illness with multiple complications People who must travel long distances daily

Diabetes-related exemptions from fasting:

Type 1 diabetes Type 2 diabetes with unstable disease Complications of diabetes Pregnancy and diabetes Older age with diabetes

Breaking the fast is recommended in the following cases:

- If blood glucose < 3.3 mmol/L (60 mg/dL) or symptoms of hypoglycemia
- If blood glucose > 16.7 mmol/L (300 mg/dL)
- If blood glucose < 3.9 mmol/L (70 mg/dL) in the morning, if patient is already on insulin or a sulfonylurea

diabetes self-management skills, and family support in case of hypoglycemia or complications.

As diabetes is a procoagulant condition, dehydration can increase the risk of thrombosis The evaluation helps to determine the patient's risk of diabetes-related complications from Ramadan fasting, which is categorized as very high, high, or moderate/low according to the criteria of the International Diabetes Federation (**Table 1**).³ Patients should be advised as to the feasibility of fasting based on this risk categorization.

Even though the recommendation is to avoid fasting if the risk is very high or high, many patients fast. But patients should be advised about Islamic regulations exempting people from fasting (**Table 2**).⁴

RAMADAN-FOCUSED DIABETES EDUCATION

Improving the patient's awareness of the risks of Ramadan fasting reduces the chance of complications. Education should include information on diet and exercise, changes in the timing and dosing of medications, signs and symptoms of hypoglycemia and hyperglycemia, the importance of monitoring blood glucose levels on fasting days, and the importance of breaking the fast in case of complications.⁵

DIET AND EXERCISE

All diabetic patients should be encouraged to remember to eat the predawn meal on fasting days. They should maintain a balanced diet, with complex carbohydrates with slow energy release for the predawn meal and simple carbohydrates for the sunset meal. Foods with a low glycemic index and high fiber content are recommended, and patients should be advised to avoid saturated fats and to drink plenty of fluids between sunset and sunrise to avoid dehydration.⁶

Diabetic patients can perform their usual physical activity, including moderate exercise, but should avoid excessive physical activity especially toward evening hours to prevent hypoglycemia.

Some patients may decide not to monitor their blood glucose as they believe that pricking the finger for blood sugar testing breaks the fast.⁷ Patients should be advised that this is a misconception.

ADJUSTING DIABETES MEDICATIONS

Oral diabetes drugs

Drugs such as metformin, alpha glucosidase inhibitors, thiazolidinediones, the short-acting insulin secretagogue nateglinide, dipeptidyl peptidase 4 inhibitors (eg, sitagliptin), and glucagon-like peptide 1 receptor agonists are associated with a lower risk of hypoglycemia and can be used during Ramadan fasting without significant changes in the daily dose (Table 3).⁸

Sulfonylureas carry a higher risk of hypoglycemia and should be used cautiously during fasting, with appropriate modification in dose and timing.^{9,10}

Sodium-glucose cotransporter 2 inhibitors, when not combined with insulin or sulfonylureas, carry a lower risk of hypoglycemia, but during Ramadan fasting there is an increased risk of dehydration, urinary tract infection, and postural hypotension since fluids cannot be taken during fasting hours.

Dipeptidyl peptidase 4 inhibitors carry a low risk of hypoglycemia and can be used during Ramadan without dosing modification. Glucagon-like peptide 1 agonists also can be used without adjusting the dosage.¹¹

TABLE 3

Recommendations for adjusting diabetes medications during Ramadan fasting

Medication	Recommendations
Metformin	Risk of hypoglycemia is low, so usually no dosage modification required Split the dose: one-third predawn, the rest at sunset
Sulfonylurea	High risk of hypoglycemia Glimepiride, gliclazide, and glipizide are preferred over conventional sulfo- nylureas such as glibenclamide because of comparatively fewer hypogly- cemic events
Thiazolidinedione	Risk of hypoglycemia is low, so usually no dosage modification required If taken with other antidiabetic drugs, take one-fourth of the dose predawn, the rest at sunset
Alpha glucosidase inhibitor	Risk of hypoglycemia is low Gastrointestinal side effects can be problematic
Nonsulfonylurea secretagogues (glinides)	Low risk of hypoglycemia, so no adjustment required for twice-daily dosing Because of faster onset and shorter duration of action, nateglinide is preferred over repaglinide during Ramadan fasting as the risk of fasting hypoglycemia is low
Glucagon-like peptide 1 receptor agonist	Risk of hypoglycemia is low, so no dosage modification required if taken alone If taken with sulfonylurea, dose reduction required
Dipeptidyl peptidase 4 inhibitor	Risk of hypoglycemia is low, so no dosage modification required
Sodium-glucose cotransporter 2 inhibitor	Avoid during Ramadan fasting due to risk of osmotic diuresis, dehydration, and ketoacidosis
Insulin	High risk of hypoglycemia Premixed 70/30 insulin during Ramadan fasting more likely to cause hypoglycemic episodes than premixed 50/50 Usual morning dose at sunset, and half of nighttime dose predawn Insulin analogues are associated with a lower risk of hypoglycemia than human insulin Reduce dose of long-acting insulin analogues by 20% During Ramadan fasting, a basal bolus regimen is preferred, including a long-acting basal insulin (eg, glargine, detemir, degludec) with a short- acting insulin (eg, glulisine, aspart, lispro) before meals

Insulins

Insulin treatment is associated with a higher risk of hypoglycemia during Ramadan fasting.¹² During fasting, the risk of hypoglycemia from premixed insulin can be minimized by changing to a multiple-dose regimen involving a basal insulin and short-acting insulin before meals, with adjustment of the shortacting insulin dose based on the anticipated carbohydrate intake for each meal.¹³

Patients taking premixed insulin preparations consisting of 70% intermediate-acting or long-acting insulin and 30% short-acting insulin should change to a 50/50 preparation during Ramadan fasting to reduce hypoglycemic risk and improve glycemic control; taking more of the fast-acting component controls postprandial hyperglycemia, and taking less of the intermediate or long-acting component minimizes the risk of hypoglycemia during fasting hours.^{14,15}

Insulin analogues carry a lower risk of hypoglycemia than human insulin. Compared with a human insulin 70/30 preparation, an analogue premix containing 75% neutral protamine lispro and 25% insulin lispro resulted in better glycemic control during Ramadan fast-

Some patients may avoid pricking the skin to test the blood as they believe, mistakenly, that it breaks the fast ing.¹⁶ This could be related to the pharmacodynamics of low-ratio premix analogues, as well as to the mealtime flexibility of analogue insulin, as the injections of the 75/25 mix were given immediately before the morning and evening meals. Insulin analogues are also less likely to cause postprandial hypoglycemia.¹⁶

A multiple-dose insulin regimen involving a long-acting basal insulin (eg, glargine, detemir, degludec) and a short-acting insulin (eg, glulisine, aspart, lispro) before meals is preferred in view of better glycemic control and lower risk of hypoglycemia.¹⁷

Use of an insulin pump during Ramadan is associated with a reduced risk of hypoglycemia.¹⁸ In patients with an insulin pump, the rate of basal insulin must be reduced during daytime, and the postprandial bolus of insulin must be increased after breaking the fast.

FREQUENT MONITORING OF BLOOD GLUCOSE DURING FASTING

Frequent monitoring reduces the risk of both hypoglycemia and hyperglycemia and helps control blood sugar levels during Ramadan fast-

REFERENCES

- Babineaux SM, Toaima D, Boye KS, et al. Multi-country retrospective observational study of the management and outcomes of patients with type 2 diabetes during Ramadan in 2010 (CREED). Diabet Med 2015; 32:819–828.
- Salti I, Benard E, Detournay B, et al; EPIDIAR Study Group. A populationbased 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; 27:2306–2311.
- 3. International Diabetes Federation and the DAR International Alliance. Diabetes and Ramadan: Practical Guidelines. Brussels, Belgium: International Diabetes Federation, 2016. www.idf.org/guidelines/diabetes-in-ramadan and www.daralliance.org. Accessed March 8, 2017.
- 4. Al-Arouj M, Bouguerra R, Buse J, et al. Recommendations for management of diabetes during Ramadan. Diabetes Care 2005; 28:2305–2311.
- Masood SN, Masood Y, Hakim R, Alvi SFD, Shera AS. Ramadan fasting related awareness, practices and experiences of a representative group of urban Pakistani Diabetics. Pak J Med Sci 2012; 28:432–436.
- 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; 27:327–331.
- Masood SN, Sheikh MA, Masood Y, Hakeem R, Shera AS. Beliefs of people with diabetes about skin prick during Ramadan fasting. Diabetes Care 2014; 37:e68–e69.
- Aravind S, Ismail SB, Balamurugan R, et al. Hypoglycemia in patients with type 2 diabetes from India and Malaysia treated with sitagliptin or a sulfonylurea during Ramadan: a randomized, pragmatic study. Curr Med Res Opin 2012; 28:1289–1296.
- Glimepiride 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; 28:421–422.
- Hassanein M, Abdallah K, Schweizer A. A double-blind, randomized trial, including frequent patient-physician contacts and Ramadan-focused advice, assessing vildagliptin and gliclazide in patients with type 2 diabetes fasting during Ramadan: the STEADFAST study. Vasc Health Risk Manag 2014;

ing. As mentioned above, pricking the finger for blood sugar testing during fasting hours does not break the fast, and this should be emphasized during Ramadan-focused diabetes education.

The exact frequency of blood sugar testing is not defined. In patients with well-controlled diabetes without complications, testing once or twice a day is enough. Patients with poorly controlled diabetes and those with complications should test more often.

ADVICE REGARDING WHEN TO BREAK THE FAST

If signs or symptoms of hypoglycemia develop, the patient should break the fast in order to avoid serious complications. This is acceptable under Islamic law.^{3,19–21}

MANAGEMENT OF COMPLICATIONS

Management of diabetic complications in patients during Ramadan fasting is similar to that for other diabetic patients and includes management of hypo- and hyperglycemia, diabetic ketoacidosis, and dehydration.

10:319–326.

- 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; 16:527–536.
- Ibrahim M, Abu Al Magd M, Annabi FA, et al. Recommendations for management of diabetes during Ramadan: update 2015. BMJ Open Diabetes Res Care 2015; 3:e000108.
- Kassem HS, Zantout MS, Azar ST. Insulin therapy during Ramadan fast for type 1 diabetes patients. J Endocrinol Invest 2005; 28:802–805.
- Hui E, Bravis V, Salih S, Hassanein M, Devendra D. Comparison of humalog mix 50 with human insulin mix 30 in type 2 diabetes patients during Ramadan. Int J Clin Pract 2010; 64:1095–1099.
- Hassanein M, Belhadj M, Abdallah K, et al. Management of type 2 diabetes in Ramadan: low ratio premix insulin working group practical advice. Indian J Endocrinol Metab 2014; 18:794–799.
- Mattoo V, Milicevic Z, Malone JK, et al; Ramadan Study Group. A comparison of insulin lispro Mix25 and human insulin 30/70 in the treatment of type 2 diabetes during Ramadan. Diabetes Res Clin Pract 2003; 59:137–143.
- Pathan MF, Sahay RK, Zargar AH, et al. South Asian Consensus Guideline: use of insulin in diabetes during Ramadan. Indian J Endocrinol Metab 2012; 16:499–502.
- Khalil AB, Beshyah SA, Abu Awad SM, et al. Ramadan fasting in diabetes patients on insulin pump therapy augmented by continuous glucose monitoring: an observational real-life study. Diabetes Technol Ther 2012; 14:813–818.
- 19. Holy Qur'an 2:195.
- 20. Holy Qur'an 4:29.
- Bashir MI, Pathan MF, Raza SA. Role of oral hypoglycemic agents in the management of type 2 diabetes mellitus during Ramadan. Indian J Endocrinol Metab 2012; 16:503–507.

ADDRESS: Raveendran A.V., MBBS, MD, Department of Internal Medicine, Govt. Medical College, Manjeri, Malappuram (DT), Kerala 670631, India; raveendranav@yahoo.co.in