Recommendations for Management of Diabetes During Ramadan

MONIRA AL-AROUJ, MD[1]
RADHIA BOUGUERRA, MD[2]
JOHN BUSE, MD, PHD[3]
SHERIF HAFEZ, MD, FACP[4]
MOHAMED HASSANEIN, FRCP[5]
MAHMOUD ASHRAF IBRAHIM, MD[6]
FARAMARZ ISMAIL-BEIGI, MD, PHD[7]
IMAD EL-KEBBI, MD[8]
OUSSAMA KHATIB, MD, PHD[9]
SUHAIL KISHAWI, MD[10]
ABDULRAZZAQ AL-MADANI, MD[11]
ALY A. MISHAL, MD, FACP[12]
MASOUD AL-MASKARI, MD, PHD[13]
ABDALLA BEN NAKHI, MD[1]
KHALED AL-RUBEAN, MD[14]

It is estimated that there are 1.1–1.5 billion Muslims worldwide, comprising 18–25% of the world population (1,2). Fasting during Ramadan, a holy month of Islam, is an obligatory duty for all healthy adult Muslims. An ~4.6% prevalence of diabetes worldwide (3) coupled with the results of the population-based Epidemiology of Diabetes and Ramadan 1422/2001 (EPIDIAR) study, which showed (in 12,243 people with diabetes from 13 Islamic countries) that ~43% of patients with type 1 diabetes and ~79% of patients with type 2 diabetes fast during Ramadan (4), lead to the estimation that some 40–50 million people with diabetes worldwide fast during Ramadan.

Ramadan is a lunar-based month, and its duration varies between 29 and 30 days. Its timing changes with respect to seasons. Depending on the geographical location and season, the duration of the daily fast may range from a few to more than 20 h. Muslims who fast during Ramadan must abstain from eating, drinking, use of oral medications, and smoking from predawn to after sunset; however, there are no restrictions on food or fluid intake between sunset and dawn. Most people consume two meals per day during this month, one after sunset, referred to in Arabic as Iftar (breaking of the fast meal), and the other before dawn, referred to as Suhur (predawn). Fasting is not meant to create excessive hardship on the Muslim individual. The Koran specifically exempts the sick from the duty of fasting (Holy Koran, Al-Bakarah, 183–185), especially if fasting might lead to harmful consequences for the individual. Patients with diabetes fall under this category because their chronic metabolic disorder may place them at high risk for various complications if the pattern and amount of their meal and fluid intake is markedly altered. This exemption represents more than a simple permission not to fast; the Prophet Mohammad said, "God likes his permission to be fulfilled, as he likes his will to be executed." Nevertheless, many patients with diabetes insist on fasting during Ramadan, thereby creating a medical challenge for themselves and their physicians. It is therefore important that medical professionals be aware of potential risks that may be associated with fasting during Ramadan. This familiarity and knowledge is as important in Indonesia, Pakistan, and the Middle East as it is in Europe, North America, New Zealand, and Australia.

The medical ramifications of fasting among patients with diabetes are largely unknown. Due to the limited information available from prospective or retrospective studies on the effects of fasting during Ramadan, a group of endocrinologists and diabetologists from a number of Muslim and non-Muslim countries met to exchange information and opinions and to propose a set of recommendations. Although recommendations for management of diabetes in patients who elect to fast during Ramadan were proposed in 1995 at a conference in Casablanca (5), the present effort was prompted by data from the EPIDIAR study (4) showing that fasting is quite common among Muslims with diabetes and by the increasing awareness that this represents a global medical issue. The purposes of the recommendations that follow are threefold: *1*) to invite an open dialogue on this important topic, *2*) to offer a set of medical opinions and suggestions, and *3*) to identify topics of research needed to answer important medical questions regarding fasting during Ramadan.

In this document, we avoid use of the terms "indications" or "contraindications" for fasting because fasting is a religious issue for which patients make their own decision after receiving appropriate advice from religious teachings and from their own health care providers. However, we emphasize that fasting, especially among patients with type 1 diabetes with poor glycemic control, is associated with multiple risks. In addition to highlighting the potential risks, we provide suggestions on how to manage the patients with diabetes who decide to fast during Ramadan.

PATHOPHYSIOLOGY OF FASTING

— Insulin secretion in healthy individuals is stimulated with feeding, which promotes the storage of glucose in liver and muscle as glycogen. In contrast, during fasting, circulating glucose levels tend to fall, leading to decreased secretion of insulin. At the same

From the [1]Ministry of Health, Amiri Hospital, Rawda, Kuwait; the [2]National Institute of Nutrition, Tunis, Tunisia; the [3]Diabetes Care Center, University of North Carolina School of Medicine, Chapel Hill, North Carolina; the [4]Department of Internal Medicine & Diabetes, Faculty of Medicine, Cairo University, Cairo, Egypt; the [5]Department of Medicine, Glan Clwyd Hospital, Rhyl, Denbighshire, U.K.; the [6]Egyptian Diabetes Center, Cairo, Egypt; the [7]Division of Clinical and Molecular Endocrinology, Case Western Reserve University, Cleveland, Ohio; the [8]Department of Medicine, Emory University School of Medicine, Atlanta, Georgia; [9]Regional Advisor/Non Communicable Diseases/World Health Organization/Eastern Mediterranean Region, Cairo, Egypt; the [10]Ministry of Health, Palestinian National Authority, Ghaza, Palestine; [11]Dubai Hospital, Dubai, United Arab Emirates; the [12]Diabetes & Endocrinology Center, Islamic Hospital, Amman, Jordan; the [13]College of Medicine, Sultan Qaboos University, Sultante of Oman; and the [14]Diabetes Center, Medical College, King Saud University, Riyadh, Saudi Arabia.

Address correspondence and reprint requests to Mahmoud Ashraf Ibrahim, MD, 19 Nasouh St., Zeitoun, Cairo 11321, Egypt. E-mail: mahmoud@arab-diabetes.com.

Abbreviations: DCCT, Diabetes Control and Complications Trial; EPIDIAR, Epidemiology of Diabetes and Ramadan 1422/2001.

time, levels of glucagon and catecholamines rise, stimulating the breakdown of glycogen, while gluconeogenesis is augmented (6). As fasting becomes protracted for more than several hours, glycogen stores become depleted, and the low levels of circulating insulin allow increased fatty acid release from adipocytes. Oxidation of fatty acids generates ketones that can be used as fuel by skeletal and cardiac muscle, liver, kidney, and adipose tissue, thus sparing glucose for continued utilization by brain and erythrocytes.

In individuals without diabetes, the processes described above are regulated by a delicate balance between circulating levels of insulin and counterregulatory hormones that help maintain glucose concentrations in the physiological range. In patients with diabetes, however, insulin secretion is perturbed by the underlying pathophysiology and often by pharmacological agents designed to enhance or supplement insulin secretion. In patients with type 1 diabetes, glucagon secretion may fail to increase appropriately in response to hypoglycemia. Epinephrine secretion is also defective in some patients with type 1 diabetes due to a combination of autonomic neuropathy and defects associated with recurrent hypoglycemia (6). In patients with severe insulin deficiency, a prolonged fast in the absence of adequate insulin can lead to excessive glycogen breakdown and increased gluconeogenesis and ketogenesis, leading to hyperglycemia and ketoacidosis. Patients with type 2 diabetes may suffer similar perturbations in response to a prolonged fast; however, ketoacidosis is uncommon, and the severity of hyperglycemia depends on the extent of insulin resistance and/or deficiency.

RISKS ASSOCIATED WITH FASTING IN PATIENTS WITH DIABETES

— Fasting during Ramadan has been uniformly discouraged by the medical profession for patients with diabetes. In keeping with this, a large epidemiological study conducted in 13 Islamic countries on 12,243 individuals with diabetes who fasted during Ramadan showed a high rate of acute complications (4). However, a few studies on this topic using relatively small groups of patients suggest that complication rates may not be significantly increased (7–11). In Table 1, we outline some of the major potential complications associated with fasting in patients with diabetes and briefly discuss them below.

Table 1—*Major risks associated with fasting in patients with diabetes*

Hypoglycemia
Hyperglycemia
Diabetic ketoacidosis
Dehydration and thrombosis

Hypoglycemia

Decreased food intake is a well-known risk factor for the development of hypoglycemia. Results of the Diabetes Control and Complications Trial (DCCT) showed a threefold increase in the risk of severe hypoglycemia in patients who were in the intensively treated group and had an average HbA_{1c} (A1C) value of 7.0% (12). It has been estimated that hypoglycemia accounts for 2–4% of mortality in patients with type 1 diabetes (13). There are no reliable estimates concerning the contribution of hypoglycemia to mortality in type 2 diabetes; however, it is felt that hypoglycemia is an infrequent cause of death in this group of patients. Rates of hypoglycemia are some several-fold lower in patients with type 2 compared with type 1 diabetes (4), with rates being even lower in patients with type 2 diabetes treated with oral agents (14).

The effect of fasting during Ramadan on rates of hypoglycemia in patients with diabetes is not known with certainty. The largest dataset is the recent EPIDIAR study (4), which showed that fasting during Ramadan increased the risk of severe hypoglycemia (defined as hospitalization due to hypoglycemia) some 4.7-fold in patients with type 1 diabetes (from 3 to 14 events · 100 people^{-1} · month^{-1}) and ~7.5-fold in patients with type 2 diabetes (from 0.4 to 3 events · 100 people^{-1} · month^{-1}). The incidence of severe hypoglycemia was probably underestimated in this study, since events requiring assistance from a third party without the need for hospitalization were not included. Furthermore, although the average A1C at the beginning of Ramadan was not given, it is unlikely that the patients in this study were in good glycemic control. Severe hypoglycemia was more frequent in patients in whom the dosage of oral hypoglycemic agents or insulin were changed and in those who reported a significant change in their lifestyle (4).

Hyperglycemia

Long-term morbidity and mortality studies in people with diabetes, such as the DCCT and the UKPDS (U.K. Prospective Diabetes Study), demonstrated the link among hyperglycemia, microvascular complications, and possibly macrovascular complications (12,15). However, there is no information linking repeated yearly episodes of short-term hyperglycemia (e.g., 4-week duration) and diabetes-related complications. Control of glycemia in patients with diabetes who fasted during Ramadan has been reported to deteriorate, improve, or show no change (7–11). The extensive EPIDIAR study showed a fivefold increase in the incidence of severe hyperglycemia (requiring hospitalization) during Ramadan in patients with type 2 diabetes (from 1 to 5 events · 100 people^{-1} · month^{-1}) and an approximate threefold increase in the incidence of severe hyperglycemia with or without ketoacidosis in patients with type 1 diabetes (from 5 to 17 events · 100 people^{-1} · month^{-1}) (4). Hyperglycemia may have been due to excessive reduction in dosages of medications to prevent hypoglycemia. Patients who reported an increase in food and/or sugar intake had significantly higher rates of severe hyperglycemia (4).

Diabetic ketoacidosis

Patients with diabetes, especially those with type 1 diabetes, who fast during Ramadan are at increased risk for development of diabetic ketoacidosis, particularly if they are grossly hyperglycemic before Ramadan (4). In addition, the risk for diabetic ketoacidosis may be further increased due to excessive reduction of insulin dosages based on the assumption that food intake is reduced during the month.

Dehydration and thrombosis

Limitation of fluid intake during the fast, especially if prolonged, is a cause of dehydration. The dehydration may become severe in hot and humid climates and among individuals who perform hard physical labor, all conditions that result in excessive perspiration. In addition, hyperglycemia can result in osmotic diuresis and contribute to volume and electrolyte depletion. Orthostatic hypotension may develop, especially in patients with preexisting autonomic neuropathy. Syncope, falls, injuries, and bone fractures may re-

Table 2—*Categories of risks in patients with type 1 or type 2 diabetes who fast during Ramadan*

Very high risk
Severe hypoglycemia within the last 3 months prior to Ramadan
Patient with a history of recurrent hypoglycemia
Patients with hypoglycemia unawareness
Patients with sustained poor glycemic control
Ketoacidosis within the last 3 months prior to Ramadan
Type 1 diabetes
Acute illness
Hyperosmolar hyperglycemic coma within the previous 3 months
Patients who perform intense physical labor
Pregnancy
Patients on chronic dialysis
High risk
Patients with moderate hyperglycemia (average blood glucose between 150 and 300 mg/dl, A1C 7.5–9.0%)
Patients with renal insufficiency
Patients with advanced macrovascular complications
People living alone that are treated with insulin or sulfonylureas
Patients living alone
Patients with comorbid conditions that present additional risk factors
Old age with ill health
Drugs that may affect mentation
Moderate risk
Well-controlled patients treated with short-acting insulin secretagogues such as repaglinide or nateglinide
Low risk
Well-controlled patients treated with diet alone, metformin, or a thiazolidinedione who are otherwise healthy

sult from hypovolemia and the associated hypotension. In addition, contraction of the intravascular space can contribute to a hypercoagulable state.

Patients with diabetes exhibit a hypercoagulable state due to an increase in clotting factors, a decrease in endogenous anticoagulants, and impaired fibrinolysis (16). Increased blood viscosity secondary to dehydration may enhance the risk of thrombosis. A report from Saudi Arabia suggested an increased incidence of retinal vein occlusion in patients who fasted during Ramadan (17). However, hospitalizations due to coronary events or stroke were not increased during Ramadan (18,19). There are no data concerning the effect of fasting on mortality in patients with or without diabetes.

MANAGEMENT — It is worth reemphasizing that fasting for patients with diabetes represents an important personal decision that should be made in light of guidelines for religious exemptions and after careful consideration of the associated risks following ample discussion with the treating physician. Most often, the recommendation will be to not undertake fasting. However, patients who insist on fasting need to be aware of the associated risks and be ready to adhere to the recommendations of their health care providers to achieve a safer fasting experience. Patients may be at higher or lower risk for fasting-related complications depending on the number and extent of their risk factors. Conditions associated with "very high," "high," "moderate," and "low" risk for adverse events in patients with type 1 or type 2 diabetes who decide to fast during Ramadan are listed in Table 2. This classification is based largely on expert opinion and not on scientific data derived from clinical studies.

I. General considerations

Several important issues deserve special attention.

Individualization. Perhaps the most crucial issue is the realization that care must be highly individualized and that the management plan will differ for each specific patient.

Frequent monitoring of glycemia. It is essential that patients have the means to monitor their blood glucose levels multiple times daily. This is especially critical in patients with type 1 diabetes and in patients with type 2 diabetes who require insulin.

Nutrition. The diet during Ramadan should not differ significantly from a healthy and balanced diet. It should aim at maintaining a constant body mass. In most studies, 50–60% of individuals who fast maintain their body weight during the month, while 20–25% either gain or lose weight (4); occasionally, the weight loss may be excessive (>3 kg). The common practice of ingesting large amounts of foods rich in carbohydrate and fat, especially at the sunset meal, should be avoided. Because of the delay in digestion and absorption, ingestion of foods containing "complex" carbohydrates may be advisable at the predawn meal, while foods with more simple carbohydrates may be more appropriate at the sunset meal. It is also recommended that fluid intake be increased during nonfasting hours and that the predawn meal be taken as late as possible before the start of the daily fast.

Exercise. Normal levels of physical activity may be maintained. However, excessive physical activity may lead to higher risk of hypoglycemia and should be avoided, particularly during the few hours before the sunset meal. If Tarawaih prayer (multiple prayers after the sunset meal) is performed, then it should be considered a part of the daily exercise program. In some patients with poorly controlled type 1 diabetes, exercise may lead to extreme hyperglycemia.

Breaking the fast. All patients should understand that they must always and immediately end their fast if hypoglycemia (blood glucose of <60 mg/dl [3.3 mmol/l]) occurs, since there is no guarantee that their blood glucose will not drop further if they wait or delay treatment. The fast should also be broken if blood glucose reaches <70 mg/dl (3.9 mmol/l) in the first few hours after the start of the fast, especially if insulin, sulfonylurea drugs, or meglitinide are taken at predawn. Finally, the fast should be broken if blood glucose exceeds 300 mg/dl (16.7 mmol/l). Patients should avoid fasting on "sick days."

II. Pre-Ramadan medical assessment and educational counseling

All patients with diabetes who wish to fast during Ramadan should undergo the nec-

essary preparations to undertake the fast as safely as possible. These include medical assessment and educational counseling.

Medical assessment. This assessment should take place within 1–2 months before Ramadan. Specific attention should be devoted to the overall well-being of the patient and to the control of their glycemia, blood pressure, and lipids. Appropriate blood studies should be ordered and evaluated. Specific medical advice must be provided to each individual patient concerning the potential risks they are accepting in deciding to fast, even if they fast against medical advice. During this assessment, necessary changes in their diet or medication regimen should be made so that the patient initiates fasting while being on a stable and effective program.

Educational counseling. It is essential that the patients and family receive the necessary education concerning self-care, including signs and symptoms of hyper- and hypoglycemia, blood glucose monitoring, meal planning, physical activity, medication administration, and management of acute complications. Adequate nutrition and hydration should be emphasized, in addition to ensuring preparedness to treat hypoglycemia promptly should it occur, even if it is mild (use of glucose gel, glucose-containing liquids, glucose tablets, or glucagons injection by family members or friends; wearing of medical alert bracelet).

III. Management of patients with type 1 diabetes

In general, patients with type 1 diabetes, especially if "brittle" or poorly controlled, are at very high risk of developing severe complications and should be strongly advised to not fast during Ramadan. In addition, patients who are unwilling or unable to monitor their blood glucose levels multiple times daily are at high risk and should be advised to not fast.

It is currently recommended that treatment regimens aimed at intensive glycemia management be used in patients with diabetes. The DCCT and its follow-up, the EDIC (Epidemiology for Diabetes Interventions and Complications) study, have shown that intensive glycemia management is protective against microvascular complications and that the benefits are long lasting (12,20). Glycemic control at near-normal levels requires use of multiple daily insulin injections (three or more) or use of continuous subcutaneous insulin infusion through pump therapy. Close monitoring and frequent insulin dose adjustments in this setting are essential to achieve optimal glycemic control and avoid hypo- or hyperglycemia in patients with type 1 diabetes.

It is unlikely that one injection of intermediate- or long-acting insulin administered before the evening meal would provide adequate insulin coverage for 24 h. Typically, patients will need to use two daily injections of NPH as intermediate-acting insulin, administered before the predawn and sunset meals, in combination with a short-acting insulin to cover food intake at the associated meals. However, there is an increased risk of hypoglycemia around midday due to peaking of the early morning insulin dose. Using the long-acting insulin ultralente is an option, with twice-daily injections at ~12-h intervals to mimic basal insulin, and a rapid- or short-acting insulin should be added before the two meals. Still, ultralente cannot be considered truly basal insulin, since it has a broad peak of action at ~8–14 h. Therefore, protracted hypoglycemia can occur, especially since ultralente exhibits wide variability in its duration of action (18–30 h).

Another option would be to use one daily injection of the long-acting insulin analog glargine or twice-daily injections of the insulin analog detemir along with premeal rapid-acting insulin analogs. Results of a study using insulin glargine in 15 relatively well-controlled patients with type 1 diabetes who fasted for 18 h showed that the mean plasma glucose declined from a value of 125 to 93 mg/dl during the fast (21). Two episodes of mild hypoglycemia occurred. Such a treatment regimen may be particularly useful since the duration of the fast in Ramadan is typically <18 h.

Clinical studies with other types of insulin during fasting are limited. A study on patients with type 1 diabetes using insulin lispro or insulin aspart instead of regular insulin in combination with intermediate-acting insulin injected twice a day led to improvement in postprandial glycemia and was associated with less hypoglycemic events (22). Subcutaneous insulin pump management is an appealing alternative strategy; however, it is more expensive and still requires frequent blood glucose monitoring.

IV. Management of patients with type 2 diabetes

Diet-controlled patients. In patients with type 2 diabetes who are well controlled with diet alone, the risk associated with fasting is quite low. However, there is still a potential risk for occurrence of postprandial hyperglycemia after the predawn and sunset meals if patients overindulge in eating. Distributing calories over two to three smaller meals during the nonfasting interval may help prevent excessive postprandial hyperglycemia. Patients controlled with diet alone usually combine this with a regular daily exercise program. The exercise program should be modified in its intensity and timing to avoid hypoglycemic episodes; the timing of the exercise could be changed to ~2 h after the sunset meal. Finally, in this usually older age-group, often with hypertension and dyslipidemia, fluid restriction and dehydration may increase the risk of thrombotic events.

Patients treated with oral agents. The choice of oral agents should be individualized. In general, agents that act by increasing insulin sensitivity are associated with a significantly lower risk of hypoglycemia than compounds that act by increasing insulin secretion.

- *Metformin*. Patients treated with metformin alone may safely fast because the possibility of hypoglycemia is minimal. However, it is suggested that the timing of the doses be modified. We recommend that two thirds of the total daily dose be administered immediately before the sunset meal, while the other third be given before the predawn meal.
- *Glitazones*. Patients on insulin sensitizers (rosiglitazone and pioglitazone) have a low risk of hypoglycemia. Usually no change in dose is required.
- *Sulfonylureas*. This group of drugs was believed to be unsuitable for use during fasting because of the inherent risk of hypoglycemia. Hence, their use should be individualized and they should be utilized with caution. Use of chlorpropamide is absolutely contraindicated during Ramadan because of the high possibility of prolonged and unpredictable hypoglycemia. Newer members of the sulfonylurea family (gliclazide MR or glimepiride) have been shown to be effective, resulting in a lower risk of hypoglycemia (23). However, it should be emphasized that the above study did not include patients who fasted. In a

recent study from Turkey, 52 patients with type 2 diabetes who fasted during Ramadan were managed with diet alone, sulfonylurea (glimepiride or gliclazide MR once daily), or repaglinide (24). One patient receiving a daily dose of 3 mg glimepiride developed a hypoglycemic event; the authors concluded that use of repaglinide might be safer than use of sulfonylureas (24). Body weight, fasting plasma glucose, fructosamine, A1C, and total cholesterol did not change during the study (24). Additional studies on the use of sulfonylureas in patients who fast during Ramadan are needed before strong recommendations on their utility can be made. Nevertheless, because of their worldwide use and relatively lower cost, these agents (especially the newer generations) may be used with caution.

- *Short-acting insulin secretagogues*. Members of this group (repaglinide and nateglinide) are useful because of their short duration of action. They could be taken twice daily before the sunset and predawn meals. One study in patients with type 2 diabetes who fasted showed that use of repaglinide was associated with less hypoglycemia compared with glibenclamide (25).

Patients treated with insulin. Problems facing patients with type 2 diabetes who administer insulin are similar to those with type 1 diabetes, except that the incidence of hypoglycemia is less. Again, the aim is to maintain necessary levels of basal insulin to remedy the prevailing relative deficiency and to overcome the existing insulin resistance. A major objective is to suppress hepatic glucose output to near-physiologic levels during the fasting period. Judicious use of intermediate- or long-acting insulin preparations plus a short-acting insulin administered before meals would be an effective strategy. Although hypoglycemia tends to be less frequent, it is still a risk, especially in patients who have required insulin therapy for a number of years, suggesting that β-cell failure has occurred and that a significant component of insulin deficiency exists. Very elderly patients with type 2 diabetes may be at especially high risk.

Using one injection of a long-acting insulin analog, such as insulin glargine, or two injections of NPH, lente, or detemir insulin before the sunset and predawn meals may provide adequate coverage as long as the dosage of each injection is appropriately individualized. A single injection of intermediate-acting insulin administered before the sunset meal may be sufficient to provide acceptable glycemic control in patients with reasonable basal insulin secretion. In such a situation, the peak action of intermediate insulin would be expected to occur at predawn and may provide adequate insulin coverage for that meal. However, most patients will still require short-acting insulin administered in combination with the intermediate- or long-acting insulin at the sunset meal to cover the large caloric load of Iftar. Moreover, many will need an additional dose of short-acting insulin at predawn. There is some evidence suggesting that use of insulin lispro instead of regular insulin before meals in patients with type 2 diabetes who fast during Ramadan is associated with less hypoglycemia and smaller postprandial glucose excursions (26,27). Again, as emphasized earlier, the overall dosage of medications, especially that of insulin, must be adjusted in conjunction with the weight loss or gain that may occur during Ramadan. Illustrative examples and recommendations for adjusting therapy during Ramadan in patients with type 2 diabetes are shown in Table 3.

V. Pregnancy and fasting during Ramadan

Pregnancy is a state of increased insulin resistance and insulin secretion and of reduced hepatic insulin extraction. Fasting glucose concentrations are lower but postprandial glucose and insulin levels substantially higher in healthy pregnant women than those who are not pregnant. Elevated blood glucose and A1C levels in pregnancy are associated with increased risk for major congenital malformations. Fasting during pregnancy would be expected to carry a high risk of morbidity and mortality to the fetus and mother, although controversy exists (28). While pregnant Muslim women are exempt from fasting during Ramadan, some with known diabetes (type 1, type 2, or gestational) insist on fasting during Ramadan. These women constitute a high-risk group, and their management requires intensive care (29).

In general, women with pregestational or gestational diabetes should be strongly advised to not fast during Ramadan. However, if they insist on fasting, then special attention should be given to their care. Pre-Ramadan evaluation of their medical condition is essential. This includes preconception care with emphasis on achieving near-normal blood glucose and A1C values, counseling about maternal and fetal complications associated with poor glycemic control, and education focused on self-management skills. Ideally, patients should be managed in high-risk clinics staffed by an obstetrician, diabetologists, a nutritionist, and diabetes nurse educators. The management of pregnant patients during Ramadan is based on an appropriate diet and intensive insulin therapy. The issues discussed above concerning the management of type 1 and type 2 diabetes also apply to this group, with the exception that more frequent monitoring and insulin dose adjustment is necessary.

VI. Management of hypertension and dyslipidemia

Dehydration, volume depletion, and a tendency toward hypotension may occur with fasting during Ramadan, especially if the fast is prolonged and is associated with excessive perspiration. Hence, the dosage of antihypertensive medications may need to be adjusted to prevent hypotension.

It is common practice that the intake of foods rich in carbohydrates and saturated fats is increased during Ramadan. Appropriate counseling should be given to avoid this practice, and agents that were previously prescribed for the management of elevated cholesterol and triglycerides should be continued.

CONCLUSIONS — Fasting during Ramadan for patients with diabetes carries a risk of an assortment of complications. In general, patients with type 1 diabetes should be strongly advised to not fast. Patients with type 1 diabetes who have a history of recurrent hypoglycemia or hypoglycemia unawareness or who are poorly controlled are at very high risk for developing severe hypoglycemia. On the other hand, an excessive reduction in the insulin dosage in these patients (to prevent hypoglycemia) may place them at risk for hyperglycemia and diabetic ketoacidosis. Hypo- and hyperglycemia may also occur in patients with type 2 diabetes but generally less frequently and with less severe consequences compared with patients with type 1 diabetes. A patient's de-

Table 3—*Recommended changes to treatment regimen in patients with type 2 diabetes who fast during Ramadan*

Before Ramadan	During Ramadan
Patients on diet and exercise control	No change needed (modify time and intensity of exercise), ensure adequate fluid intake
Patients on oral hypoglycemic agents	Ensure adequate fluid intake
Biguanide, metformin 500 mg three times a day, or sustained release metformin (glucophage R)	Metformin, 1,000 mg at the sunset meal (Iftar), 500 mg at the predawn meal (Suhur)
TZDs, pioglitazone or rosiglitazone once daily	No change needed
Sulfonylureas once a day, e.g., glimepiride 4 mg daily, gliclazide MR 60 mg daily	Dose should be given before the sunset meal (Iftar); adjust the dose based on the glycemic control and the risk of hypoglycemia
Sulfonylureas twice a day, e.g., glibenclamide 5 mg or gliclazide 80 mg, twice a day (morning and evening)	Use half the usual morning dose at the predawn meal (Suhur) and the full dose at the sunset meal (Iftar), e.g., glibenclamide 2.5 mg or gliclazide 40 mg in the morning, glibenclamide 5 mg or gliclazide 80 mg in evening
Patients on insulin	Ensure adequate fluid intake
70/30 premixed insulin twice daily, e.g., 30 units in morning and 20 units in evening	Use the usual morning dose at the sunset meal (Iftar) and half the usual evening dose at predawn (Suhur), e.g., 70/30 premixed insulin, 30 units in evening and 10 units in morning; also consider changing to glargine or detemir plus lispro or aspart

The recommendations given in this table are for illustrative purposes and are largely based on expert clinical opinion and not on scientific data derived from clinical studies. The recommendations must be adjusted for each specific patient. Adapted from Akbani et al. (30). TZD, thiazolidinedione.

cision to fast should be made after ample discussion with his or her physician concerning the risks involved. Patients who insist on fasting should undergo pre-Ramadan assessment and receive appropriate education and instructions related to physical activity, meal planning, glucose monitoring, and dosage and timing of medications. The management plan must be highly individualized. Close follow-up is essential to reduce the risk for development of complications.

Further research is needed to help expand our knowledge concerning the risks and management issues related to fasting in patients with diabetes. Interventional studies can help define new approaches that minimize the complications associated with fasting. Surveys such as the EPIDIAR study should be encouraged and extended to population-based samples and clinical trials. In addition to obtaining data in these surveys on the adverse events during fasting in patients with diabetes, it would be essential to obtain information on the risk factors that predispose to the occurrence of these events. Such data would help refine management guidelines by providing objective criteria for assigning patients to the different risk categories with the aim of minimizing complications.

Acknowledgments— The Egyptian Diabetes Center, with a support from Les Laboratoires Servier, made this work possible.

We are grateful to Drs. Abdulnabi Alattar (Ministry of Health, Amiri Hospital, Rawda, Kuwait), Baha Arafah and Saul Genuth (Cleveland, OH), Mahdi Gibani (North West Wales NHS Trust, Bangor, U.K.), and Rayaz Malik (Manchester Royal Infirmary, Manchester, U.K.) for their critical review of the manuscript and useful suggestions.

References

1. The Canadian Society of Muslims: Muslim population statistics [article online], 2000. Available from http://muslim-canada.org/muslimstats.html. Accessed 14 April 2005
2. An analysis of the world Muslim population by country/region [article online]. Available at http://www.factbook.net/muslim_pop.php. Accessed 14 April 2005
3. Wild S, Roglic G, Green A, Sicree R, King H: Global prevalence of diabetes, estimates for the year 2000 and projections for 2030. *Diabetes Care* 27:1047–1053, 2004
4. Salti I, Benard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C, Jabbar A, the EPIDIAR Study Group: 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* 27:2306–2311, 2004
5. International Meeting on Diabetes and Ramadan Recommendations: *Edition of the Hassan II Foundation for Scientific and Medical Research on Ramadan*. Casablanca, Morocco, FRSMR, 1995
6. Cryer PE, Davis SN, Shamoon H: Hypoglycemia in diabetes (Review). *Diabetes Care* 26:1902–1912, 2003
7. Uysal AR, Erdogan MF, Sahin G, Kamel N, Erdogan G: Clinical and metabolic effects of fastingin 41 type 2 diabetic patients during Ramadan (Letter). *Diabetes Care* 21:2033–2034, 1998
8. Laajam MA: Ramadan fasting and non-insulin-dependent diabetes: effect on metabolic control. *East Afr Med J* 67:732–736, 1990
9. Mafauzy M, Mohammed WB, Anum MY, Zulkifli A, Ruhani AH: A study of the fasting diabetic patient during the month of Ramadan. *Med J Malaysia* 45:14–17, 1990
10. Belkhadir J, el Ghomari H, Klocker N, Mikou A, Nasciri M, Sabri M: Muslims with non-insulin-dependent diabetes fasting during Ramadan: treatment with glibenclamide. *BMJ* 307:292–295, 1993
11. Katibi IA, Akande AA, Bojuwoye BJ, Okesina AB: Blood sugar control among fasting Muslims with type 2 diabetes mellitus in Ilorin. *Niger J Med* 10:132–134, 2001
12. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993
13. Laing SP, Swerdlow AJ, Slater SD, Botha JL, Burden AC, Waugh NR, Smith AW, Hill RD, Bingley PJ, Patterson CC, Qiao Z, Keen H: The British Diabetic Association Cohort Study. II. Cause-specific mortality in patients with insulin-treated diabetes mellitus. *Diabet Med* 16:466–471, 1999
14. Miller CD, Phillips LS, Ziemer DC, Gallina DL, Cook CB, El-Kebbi IM: Hypoglycemia in patients with type 2 diabetes. *Arch Int Med* 161:1653–1659, 2001
15. UK Prospective Diabetes Study (UKPDS)

Group: Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352:837–853, 1998
16. Beckman JA, Creager MA, Libby P: Diabetes and atherosclerosis: epidemiology, pathophysiology and management. *JAMA* 287:2570–2581, 2002
17. Akhan G, Kutluhan S, Koyuncuoglu HR: Is there any change in stroke incidence during Ramadan? *Acta Neurol Scandin* 101:259–261, 2000
18. Alghadyan AA: Retinal vein occlusion in Saudi Arabia: possible role of dehydration. *Ann Ophthalmol* 25:394–398, 1993
19. Temizhan A, Donderici O, Ouz D, Demirbas B: Is there any effect of Ramadan fasting on acute coronary heart disease events? *Int J Cardiol* 70:149–153, 1999
20. Writing team for the Diabetes Control and Complications Trial/Epidemiology for Diabetes Interventions and Complications Research Group: Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA* 290:2159–2167, 2003
21. Mucha GT, Merkel S, Thomas W, Bantle JP: Fasting and insulin glargine in individuals with type 1 diabetes (Brief Report). *Diabetes Care* 27:1209–1210, 2004
22. Kadiri A, Al-Nakhi A, El-Ghazali S, Jabbar A, Al Arouj M, Akram J, Wyatt J, Assem A, Ristic S: Treatment of type 1 diabetes with insulin lispro during Ramadan. *Diabetes Metab* 27:482–486, 2001
23. Schernthaner G, Grimaldi A, Di Mario U, Drzewoski J, Kempler P, Kvapil M, Novials A, Rottiers R, Rutten GE, Shaw KM: GUIDE study: double-blind comparison of once-daily gliclazide MR and glimepiride in type 2 diabetic patients. *Eur J Clin Invest* 34:535–542, 2004
24. Sari R, Balci MK, Akbas SH, Avci B: The effects of diet, sulfonylurea, and repaglinide therapy on clinical and metabolic parameters in type 2 diabetic patients during Ramadan. *Endocr Res* 30:169–177, 2004
25. Mafauzy M: Repaglinide versus gliben-clamide treatment of type 2 diabetes during Ramadan fasting. *Diabetes Res Clin Pract* 58:45–53, 2002
26. Mattoo V, Milicevic Z, Malone JK, Schwarzenhofer M, Ekangaki A, Levitt LK, Liong LH, Rais N, Tounsi H, the 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* 59:137–143, 2003
27. Akram J, De Verga V: Insulin lispro in the treatment of diabetes during the fasting month of Ramadan. *Diabet Med* 16:861–866, 1999
28. Malhotra APH, Scott J, Scott H, Wharton BA: Metabolic changes in Asian Muslim pregnant mothers observing Ramadan fast in Britain. *Br J Nutr* 61:663–672, 1989
29. Azizi F: Research in Islamic fasting and health. *Ann Saudi Med* 22:186–191, 2002
30. Akbani MF, Saleem M, Gadit WU, Ahmed M, Basit A, Malik RA: Fasting and feasting safely during Ramadan in the diabetic patient. *Pract Diab Int* 22:100–104, 2005