

Canadian Diabetes and Ramadan Fasting Position Statement

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ABSTRACT

Objective: Fasting in Ramadan from dawn to dusk, including abstaining from water and food, is one of the pillars of Islam and is observed by the majority of Muslims. Most research on diabetes and fasting in Ramadan originates from Middle Eastern or South Asian countries; however, differences exist in hours of work and fasting, pharmacotherapy and blood glucose monitoring between these countries and Canada.

Methods: An expert forum of seven Canadian and one international expert collaborated to develop Canadian guidelines using the same evidence-based principles, with the exception of an independent methods review, used for the Diabetes Canada Clinical Practice Guidelines. Diabetes Canada scientific leadership and Canadian healthcare providers performed independent external reviews. Religious leaders endorsed the position statement and provided letters of support. An informed patient participated in the position statement development. Each recommendation was approved with 100% consensus of the expert forum.

Results: Recommendations for risk stratification, education, pharmacotherapy and blood glucose monitoring for adults with type 1 and type 2 diabetes who intend to fast during Ramadan have been developed.

Conclusions: This is the first Canadian position statement on the topic of Ramadan fasting and diabetes, developed by an expert faculty and endorsed by Diabetes Canada. It provides guidance on pharmacotherapy and glucose monitoring for health-care providers, so that they can assist Canadian Muslims living with diabetes to safely observe fasting during Ramadan.

Pre-Ramadan diabetes management planning

Recommendations:

1. For adults with type 1 or type 2 diabetes intending to fast, a pre-Ramadan individualized assessment should be performed 1 to 3 months prior to the start of fasting to reduce the risk of hypoglycemia, with maintenance of stable glycemic control [Grade C, Level 3 [13]]. The assessment should include:
 - a. Appropriate risk stratification
 - b. Review of positive and adverse experiences from previous fasting
 - c. Formulate an individualized treatment plan
 - d. Discuss the importance of antihyperglycemic medication adjustment, meals, physical activity, frequency of self-monitoring of blood glucose, and situations where it would be medically indicated to break the fast [Grade D, Consensus for all].
2. Dietary counselling should be provided based on IDF-DAR and Diabetes Canada Clinical Practice Guidelines [Grade D, Consensus].
3. Risk stratification for people living with diabetes, including very high-risk special populations (i.e. frail individuals, pregnancy, etc) should be based on the published IDF-DAR guidelines (see Table 1) [Grade D, Consensus].
4. For individuals who intend to fast despite being advised of a high-risk stratification, scheduled contact during Ramadan (either in clinic, virtually or over the phone) with their health-care provider or diabetes health-care team is recommended to review glucose records and make further adjustments to therapy [Grade D, Consensus].
5. People in any risk strata of IDF-DAR guidelines should be advised to break their fast and seek immediate medical attention if they experience any documented episode of hypoglycemia or symptomatic hyperglycemia during Ramadan [Grade D, Consensus].
6. A post Ramadan follow-up health-care visit should be considered to review any concerns with diabetes management and help formulate a strategy for future fasting [Grade D, Consensus].

Table 1: Risk stratification for fasting during Ramadan for people living with diabetes

Classification of Risk	Risk Factors
<p>Very High Risk MUST NOT FAST</p>	<ul style="list-style-type: none"> • Poorly controlled T1DM (defined as a pre-Ramadan A1C >9%) • Severe hypoglycemia within 3 months, recurrent hypoglycemia, and/or unawareness of hypoglycemia • Ketoacidosis within 3 months • Hyperosmolar hyperglycemic coma within 3 months • Acute illness • Advanced macrovascular complications, renal disease (on dialysis, stage IV or V), cognitive dysfunction, or uncontrolled epilepsy • Pregnancy in diabetes or GDM - treated with insulin
<p>High Risk SHOULD NOT FAST</p>	<ul style="list-style-type: none"> • T2DM with sustained poor glycemic control* • Well-controlled T2DM on MDI or mixed insulin • Pregnant T2DM or GDM controlled by diet only • CKD stage 3 or stable macrovascular complications • Performing intense physical labour • Well-controlled T1DM
<p>Moderate/Low Risk CAN FAST WITH MEDICAL ADVICE</p>	<ul style="list-style-type: none"> • Well-controlled diabetes • Treated with lifestyle alone, or with: metformin, acarbose, incretin-therapies (DPP-4 inhibitors or GLP-1 RA), second generation SU, SGLT2 inhibitors, TZD or basal insulin in otherwise healthy individuals

CKD, chronic kidney disease; *DPP-4*, dipeptidyl peptidase; *GDM*, gestational diabetes mellitus; *GLP-1 RA*, glucagon-like peptide-1 receptor agonist; *MDI*, multiple daily injections; *SGLT2*, sodium glucose transporter-2; *SU*, sulfonylurea; *T1DM*, type 1 diabetes mellitus; *T2DM*, type 2 diabetes mellitus; *TZD*, Thiazolidinedione

*The level of glycemic control is to be agreed upon between the health-care provider and the person living with diabetes.

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Non-insulin pharmacotherapy for type 2 diabetes during Ramadan

1. Agents that have a low risk of hypoglycemia or orthostasis (metformin, DPP-4 inhibitors, alpha glucosidase inhibitors and thiazolidinediones) can be used safely during Ramadan [Grade B, Level 2 [14,15] for sitagliptin; Grade B, Level 2 [25] for pioglitazone; Grade D, Consensus for all others]
2. When feasible, insulin secretagogues should be switched to an antihyperglycemic agent with a lower risk of hypoglycemia for the duration of Ramadan to reduce the risk of hypoglycemia [Grade B, Level 2 [14,15] for sitagliptin; Grade B, Level 2 [19,20] for liraglutide; Grade B, Level 2 [23] for canagliflozin; Grade B, Level 2 [24] for dapagliflozin; Grade D, Consensus for others], especially for individuals with a higher risk of hypoglycemia [Grade D, Consensus]. If it is not feasible to switch to a different class, insulin secretagogues with a lower risk of hypoglycemia (gliclazide, repaglinide) should be used to reduce risk of hypoglycemia [Grade C, Level 2 [14,15] for gliclazide; Grade C, Level 2 [22] for repaglinide] along with a concomitant dose reduction of 25-50% [Grade D, Consensus]. Repaglinide dosage should be adjusted according to alteration of meal times and sizes during Ramadan [Grade D, Consensus]. If glyburide is continued during fasting, the morning dose should be held or reduced by $\geq 50\%$ depending on the carbohydrate content of the pre-dawn meal [Grade D, Consensus].
3. GLP-1 receptor agonists can be continued during Ramadan to maintain glycemic control with low rates of hypoglycemia [Grade C, Level 2 [19,20] for liraglutide; Grade D, Consensus for others], but should not be started within 4 weeks prior due to possible gastrointestinal adverse effects [Grade D, Consensus]. If adverse gastrointestinal effects occur during Ramadan, dose reduction or temporary discontinuation of this class should be considered [Grade D, Consensus].
4. SGLT2 inhibitors can be continued during Ramadan to maintain glycemic control with low rates of hypoglycemia [Grade C, Level 2 [23] for canagliflozin; Grade C, Level 2 [24] for dapagliflozin; Grade D, consensus for empagliflozin] . Dose reduction or a temporary hold of SGLT2 inhibitor medication should be considered for people at high risk for volume depletion

(age > 75 years, eGFR < 60 mL/min/1.73m², and/or or loop diuretics) [Grade D, Consensus]. For people with clinical cardiovascular disease, SGLT2 inhibitors should not be held during Ramadan due to their role in reducing major CV events and heart failure hospitalization [Grade D, Consensus].

5. People living with type 2 diabetes who develop vomiting, diarrhea or orthostasis during Ramadan should break their fast immediately, hold certain antihyperglycemic medications (metformin, secretagogues, GLP-1 receptor agonists, SGLT2 inhibitors), continue blood glucose monitoring and seek immediate medical attention [Grade D, Consensus].

Insulin management of type 2 diabetes during Ramadan

1. For adults with type 2 diabetes needing insulin initiation just prior to or during Ramadan, a basal, long-acting analog insulin (detemir, glargine) or ultra-long analog insulin (degludec, glargine U300) may be preferred over intermediate acting basal or premixed insulin options during the fasting month to reduce the risk of hypoglycemia [Grade D, Consensus].
2. For those individuals already on a regimen containing intermediate acting insulins (NPH, premixed)
 - a. Consider switching to a long acting or ultra-long insulin basal analogs 1 to 3 months prior to Ramadan, when feasible, to lower the risk of hypoglycemia [Grade D, Consensus]
 - b. U500 formulation of human regular insulin should be treated like intermediate acting insulin and consideration should be given to switching to an alternate insulin regimen pre-Ramadan [Grade D, Consensus]
 - c. When switching from premixed or self-mixed insulin, the choice of regimen options (basal insulin-oral antihyperglycemic agents, basal insulin-GLP-1 receptor agonists, basal insulin-plus one mealtime bolus insulin or basal-bolus insulin given with each meal) should be individualized [Grade D, Consensus]

- d. If a switch is not feasible, the dose of NPH or premixed insulin taken with the pre-dawn meal should be reduced by 25 to 50% depending on carbohydrate content, timing of last insulin dose and risk of hypoglycemia [Grade D, Consensus]
3. For those individuals already on a regimen containing long acting basal insulin analogs (degludec, detemir, glargine, glargine U300), a dose reduction of 15 to 30% should be considered on fasting days to reduce the risk of hypoglycemia [Grade D, Consensus].
4. For those individuals already on a regimen containing bolus insulin
 - a. A rapid-acting insulin analog (aspart, faster acting aspart, glulisine, lispro) is preferred over human regular insulin to lower the risk of hypoglycemia and post-meal hyperglycemia [Grade C, Level 2 [29, 30] for lispro; Grade D, Consensus for aspart, faster acting aspart, glulisine]
 - b. Patients should be advised to take their normal bolus dose with sunset meal, omit their lunch-time bolus dose, and lower their pre-dawn meal dose by 5 to 50% depending on carbohydrate intake and glucose readings [Grade D, Consensus].
5. For those individuals managed on any insulin regimen, less intensive glycemic targets during Ramadan, aiming for fasting and pre-meal SMBGs of 5.5 to 7.5 mmol/L, are preferred to reduce the risk of hypoglycemia [Grade D, Consensus]. Insulin dose adjustment to achieve these conservative targets should be individualized taking into consideration insulin sensitivity and total daily insulin dose as well as the duration of fast [Grade D, Consensus].
6. Individuals on a complex insulin regimen, especially those with increased risk of hypoglycemia, should be evaluated by a diabetes management team pre-Ramadan [Grade D, Consensus].

Type 1 Diabetes management during Ramadan

1. For people with type 1 diabetes who intend to fast, a medical assessment should be performed 1 to 3 months prior to Ramadan to evaluate individual risks for fasting and to optimize insulin management [Grade D, Consensus].

2. People with poorly controlled type 1 diabetes (i.e. pre-Ramadan A1C >9.0%, infrequent blood glucose monitoring or those with hypoglycemia unawareness) should be advised to not fast [Grade D, Consensus]
3. For those using regular human insulin as their bolus insulin, switching to a rapid-acting insulin analog (aspart, faster acting aspart, glulisine, lispro) should be considered to reduce rates of hypoglycemia [Grade C, Level 2 [36] for lispro; Grade D, Consensus for for aspart, faster acting aspart, glulisine] 1 to 3 months prior to Ramadan.
4. For those using basal-bolus injection therapy, a basal analog insulin (detemir, glargine) is preferred over intermediate-acting insulin during Ramadan [Grade D, Consensus]. Alternatively, a once daily ultra-long acting basal insulin (degludec, glargine U300) may be used to further reduce the risk of hypoglycemia and minimize the chance of missed insulin doses or periods of inadequate background insulin on board during prolonged fasting periods [Grade D, Consensus].
5. Insulin-to-carbohydrate ratio and insulin sensitivity factor should remain unchanged during fasting if stable and well controlled [Grade D, Consensus].
6. All basal insulin doses, or daytime basal doses on insulin pump therapy, should be reduced by a minimum of 20% for fasting days to reduce the risk of hypoglycemia [Grade D, Consensus] and reassessed weekly for further adjustments [Grade D, Consensus].
7. People with type 1 diabetes should monitor blood ketones when SMBG readings are elevated >14.0 mmol/L to screen for DKA. Those with blood ketones > 0.6mmol/L should break their fast, take a supplemental dose of rapid-acting insulin for correction of blood ketones and re-evaluate their ability to safely fast during Ramadan [Grade D, Consensus].

Monitoring glycemic control while fasting in Ramadan

1. For individuals fasting during Ramadan who use insulin
 - a. Education on frequency of SMBG testing during fasting should be provided to improve A1C and reduce rates of hypoglycemia [Grade C, Level 3 [13,48]]. SMBG should be undertaken at

- least 5 times per day for people living with type 1 diabetes [Grade D, Consensus] and between 2 to 5 times per day for those living with type 2 diabetes [Grade D, Consensus], in addition to periods of symptomatic hyper/hypoglycemia [Grade D, Consensus].
- b. In the short-term, real-time CGM or FGM during fasting to adjust insulin doses and prevent hypoglycemia risk may be considered for people living with type 1 or type 2 diabetes on complex insulin regimen defined as basal plus at least one additional administration of bolus insulin [Grade D, Consensus].
2. For individuals with diabetes not requiring insulin, SMBG should be individualized depending on the type of therapy, risk of hypoglycaemia or hyperglycemia, level of glycemic control and duration of fast [Grade D, Consensus].

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