PHARMACIST'S LETTER / PRESCRIBER'S LETTER

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Fasting and Patients With Diabetes

Introduction

For patients with diabetes, medically required and religious dietary fasting introduces increased risk for hypoglycemia and hyperglycemia. Fasting is sometimes necessary prior to laboratory tests, procedures, or surgery. Fasting is also part of religious observances for many people. However, there is little literature on what to do with diabetes medications when people fast, and the guidelines that do exist are based mostly on expert opinion. It is vital that patients with diabetes know the importance of managing their blood sugar levels during a fast and that they understand what they should do to accomplish this. This document discusses the issues of dietary fasting and patients with diabetes.

Fasting for Blood Tests or Surgical Procedures

Patients are sometimes required to fast for eight to 12 hours prior to certain blood tests (e.g., cholesterol tests) or prior to surgical procedures. These fasts can require some planning for patients with diabetes.

Some retrospective, observational studies have found that many patients with diabetes receive no counseling on making adjustments to their diabetes medications prior to fasting blood work. This can cause morning hypoglycemia for many of these patients.[1]

Despite the lack of published information, there are a number of recommendations for potential interventions which may reduce the incidence of hypoglycemia. Lab tests/procedures should be scheduled as early in the morning as possible, to reduce the duration of the fast. Patients should be instructed to monitor blood glucose concentrations more frequently on the morning of the blood test or surgery. If severe, symptomatic hypoglycemia occurs, the patient may have to ingest carbohydrates and cancel the laboratory test or surgical procedure.[1]

Sulfonylureas have a relatively long half-life (up to 24 hours, more in some patients) and are known to cause hypoglycemia. If a patient needs to fast for a longer period, such as for some surgeries or afternoon blood work, consider reducing or omitting the evening dose of a sulfonylurea.[1] However, it is not always necessary to hold or reduce the dose of sulfonylurea the evening before early morning lab work. In fact, keeping meds (including sulfonylureas and insulin) as normal as possible the evening before lab work can allow the clinician to see what the fasting blood glucose is under normal circumstances. All other oral diabetes medications, as well as GLP-1 agonists, are taken on the evening before the fast but it is recommended that they usually be withheld on the morning of surgical procedures and sometimes for blood tests.[3,11] Diabetes medications should be restarted, with a meal, as soon as the lab test or procedure is over.

Short- or rapid-acting insulins should be withheld on the morning of the fast, restarting with food after the blood work/procedure is complete.[1,2] Most patients will require their basal insulin in the morning; however, the dose can be reduced to one-half to one-third of their usual dose.[2] Patients with well controlled blood glucose levels can use less basal insulin (i.e., closer to one-third their usual dose).[2] It is important to avoid hypoglycemia so overall targets should be slightly high, particularly in those prone to hypoglycemic episodes.[2] There may also be a need for a reduction of the dose of intermediate-acting or mixed insulins on the evening before the laboratory test or surgery. For this adjustment, consider the timing of the lab test/procedure (i.e., the estimated time of the fast), the patient's level of glucose control, and their history of hypoglycemia.

Fasting for Colonoscopies

The management of patients with diabetes undergoing colonoscopies is somewhat different

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than other procedures due to the restricted dietary intake, fasting, and bowel evacuation preparation required on the day prior to the procedure. There are also no evidence-based guidelines for patients with diabetes for diagnostic procedures such as colonoscopies. However, a number of institutions have patient handouts on their protocols, which are mainly based on clinical experience of the institution and expert opinion.[3-5,12,13]

As with blood tests and surgical procedures, patients with diabetes who must fast prior to a diagnostic procedure should schedule the procedure early in the day, so there is minimal interruption in timing of meals and medications. Patients should be instructed to test their blood glucose more frequently (e.g., before meals and at bedtime on the day before the procedure and every one to two hours on the day of procedure, plus at any time if the patients has any symptoms of hypo- or hyper- glycemia).[3]

On the day prior to a colonoscopy, called "prep day," patients are on a clear liquid diet.[14] Patients with diabetes need to be sure that their clear diet includes 45 g of carbohydrate at meals and 15 g to 30 g of carbohydrate for snacks.[5] Patients should check the labels of their clear liquid choices to see the carbohydrate content of each product.

Sulfonylureas (glyburide, glimepiride, glipizide, gliclazide) have a long duration of action (up to 24 hours and sometimes longer) and are known to cause hypoglycemia. Many recommend that any morning doses of these agents be given on prep day at half their usual dose and to withhold the evening dose.[5,12,13] Other oral agents, such as metformin, thiazolidinediones (pioglitazone, etc), DPP-4 inhibitors (linagliptin, saxagliptin, etc), SGLT2 inhibitors (canagliflozin, empagliflozin, etc), acarbose (*Precose* [U.S.], *Glucobay* [Canada]), or bromocriptine (*Cycloset* [U.S.]) can be taken at their normal doses on the day of the prep because these medications do not usually cause hypoglycemia when taken without insulin or sulfonylureas.[4,12,18] GLP-1 agonists (exenatide, liraglutide, etc) and pramlintide (*Symlin* [U.S.]) can be taken at their usual doses on prep day as well.[13] For insulin dosing on prep day, the usual morning dose should be given and the evening dose should be given as one-half the usual dose.[5,12]

On the day of the colonoscopy all oral diabetes medications can be withheld and then later taken with a meal, as soon as the procedure is over.[3,4,12,13] Many recommend taking one-third to one-half of intermediate-acting or long-acting morning insulin dose (i.e., basal insulin, such as *Lantus* or *Levemir*) on the day of the procedure; however, any short-acting, rapid-acting and mixed insulins (i.e., mealtime boluses) should be withheld until the patient resumes eating.[2,4,5] On the morning of the procedure basal insulin, even in the fasted state, is necessary to prevent diabetic ketoacidosis, especially in patients with type 1 diabetes. Blood glucose should be closely monitored on the day of the procedure. Hyperglycemia should be treated with short- or rapid-acting insulin. Hypoglycemia should be treated with clear juices, regular soda, glucose gel, or glucose tablets, being sure to avoid any products with red dyes.[13]

Fasting for Religious Holidays

There are a number of religions (e.g., Islam, Judaism, Mormon, etc) that observe different periods of fasting. The duration of these fasts vary and patients with diabetes must understand how to adjust their medications and monitor blood glucoses in order to avoid hypoglycemia and hyperglycemia during these periods. It is important to note that most religions will exempt patients with medical conditions from fasting. While this would often be the safest option for patients with diabetes, many will make the decision to fast for personal reasons. Patients with diabetes who should be advised not to fast include those with type 1 diabetes; who have poor glycemic control; who have recurrent, severe, or unawareness of hypoglycemia; or who are pregnant.[17] In general, if significant hypoglycemia develops (usually defined as a blood glucose of 70 mg/dL to 90 mg/dL [3.9 mmol/L to 5 mmol/L], depending on the patient), the fast should be broken immediately and a carbohydrate should be consumed.[2]

In the Jewish religion, fasting is performed on one to six holy days. Some of these fasts are only during daytime hours, while others last from sundown to sundown. On these days of fasting, restriction of intake of all food and liquid (especially on Yom Kippur) is observed.[2,6]

For <u>daytime only fasts:</u>[2,6]

- Eat a normal meal on the evening before the fast.

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- Take short-acting medications (short- or rapid-acting insulin, mealtime meds) with the evening meal.
- Evening dose of intermediate or basal insulin should be reduced by about 20%.
- On the day before the fast, the bedtime dose of a sulfonylurea should be omitted.
- On the morning of the fast, do not take any diabetes medications, except insulin (see below).
- On the day of the fast, take one-half to one-third of the intermediate-acting or basal insulin.
- For those taking insulin, blood glucose should be monitored frequently, and short-acting insulin should be used for blood glucose values greater than 250 mg/dL (13.9 mmol/L).
- After the fast, all medications and meals should be resumed, as usual.

In extended fasts (e.g., sundown to sundown) such as on Yom Kippur and Ninth of Av, patients should be instructed to follow the same instructions as those with the daytime fast, except evening doses of intermediate-acting or basal insulin should be reduced to one-half to one-third of the usual dose.[2,6] Patients whose diabetes is well controlled should use closer to one-third their dose, while those who are less well-controlled should take closer to one-half their usual dose.[15]

Fasting during the holy month of Ramadan is a situation which requires even more education and planning. Fasting during Ramadan for patients with diabetes is discouraged and these patients are medically exempt, but many patients will still choose to fast.[7,8] Ramadan is a lunar-based month during which patients who are Muslim fast from predawn to after sunset for 29 to 30 consecutive days. Because the dates of Ramadan vary with the moon cycles, they change each year. In 2016, Ramadan starts in June, so the days are the longest days of the year in the Northern hemisphere. This increases the impact to patients with diabetes who choose to fast, as longer days mean longer fasting time.

As with all situations of fasting in patients with diabetes, literature is limited.[7,8] There is, however, one large, population-based Epidemiology of Diabetes and Ramadan 1422/2001 (EPIDIAR) study, which included 12,243 patients with diabetes from 13 Islamic countries.[9] They found that fasting during Ramadan increased the risk of severe hypoglycemia, requiring hospitalization 4.7-fold in patients with type 1 diabetes (from 3 events per 100 people per month to 14 events per 100 people per month) and 7.5-fold in patients with type 2 diabetes (from 0.4 events per 100 people per month to 3 events per 100 people per month). These numbers are likely underestimated, because patients who developed hypoglycemia but were cared for by family and friends rather than seeking medical care were not included. Severe hypoglycemia was more common in patients in whom recent dosage changes of oral antidiabetic agents or insulin were made.[9]

As with hypoglycemia, the incidence of hyperglycemia is also increased in patients with diabetes who fast during Ramadan. In the EPIDIAR study mentioned above, there was a 5-fold increase in hyperglycemia requiring hospitalization in patients with type 2 diabetes (from 1 event per 100 patients per month to 5 events per 100 people per month). In patients with type 1 diabetes, the incidence of severe hyperglycemia with or without ketoacidosis was 3-fold higher during Ramadan (from 5 events per 100 people per month to 17 events per 100 people per month). It has been proposed that the increases were a result of excessive reductions in antidiabetic medications.[9]

Prior to the holy month of Ramadan, patients with diabetes who wish to fast should undergo a complete medical evaluation including assessment of glycemic control, blood pressure, and lipids.[7,8] Any changes to diet, exercise, or medication regimens should be made during this period so that the patient is on a stable and effective regimen when fasting begins. Extensive education regarding the importance of glucose monitoring during fasting and non-fasting hours, when to stop the fast, meal planning to avoid hypoglycemia and dehydration, appropriate meal choices to avoid postprandial hyperglycemia, and timing and intensity of physical activity is vital.[7,8]

The management of patients with **type 2 diabetes** will vary depending on which diabetes medications they are taking. The table below summarizes adjustments to medications for patients with **type 2 diabetes** during Ramadan.[7,8,16,17]

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Adjusting Medications for Patients with Type 2 Diabetes who Fast During Ramadan[7,8,16,17]

Patient Characteristics	Medication Adjustments
Diet controlled	• Divide calories over two to three smaller meals during non-fasting hours to avoid postprandial hyperglycemia.
Metformin	• Total dose of metformin unaffected, but the timing of ingestion should be altered. • Take two-thirds of the total daily dose with the sunset meal, and remaining one-third with predawn meal.
Sulfonylureas	• Avoid chlorpropamide. • Once daily sulfonylureas – take with sunset meal. • Twice daily sulfonylureas – take usual dose with the sunset meal, one-half of morning dose with the predawn meal. • Adjust dose based on blood glucose concentrations. • Consider reducing dose if history of hypoglycemia.
Alpha-glucosidase inhibitors • acarbose, miglitol Meglitinides • nateglinide, repaglinide	• Take only when ingesting a meal.
Sodium-glucose co-transporter 2 (SGLT2) inhibitors • canagliflozin, dapagliflozin, empagliflozin	• No change in dose • Encourage water intake, if possible, to lessen risk of dehydration and syncope • Be alert for signs of ketoacidosis
Insulin	• Limited evidence suggests that rapid-acting insulin (aspart, glulisine, lispro) produces less hypoglycemia than short-acting insulin before meals. • If using basal insulin (glargine, detemir), take 80% of dose with evening meal and use regular dose of rapid-acting before meals. • If using twice daily insulin or mixed insulin, consider switching to basal insulin, with rapid-acting insulin before meals. Otherwise, take usual dose at sunset meal and half usual dose at predawn meal.
Dipeptidyl peptidase-4 inhibitors • linagliptin, saxagliptin, etc GLP-1 agonists • albiglutide, exenatide, etc Thiazolidinediones (TZD) • pioglitazone, rosiglitazone Bromocriptine (*Cycloset* [U.S.]) Pramlintide [U.S. only] (*Symlin*)	• No adjustment necessary.

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It is recommended that patients with **type 1 diabetes** do not fast. However, as was shown in the EPIDIAR study, fasting for Ramadan remains common in this group. Patients with type 1 diabetes who do decide to fast during Ramadan, must continue their insulin to avoid diabetic ketoacidosis (DKA). It is suggested that patients with type 1 diabetes reduce their basal long-acting insulin by about 20%, given with the evening meal. Any rapid-acting insulin usually scheduled for midday should not be given.[16] Insulin pumps should also have the basal rate reduced by about 20%.[16] The adjustment of basal insulin in these patients should be individualized, based on patient factors (i.e., glucose control, history of hypoglycemia, etc) and blood glucose monitoring during the fast (reductions can range from 10% to 30%, or even up to 50%).[10,17]

Conclusion

Fasting in the patient with diabetes is common for a variety of reasons. Fasting can be performed safely by most patients [Evidence level C; consensus].[2,6-8,15] In order to prevent issues with hypoglycemia or hyperglycemia, it is vital that a patient with diabetes understands what to do when fasting is necessary. Education should include the importance of more frequent blood sugar monitoring, what medicines and doses to take before and during the fast, information about exercise or activity before and during the fast, the signs and symptoms of hypoglycemia and hyperglycemia, and what to do if hypoglycemia and hyperglycemia occur.

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References

1. Aldasouqi S, Sheikh A, Klosterman P, et al. Hypoglycemia in patients with diabetes on antidiabetic medications who fast for laboratory tests (letter). *Diabetes Care* 2011:34;e52.
2. Grajower MM. 24-hour fasting with diabetes: management of religious observances and of the preoperative patient. *Diabetes Metab Res Rev* 2011. Published on-line ahead of print. doi: 10.1002/dmrr.1169.
3. Sylvest L. University of Michigan Health System. Instructions for patients with diabetes having outpatient procedures/tests. April 2008. https://www.med.umich.edu/1libr/aha/umdiabetesnoinsulin.htm. (Accessed April 12, 2016).
4. Concord Hospital. Diabetes medication instructions for colonoscopy preparation and procedure. May 2015. http://www.concordhospital.org/wellness-resources/health-library/healthwise-document-viewer/?id=abl0488. (Accessed April 11, 2016).
5. Concord Endoscopy Center. Diabetes instructions for colonoscopy preparation and procedure. http://giaofnh.com/pdf/Diabetes_InstructionsforColonoscopy.pdf. (Accessed April 11, 2016).
6. Grajower MM. Management of diabetes mellitus on Yom Kippur and other Jewish fast days. *Endocr Pract* 2008;14:305-11.
7. Hui E, Bravis V, Hassanein M, et al. Management of people with diabetes wanting to fast during Ramadan. *BMJ* 2010;340:c3053.
8. Al-Arouj M, Assaad-Khalil S, Buse J, et al. Recommendations for management of diabetes during Ramadan: update 2010. *Diabetes Care* 2010;33:1895-902.
9. Salti I, Bénard E, Detournay B, et al (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* 2004;27:2306-11.
10. Kobeissy A, Zantout MS, Azar ST. Suggested insulin regimens for patients with type 1 diabetes mellitus who wish to fast during the month of Ramadan. *Clin Ther* 2008;30:1408-15.
11. Khan NA, Ghali WA, Cagliero E. Perioperative management of blood glucose in adults with diabetes mellitus. March 2016. In UpToDate, Post TW (ed), UpToDate, Waltham, MA 02013.
12. University College London Hospitals. Advice for people with diabetes when taking bowel preparation medication for a colonoscopy. June 2012. https://www.uclh.nhs.uk/PandV/PIL/Patient%20information%20leaflets/Colonoscopy%20bowel%20preparation%20advice%20for%20diabetics.pdf. (Accessed April 12, 2016).
13. Mayo Clinic. Colonoscopy – medication directions for patients with diabetes. September 2012. http://mayoclinichealthsystem.org. (Accessed April 12, 2016).

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14. Duke Medicine. Colonoscopy preparation instructions. March 2010. http://www.dukehealth.org/repository/dukehealth/2010/04/21/09/27/53/2089/colonoscopy_preparation_with_miralax.pdf. (Accessed April 12, 2016).
15. Grajower MM, Zangen D. Expert opinion and clinical experience regarding patients with type 1 diabetes mellitus fasting on Yom Kippur. *Pediatr Diabetes* 2011;12:473-7.
16. Sunni M, Brunzell C, Nathan B, Moran A. Management of diabetes during Ramadan, practical guidelines. *Minn Med* 2014;97:36-8.
17. Ali S, Davies MJ, Brady EM, et al. Guidelines for managing diabetes in Ramadan. *Diabet Med* 2016 Jan 23. doi: 10.1111/dme.13080. [Epub ahead of print].

Levels of Evidence

In accordance with the trend towards Evidence-Based Medicine, we are citing the **LEVEL OF EVIDENCE** for the statements we publish.

Level	Definition
A	High-quality randomized controlled trial (RCT) High-quality meta-analysis (quantitative systematic review)
B	Nonrandomized clinical trial Nonquantitative systematic review Lower quality RCT Clinical cohort study Case-control study Historical control Epidemiologic study
C	Consensus Expert opinion
D	Anecdotal evidence In vitro or animal study

Adapted from Siwek J, et al. How to write an evidence-based clinical review article. *Am Fam Physician* 2002;65:251-8.

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