

Strategies for management of intermittent fasting in patients with diabetes

ISLAM IS THE SECOND most common religion in the world, and there are 1.6 billion Muslims, many in areas where diabetes is prevalent. Each year observant Muslims fast during the daylight hours for the holy month of Ramadan. It is estimated that 50 million diabetic people fast between dawn and sundown during Ramadan, and Muslims are not the only group of patients who fast for religious or other reasons. It is important for healthcare providers to guide patients with diabetes in avoiding problems related to prolonged fasting.

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In this issue of the *Cleveland Clinic Journal of Medicine*, Drs. A.V. and Zagar address management of diabetes specifically relating to Ramadan fasting, with considerations that also apply to other diabetic patients who fast for religious or for medical reasons.

Fortunately, we now have antihyperglycemic agents that are unlikely to cause hypoglycemia if used alone or in combination, as long as the regimen does not include insulin or a sulfonylurea. These include:

- Metformin and thiazolidinediones (pioglitazone and rosiglitazone), which improve insulin sensitivity
- Glucagon-like peptide 1 (GLP-1) agonists (exenatide, liraglutide, dulaglutide, and albiglutide), which facilitate insulin release in a glucose-dependent fashion
- Dipeptidyl peptidase 4 inhibitors (sitagliptin, saxagliptin, alogliptin, and lina-

gliptin), which augment endogenous incretin hormones, primarily GLP-1, and also facilitate insulin production in a glucose-dependent fashion

- Alpha glucosidase inhibitors (acarbose and miglitol), which slow carbohydrate absorption.

Introduced in recent years, the sodium-glucose cotransporter 2 (SGLT-2) inhibitors canagliflozin, dapagliflozin, and empagliflozin lower blood glucose by reducing the renal threshold for reabsorption of glucose, coupled with reabsorption of sodium leading to daily urinary excretion of about 200 calories. These agents alone or taken with any of the agents above should not cause hypoglycemia. However, they can lead to dehydration if fasting precludes the intake of water as well as food.

The primary concern during fasting is hypoglycemia when diabetes regimens involve insulin or insulin secretagogues, most commonly sulfonylureas. Long-acting basal insulin should not require adjustment during fasting if the dose is not excessive. The amount and timing of short-acting analogues administered before meals should be adjusted to the timing of meals, and doses should be adjusted proportionally to the anticipated carbohydrate intake. Premixed insulins such as intermediate-acting (protamine suspension) insulin and a short-acting insulin in 70/30, 75/25, or 50/50 ratios should be avoided. They do not lend themselves to changes in timing, and the short-acting component is fixed and cannot be changed for varied intake without changing the intermediate-acting portion, which

The main concern is to avoid hypoglycemia, but diabetic patients also need to be aware of the risks of hyperglycemia and ketoacidosis

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functions as the basal insulin.

Sulfonylurea doses can be reduced or the larger dose moved to before the evening meal, but these agents still pose a risk of hypoglycemia during fasting hours. And as Drs. A.V. and Zagar state, glimepiride, glipizide, and gliclazide are the only agents in the class that should be considered; glyburide (ie, glibenclamide) poses too great a risk of hypoglycemia. On the other hand, the short-acting secretagogue nateglinide can be used safely before meals without much risk of hypoglycemia.

We have focused primarily on hypoglycemia risk. But if antihyperglycemic agents are

halted completely or if the reduction is too severe, patients are at risk for hyperglycemia and even diabetic ketoacidosis. Careful monitoring of blood glucose levels during the fasting period is most important for patients taking agents that can cause hypoglycemia, and patients should be advised to break the fast if dangerously low glycemic levels occur. Similarly, if severe hyperglycemia or ketoacidosis develops, patients should be advised to seek medical advice promptly. ■

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