Management of Diabetes in the Patient With Cancer

PRESENTED BY LORENA A. WRIGHT, MD, FACE

Abstract

During JADPRO Live Virtual 2020, Lorena A. Wright, MD, FACE, reviewed the principles of antihyperglycemic management and discussed the importance of working as a team to collaborate in the management of patients with cancer.

Understanding the optimal management of hyperglycemia in patients with cancer is an essential responsibility of advanced practitioners. During JADPRO Live Virtual 2020, Lorena A. Wright, MD, FACE, of the University of Washington Diabetes Institute in Seattle, discussed the importance of glycemic control in patients with cancer and outlined the principles of antihyperglycemic management and treatment.

HYPERGLYCEMIA AND CANCER

As Dr. Wright reported, hyperglycemia is emerging as a potential risk factor for the development of cancer and may be associated with poor cancer treatment outcomes. Patients with diabetes, especially those with poorly controlled hyperglycemia, are associated with an elevated risk of pancreatic, liver, colon, breast, and endometrial cancer (Barone et al., 2010). There's also a greater risk of cancer mortality in adults with prior glucose intolerance than in those with a normal response.

According to Dr. Wright, there are several cancer treatments in use that might either exacerbate hyperglycemia in patients with diabetes or cause newly induced diabetes, but corticosteroids are by far the most common. Corticosteroids do this by increasing insulin resistance, which puts stress on the pancreas that might already be at risk for development of hyperglycemia. Although this is often reversible by stopping these medications, said Dr. Wright, in patients with several risk factors, this could induce a permanent diagnosis of diabetes requiring insulin.

Immune checkpoint inhibitors are also capable of causing abrupt and dramatic presentation of hyperglycemia. There are several cases of immune checkpoint inhibitors causing fulminant hyperglycemia with ketoacidosis, which requires prompt recognition and treatment, said Dr. Wright (Table 1).

Table 1. Diabetes Related to Cancer Treatments

Causes	Mechanism	Features	Treatment
Corticosteroids	Increased insulin resistance	Common; reversible; postprandial > fasting elevations	Insulin often needed
P13K/AKT, mTOR, IR/IGFR1R inhibitors	Increased insulin resistance and impaired secretion	Reversible when drug stopped	–
Immune checkpoint inhibitors	Autoimmune destruction of beta cells	Several cases reported; potentially fulminant with ketoacidosis	Insulin required
Unresectable pancreatic cancer	Destruction or impairment of islet cells due to inflammation	Poor patient oral intake often limits its severity and allows less aggressive treatment	Insulin
Pancreatic cancer resection	Removal of part of pancreas	Treat as Type 1 phenotype initially; may recover some function; good glycemic control improves outcome	Endocrine should be consulted

Note. Other agents: interferon-alpha, L-asparaginase, streptozocin, octreotide, tacrolimus, cyclosporine, pentamidine, antipsychotics, thiazide diuretics, and megace. Information from Flory & Farooki (2016).

WHEN TO INITIATE INSULIN THERAPY IN TYPE 2 DIABETES

Two separate organizations have recommendations about when to initiate insulin. The American Diabetes Association (ADA) recommends initial therapy in patients with the following characteristics: significant symptoms associated with hyperglycemia; dramatically elevated glucose concentrations (> 300–350 mg/dL) or A1C ≥ 10.0%; failure of noninsulin therapies; and unintentional weight loss. The American Association of Clinical Endocrinology (AACE) recommends initial therapy in patients an A1C > 9.0%, with symptoms associated with hyperglycemia, or when triple therapy fails to achieve control.

INTENSIVE INSULIN MANAGEMENT

In order to individualize insulin management, Dr. Wright emphasized the importance of understanding the basic physiology of the pancreas. With every meal, the pancreas senses spikes in blood sugars and secretes a burst of insulin in response. During periods of fasting, the pancreas also responds to basal (background) glucose with a steadier dose of insulin.

In order to mimic this function, intensive insulin management must thus provide basal insulin to maintain constant blood sugar levels during fasting and bolus (prandial) insulin as coverage for meals for the postmeal glucose rise. There is also a correction component to adjust for hyperglycemia.

As Dr. Wright explained, insulin is the preferred treatment for glycemic control in the ill patient for a number of reasons: the pharmacodynamics of insulin allow it to be adaptable to the changing physiology of the sick patient; there is easy titration and no dosage threshold; it has rapid onset and minimal side effects, except hypoglycemia; and there are minimal drug interactions.

STEROID-INDUCED HYPERGLYCEMIA

Glucocorticoids are by far the most common cause of medication-induced hyperglycemia and development of newly diagnosed diabetes, with some studies showing more than double the risk (Clore & Thurby-Hay, 2009). Knowing that hyperglycemia will have an effect on metabolic deterioration in a patient with diabetes underscores the importance of surveillance of blood sugars in patients receiving high-dose steroids, said Dr. Wright, who noted that the half-life of steroids is used to determine duration of surveillance.

In patients with no preexisting diabetes, risk depends on the dose and duration of the steroid as well as the risk factors of the patient, but providers cannot predict how an individual patient is going to respond, said Dr. Wright.

Patients are first asked to monitor their glucose fasting and before meals for 24 hours. If blood sugars are less than 140, blood glucose testing can be discontinued. For patients with blood sugars higher than 140, however, a correctional dose is recommended.

"For patients using more than 20 units of correctional insulin after 24-hour follow-up, a preset dose needs to be set before eating," said Dr. Wright. "These patients need to be followed very closely."

For patients with blood sugars above 180 in the first 24 hours of testing, scheduled subcutaneous insulin is required, not just correctional insulin.

"In patients with preexisting diabetes, on the other hand, we know that their blood sugars are going to significantly deteriorate and most of them will need insulin," said Dr. Wright.

For patients with Type 1 diabetes with a total pancreatectomy, the recommendation is to continue with the regimen, but more prandial insulin will be needed. Steroid-induced hyperglycemia is characterized mainly by postprandial hyperglycemia, said Dr. Wright, so these will need to be adjusted.

Patients with Type 2 diabetes who are on home insulin but poorly controlled or on noninsulin antidiabetic medications will need to switch to subcutaneous insulin. Well-controlled patients with an A1C < 7, on the other hand, can be managed with lifestyle or noninsulin diabetes medications. Low correctional insulin is used first followed by a preset dose before eating,

"For steroid-induced hyperglycemia, NPH insulin is really a great choice because it will cover the time period that is affected the most with the steroids," said Dr. Wright (Table 2).

MANY MOVING TARGETS

Finally, Dr. Wright noted that there are many moving targets with steroid-induced hyperglycemia. Because patients with a prior history do not always develop hyperglycemia on steroids, even at extremely high doses, monitoring is important. Providers should also remember that there is no perfect formula to predict the exact insulin doses needed.

"Use the formula as a guide, consider the number of correction units being used, and use your clinical judgment," said Dr. Wright, who emphasized that self-monitoring of blood glucose is critical to calculate and titrate the doses.

Dr. Wright also noted that as steroids are tapered down, glucose will improve and insulin doses need to be adjusted to avoid hypoglycemia.

"Very close follow-up is needed for these high-risk patients as things change on a daily basis," Dr. Wright concluded. "When management of these patients is quite intensive, you can consider endocrinology." ●

Disclosure

Dr. Wright had no conflicts of interest to disclose.

References

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Table 2. Determining Insulin Dose for Steroid-Induced Hyperglycemia	
Prednisone (mg/day)	**NPH (units/kg/day)**
> 40	0.4 units
30	0.3
20	0.2
10	0.1

Note. If choosing basal-bolus insulin, estimated total daily dose (TDD) = 0.4 unit/kg/day. ~30% basal (glargine or detemir) and ~70% prandial (lispro, aspart, glulisine).