Management Strategy for Steroid-Induced Malglycemia During Cancer Treatment

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Malglycemia is a temporary problem that has significant negative sequelae. This article attempts to clarify and educate oncology nurses about the impact and management of steroid-induced malglycemia on patients with cancer receiving treatment. A management algorithm is provided to aid in evaluation and treatment decisions.

A patient named J.K., who also is an RN, was diagnosed with a pancreatic neuroendocrine carcinoid tumor. As is common with diseases of the pancreas, J.K.’s blood sugars started to become elevated. She was concerned, but when she brought her concerns to her oncologist, he stated that it was a problem for the endocrinologist and to call him instead. After waiting six weeks for an appointment, the endocrinologist told her that her malglycemia was from the cancer treatments and a temporary problem. He advised her to “just leave it alone.” J.K. declined physically with rapid tumor growth, increase in symptoms, and blood sugars as high as 500 mg/dl. She knew something had to be done, and she was frustrated by the “hot potato game.” In response, her clinic nurse began researching ways to manage malglycemia.

Malglycemia

Healthcare professionals are well aware of the consequences of unmanaged hyperglycemia. The term malglycemia is used to describe a hyperglycemic state in a patient that is not known to have diabetes. Cancers of the pancreas, either primary pancreatic cancers or neuroendocrine tumors of the pancreas, can result in glucose intolerance, insulin resistance, or failure of the pancreas to function properly (Wang, Larsson, & Herrington, 2003). Use of Steroids

Corticosteroids and glucocorticoids are used for two main purposes in cancer treatments. The first is to increase the cell kill process in diseases such as multiple myeloma, lymphomas, and some solid tumors (Faiman, Bilotti, & Rogers, 2008). The steroid works by inhibiting the expression of cytokines such as interleukin, which is a major growth factor (Faiman et al., 2008). The suppression of the growth factor reduces the activity of other signaling systems, and natural cell death occurs. The second reason for the use of steroids in cancer treatments is for side-effect mitigation. The steroids work to suppress allergic and hypersensitivity responses, as well as decrease inflammation and potentiate the effect of antiemetic medications.

Concerns With Steroids

Steroid-induced malglycemia is a temporary problem that can lead to poor patient outcomes. The pathophysiology of the steroid effects includes “down regulation of glucose transport in the muscle, so that more insulin is needed for the uptake of glucose in the cells” (Oyer, Shah, & Bettenhausen, 2006, p. 479). Steroids stimulate the release of glucose from the glycogen stores in the liver (gluconeogenesis), resulting in increased circulating glucose and, ultimately, development of insulin resistance (Mackay & Barrow, 2010). In insulin resistance, the insulin molecule has difficulty binding to the insulin receptor on muscle, fat, or liver

Note. Based on information from Faiman et al., 2008; Hammer & Voss, 2012; Stevens et al., 2011.
Vegetables: spinach, tomatoes, eggplant, squash, broccoli, cabbage, beets, mushrooms, peppers, bean sprouts, green beans, carrots, okra, chard, pea pods, kale, cauliflower.

Protein: meat (beef, chicken, pork, fish, lamb), nuts, soy or tofu, cottage cheese, eggs and egg whites, cheese, plain yogurt

Carbohydrates: fruit, grains, cereal, pasta, rice, bread, flour, beans, starchy vegetables

Sweets, fruit juice, sweeteners

FIGURE 3. Food Choices for Carbohydrate Control
Note. Based on information from Chase, 2011a, 2011b; Novo Nordisk, 2013.

All patients given corticosteroids will be screened with two-hour postprandial blood glucose on day 2 of the first chemotherapy cycle.

Two-hour postprandial blood glucose greater than 200 mg/dl

Patient to come to clinic to receive:
• Education about glucose monitoring, use of the insulin pen, and dietary carbohydrate control
• Blood glucose monitoring before each meal
• Dietary carbohydrate control of 30 g per meal
• Subcutaneous insulin injections given before each meal using the insulin lispro pen; dose per project-designed scale

Two-hour postprandial blood glucose ranging from 140–199 mg/dl

Patient to come to clinic to receive:
• Blood glucose meter and education on its use
• Blood glucose monitoring two hours after the largest meal of the day, along with dietary carbohydrate control of 30 g per meal

Two-hour postprandial blood glucose less than 140 mg/dl

No intervention needed; continue to monitor blood glucose with pretreatment laboratory results.

FIGURE 2. Management Strategy for the Treatment of Malglycemia
Note. Based on information from Gannon & Dando, 2010; Genolet & Petite, 2012; Oyer et al., 2006.

Two-hour postprandial blood glucose greater than 200 mg/dl

Two-hour postprandial blood glucose ranging from 140–199 mg/dl

Two-hour postprandial blood glucose less than 140 mg/dl

No intervention needed; continue to monitor blood glucose with pretreatment laboratory results.

Screening and Intervention

According to Genolet and Petite (2012), “steroid-induced hyperglycemia is a common clinical problem without an evidence-based solution” (p. 800). Figure 2 was designed by the authors of the current article to address a management strategy that can be conducted in all treatment settings. The steps are initiated by the nurse—with the use of a finger stick—and progresses from there. The use of a two-hour postprandial blood glucose level

has conducted extensive laboratory research on this concept.

Malglycemia has significant harmful effects on the human body. Complications include impaired cell repair (delayed recovery from chemotherapy and wound healing); increased clotting of red cells; increased aggregation of platelets (increased risk of deep vein thrombosis and pulmonary embolism); increased inflammation (Hammer & Voss, 2012); decreased ability to fight infection; increased load on major organs, including kidney, liver, and heart; and, most important for patients with cancer, increase in cellular proliferation (cancer growth) and mortality (Stevens, Dinkel, & Catanzaro, 2011) (see Figure 1). In other words, cancer cells grow faster with unmanaged malglycemia (Faiman et al., 2008) and apoptosis (programmed cell death) is suppressed (Hammer & Voss, 2012).

The role of insulin-like growth factor (ILGF) cannot be overlooked. Maki (2010) presented data regarding the influence of ILGF on the proliferation of cancer cells. The process of insulin resistance creates an atmosphere of hyperglycemia as well as hyperinsulinemia. Each is a proliferative agent. Hursting (2012)
has been validated as the most effective time interval to assess for steroid insulin resistance (Gannon & Dando, 2010; Oyer et al., 2006). To date, insulin remains the best management option available to prevent middle- and long-term consequences of repeated hyperglycemia (Genolet & Petite, 2012; Oyer et al., 2006).

The quality improvement initiative entailed the development of a protocol based on the current literature for the treatment of steroid-induced insulin resistance. A combination of diabetic literature and oncology literature, as well as some general medicine journals, were reviewed. The proposal was presented to the physicians at PCR Oncology, and verbal permission was received to implement screening for and treatment of steroid-induced malglycemia for patients that fit the criteria. Verbal consent was obtained from each patient. No institutional review board approval was sought and no consent forms were used. All patients who had received glucocorticoids or corticosteroids as part of their day 1 treatment regimen, regardless of the reason, were screened for malglycemia with a two-hour postprandial glucose reading on day 2 of treatment. The two-hour postprandial blood glucose reading was taken in the clinic by finger stick and measured by a glucose meter two hours after the lunch meal. This time period was reasonable to patients, as many needed to return to the clinic for growth factor injections as well. Patients that recorded a blood glucose result of 140 mg/dl or lower were placed in the nonintervention group. Their follow-up would occur during random blood collection before cancer treatment doses. Patients that recorded a blood glucose level of 141–200 mg/dl were provided with an educational intervention that included daily glucose monitoring and dietary carbohydrate control. Carbohydrate control of 30–45 g of carbohydrates per meal was used as the model.

Patients were given guidelines for food choices. The authors developed a graphic showing food choices for carbohydrate control (see Figure 3). In addition, patients were given one-on-one education, a glucometer for home use, and a demonstration on its use. Handouts were provided with examples of food lists, carbohydrate sources and gram amounts, a food diary, and signs and symptoms of hypoglycemia along with treatment. Patients who had glucose readings of 201 mg/dl or higher were provided with the same dietary instruction and glucometers, but also were placed on insulin lispro. They were instructed to test their blood sugars before each meal and to treat each blood sugar according to instructions on the insulin scale (see Figure 4). The rationale for testing and treatment was to mimic what the pancreas should be doing naturally. Patients were asked to follow up weekly with the nurse and to bring their blood glucose log to the clinic to evaluate the management of their malglycemia. This was done by tracking the oral intake of food with the blood glucose recordings at the appointed time points during the day in addition to evaluating the effects of insulin, if insulin was in use. A conservative insulin scale was developed specific for this population and was used for each patient placed on insulin.

This quality improvement initiative focused on management of malglycemia. The authors did not collect baseline information (gender, age, race, or cancer diagnosis) on all 30 patients. This was a limitation of the data. The authors will collect that type of data with future research. Thirty patients were screened, and 10 of the 30 needed intervention. All of the patients were asymptomatic when screened. Nine patients showed improvement in overall glucose control. Seven patients required insulin, whereas the other three patients were able to keep their glucose readings between 140–170 mg/dl with carbohydrate counting. The patients receiving any intervention were successfully kept euglycemic for the remainder of their cancer treatment, with the exception of one type 1 diabetic who remained fragile. Patients were transitioned back to their primary care providers once cancer treatments stopped. At least three of the seven patients who required insulin needed to be placed on oral antiglycemic agents to manage blood glucose levels once steroids were discontinued. None of the screened patients experienced symptoms of elevated blood glucose; however, 35% of the patients screened required intervention.

### Practice Implications

Nurses can be proactive and screen patients on day 2 if a cancer regimen contains corticosteroids. Patients will most likely be asymptomatic, so additional patient education and patient assessment will be necessary at that time. The recognition and management of malglycemia is an opportunity for nurses to lead a change in their local practices. Nurses should collaborate with their

| Blood glucose less than 75 mg/dl before any meal |
|-------------------------------------------------|--------------------------------------------------|
| • Treat with 1/2 cup of fruit juice or 3–4 glucose tablets and notify doctor. |

| Blood glucose 75–130 mg/dl before any meal |
|------------------------------------------|--------------------------------------------------|
| • Treat with three units of insulin lispro by subcutaneous injection. |

| Blood glucose 131–170 mg/dl before any meal |
|-------------------------------------------|---------------------------------------------------|
| • Treat with four units of insulin lispro by subcutaneous injection. |

| Blood glucose 171–210 mg/dl before any meal |
|-------------------------------------------|--------------------------------------------------|
| • Treat with five units of insulin lispro by subcutaneous injection. |

| Blood glucose 211–250 mg/dl before any meal |
|-------------------------------------------|--------------------------------------------------|
| • Treat with six units of insulin lispro by subcutaneous injection. |

| Blood glucose 251–299 mg/dl before any meal |
|-------------------------------------------|--------------------------------------------------|
| • Treat with seven units of insulin lispro by subcutaneous injection and notify doctor. |

| Blood glucose 300 mg/dl or higher before any meal |
|---------------------------------------------------|--------------------------------------------------|
| • Treat with eight units of insulin lispro by subcutaneous injection and notify doctor. |

Note. Based on a formula of 1 U of insulin for every 10 g of carbohydrate, and 1 U of insulin drops the blood glucose by 40 points.

**FIGURE 4. Screening and Intervention Insulin Scale**
interdisciplinary team and institute a plan or create a protocol/algorithm that can be used to identify and manage malglycemia. They also should consider establishing proactive screening of all patients with cancer receiving steroids with a day 2 post-prandial finger stick. Identifying those patients who continue to have malglycemia once steroids are discontinued may require additional education, treatment, and follow-up with an endocrinologist and the primary care team to manage blood glucose levels to improve quality of life and outcomes.

Conclusion

Nurses are encouraged to take this information into their practice, discuss it with colleagues, consider conducting a quality improvement initiative, and open a dialogue about malglycemia.

Finally, regarding J.K., she was placed on the protocol and her blood sugars came under control, her tumor progression halted, she began to respond to treatment, and her symptoms began to resolve. J.K. was alive one year later.

References


Do You Have an Interesting Topic to Share?

Safety provides readers with information on safety issues affecting patients with cancer and those caring for them. Length should be no more than 1,000–1,500 words, exclusive of tables, figures, insets, and references. If interested, contact Associate Editor David Glenn, RN, MS, at david.glenn@umaryland.edu.