CADRE'S "DIABETES TACTICS"

In December 2007, the Council for the Advancement of Diabetes Research and Education (CADRE) implemented a new Web site initiative—a "Diabetes Tactics" case study each month that explores a different challenge in diabetes treatment. The scenarios presented are among those a health care provider is likely to encounter in practice, and each treatment challenge is followed by practical treatment information and suggestions from the experts on the CADRE Advisory Board. All case studies are available on the CADRE Web site (www.cadre-diabetes.org) free of charge. Cases currently available on the Web site include:

- A 37-year-old white man with a 17-year history of type 1 diabetes mellitus (DM), frequent hypoglycemic reactions, and a glycosylated hemoglobin (A1C) level of 8.3%. He recently experienced a severe hypoglycemic reaction, but remains reluctant to change his treatment regimen because he fears that the frequency of his hypoglycemic episodes would increase. Davida F. Kruger, MSN, a Certified Nurse Practitioner at the Henry Ford Health System (Detroit, Michigan), explores a recommendation for treatment with an intensive insulin regimen and pramlintide.
- A 25-year-old Hispanic woman with a 5-year history of type 2 DM and an A1C of 7.8% despite being treated with 3 oral antihyperglycemic medications. The patient has a family history of type 1 DM and is concerned that she may have been misdiagnosed. Matthew Riddle, MD, Professor of Medicine at Oregon Health & Sciences University (Portland, Oregon), discusses latent autoimmune diabetes in adults.
- A 47-year-old white woman with a 10-month history of type 2 DM being treated with diet and exercise. Although treatment with lifestyle modifications was successful initially, she has regained 6 of the 14 lb lost and her A1C, after dropping from 7.4% at diagnosis to 6.5%, has increased to 6.8%. William Cefalu, MD, Chief of the Division of Nutrition and Chronic Diseases at Pennington Biomedical Research Center in the Louisiana State University system (Baton Rouge, Louisiana), reviews adjustment of postprandial glucose levels without negatively affecting weight.
- A 63-year-old African American man with a 15-year history of hypertension and a 3-month history of type 2 DM. Although this patient was treated initially with metformin and changes in diet and exercise, he presents at a follow-up visit with an A1C of 10.4%. Derek LeRoith, MD, PhD, Chief of the Division of Endocrinology, Diabetes, and Bone Diseases at Mount Sinai School of Medicine (New York, New York), explores the rationale for aggressive treatment with insulin in this patient.

This month's "Diabetes Tactics" case discusses the treatment challenge created when an adolescent male with type 1 DM participates in sports and exercise programs. The treatment discussion was provided by Desmond Schatz, MD, Professor and Associate Chairman of Pediatrics, and Medical Director, Diabetes Center at the University of Florida (Gainesville, Florida); scientific research and writing assistance was provided by Julie Martin, MS.

CASE PRESENTATION

A 17-year-old white male with a 3-year history of type 1 DM visits the clinic after experiencing 2 severe hypoglycemic reactions (both requiring assistance) during the past month. The patient is an active high school junior who has played on the varsity basketball team since the start of the season 6 weeks earlier. At this visit, his height is 74 inches and he weighs 170 lb (body mass index, 22 kg/m^2). He has been using a continuous subcutaneous insulin infusion (CSII) pump for the previous 2 years. His A1C is 7.3%. The patient consistently monitors his blood glucose 4 to 6 times daily, and readings range from 62 to 190 mg/dL during the day. His problem times for hypoglycemia are typically in the late evening and during the night; problems usually occur following afternoon basketball practice or a strenuous evening basketball game.

The patient currently takes a rapid-acting insulin analogue, and ~50% of his total daily insulin is administered as basal insulin. He uses 4 basal rates (1.4 units/hour [midnight–4 AM], 1.8 units/hour [4 AM–7 AM], 1.7 units/hour [7 AM–3 PM], and 1.5 units/hour [3 PM–midnight]) and insulin boluses for meals. The boluses are based on carbohydrate counting, where 1 unit of insulin is given for every 10 grams of carbohydrate consumed. The insulin pump is detached (ie, no insulin is infused) during basketball practices and games (~2 hours each time). Practices are less strenuous than games and occur in the afternoon immediately after school. The patient finds that if he does not drink a sports drink that contains ~15 grams of carbohydrate during his practices, his blood glucose can drop to 50 to 70 mg/dL immediately after exercise. After playing a strenuous evening game, the patient often finds that his blood glucose increases to 160 to 180 mg/dL; as a result, he drinks only unsweetened beverages during and immediately after games. If his blood glucose level is <100 mg/dL before bedtime, he eats a snack that contains carbohydrates (usually a bowl of cereal or a granola bar) and does not take bolus insulin for these carbohydrates. Despite this regimen, his blood glucose has been decreasing to levels as low as 40 mg/dL during the night while he is asleep. His parents have been waking him every 2 to 3 hours to check his blood glucose. They have decided that he will have to stop playing basketball if his hypoglycemia does not improve, because they feel this is putting his health at risk and creating too much stress on the family.

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Analysis

With the added physical demands of sports participation, this patient's current CSII regimen is not meeting his needs. However, he should be able to reduce his risk of postexercise hypoglycemia with some adjustments to the amounts of his basal and bolus insulin and to the timing of his carbohydrate intake. He actually needs 2 separate regimens to manage his exercise, one for the mildly to moderately intense practice sessions and another for the more intense exertion and stress associated with games. His A1C level (7.3%) is fairly good for an adolescent (American Diabetes Association A1C goal for ages 13–19: <7.5%) and, although a lower A1C would be preferred, it is more important at this time to reduce his risk of severe hypoglycemia.

Recommendations

There are several ways to manage hypoglycemia in this patient; the following is one approach. On days that the patient has afternoon basketball practice, he should reduce his prelunch insulin bolus by 20%. During practice, he should take an extra 15 to 30 grams of carbohydrate for every 30 to 60 minutes of exercise. If his blood glucose decreases during or after practice, he should consume an additional 30 to 45 grams of oral glucose. Frequent blood glucose monitoring is essential.

For the more intense night games, the patient should consider decreasing his insulin-to-carbohydrate ratio at dinner to 1:15. During the game he should drink water (instead of a drink that contains carbohydrates) to replenish his fluids, as long as his blood glucose level is not dropping. If nocturnal hypoglycemia persists, he should start a temporary basal rate immediately after exercise (decreasing up to 50% for at least 4 hours or longer if necessary). Before bedtime, he should check his blood glucose; if it is <130 mg/dL, the patient should eat a snack that is larger than his usual snack—one that includes protein and fat as well as complex carbohydrates. In addition, he should make sure that the CSII injection site is in an area away from intense muscle activity (eg, the abdomen instead of the leg).

If hypoglycemia continues to be a problem, a continuous glucose monitoring system (CGMS) could be considered. A CGMS would monitor subcutaneous tissue interstitial glucose levels, recording glucose values approximately every 5 minutes and setting off an alarm if the blood glucose level falls below a pre-set level. This will reduce the need for frequent blood glucose checks during the night and may allow the patient and family to sleep better, although it should be noted that these devices may have limited accuracy at low blood glucose levels and should not be substituted for self-monitoring of blood glucose. Even if the patient did not want to wear the CGMS all the time, it would be good for him to wear it after practice and intense games while an appropriate and more exact exercise-related treatment plan is being formulated.

Rationale

Children and adolescents with type 1 DM should not be restricted from regular physical activity and sports participation, as long as blood glucose is monitored frequently and therapy is adjusted to decrease the risk of hypoglycemia. In fact, youths should be encouraged to participate in moderate to vigorous physical activity for a total of 30 to 60 minutes daily to improve their body composition and self-esteem, and to reduce their risk of long-term diabetes complications.

Multiple factors influence the metabolic and hormonal responses to exercise in patients with type 1 DM, including the level of baseline metabolic control, the duration and intensity of the exercise, the type and dose of insulin delivered before and after exercise, the site of the insulin injection, and the timing of food intake relative to exercise. Although general guidelines can be given to reduce the risk of postexercise hypoglycemia, because the metabolic response to exercise is so complex, increased blood glucose monitoring is needed during and after exercise to individualize the treatment plan.

The metabolic response to exercise differs depending on whether the activity is aerobic or anaerobic. Mild to moderate activities, like walking, running, swimming, and cycling, are primarily *aerobic*; they are characterized by lower rates of muscle contraction over a longer duration and require a great deal of oxygen to make the energy needed. The increase in oxygen uptake by muscles during this type of exercise increases the requirement of glucose, and the muscles use carbohydrate, fat, and some protein for oxidation within the muscle. In athletes without DM, plasma insulin usually remains constant or declines slightly, but then increases rapidly during the recovery period after exercise, leading to a restoration of normal blood glucose and replenishment of muscle glycogen. In athletes with type 1 DM, hypoglycemia may occur during or immediately after aerobic exercise because of an inability to regulate insulin secretion in response to the increased rate of muscle glucose transport. Late-onset postexercise hypoglycemia may also occur 6 to 15 hours after aerobic exercise; this may be caused by an increase in glucose uptake by muscles for the replenishment of muscle glycogen stores and an increase in insulin sensitivity after exercise.

Anaerobic exercise, on the other hand, does not use oxygen for energy and therefore refers to exercise that uses muscles at high intensity and a high rate of work for only a short period of time. Examples include weight lifting, sprinting, and any rapid burst of hard exercise. In this type of exercise, glucose is mobilized from muscles and the liver, and anaerobic oxidation occurs. In some cases, the increase in glucose production is higher than the rate of glucose utilization, resulting in hyperglycemia during and immediately after exercise. In addition, the stress of strenuous exercise may have effects on insulin counterregulatory hormones such as cortisol, glucagon, and norepinephrine, which can affect hepatic glucose output and may increase the risk of late-onset postexercise hypoglycemia.

In this case, the patient's basketball practices involved moderate activities (primarily aerobic exercise), whereas the basketball games involved short periods of intense activity followed by brief intervals of rest (primarily anaerobic exercise). Thus, different treatment scenarios are required to address the fluctuations in blood glucose created by this patient's participation in 2 different types of exercise.

Key Messages

- Children with type 1 DM should be encouraged to exercise and participate in sports activities. Insulin regimens and food intake can be adjusted to reduce the risk of hypoglycemia.
- Blood glucose should be monitored carefully before, immediately after, and at regular intervals (eg, every 2 hours) after activities that are moderate or vigorous in intensity, until predictable blood glucose patterns can be identified.
- The metabolic response to exercise and the recommended interventions may vary depending on the intensity and duration of the activity.
- Consider a CGMS if hypoglycemia persists despite therapeutic intervention.

RECOMMENDED READING

1. Rachmiel M, Buccino J, Daneman D. Exercise and type 1 diabetes mellitus in youth; review and recommendations. *Pediatr Endocrinol Rev.* 2007;5:656–665.
2. Silverstein J, Klingensmith G, Copeland K, et al. Care of children and adolescents with type 1 diabetes: A statement of the American Diabetes Association. *Diabetes Care*. 2005;28:186–212.
3. Marcus AO. The art and science of insulin-pump therapy. In: Leahy JL, Cefalu WT, eds. *Insulin Therapy.* New York, NY: Marcel Dekker, Inc; 2002:223–244.
4. Tsalikian E, Mauras N, Beck RW, et al. Impact of exercise on overnight glycemic control in children with type 1 diabetes mellitus. *J Pediatr.* 2005;147:528–534.
5. McMahon SK, Ferreira LD, Ratnam N, et al. Glucose requirements to maintain euglycemia after moderate-intensity afternoon exercise in adolescents with type 1 diabetes are increased in a biphasic manner. *J Clin Endocrinol Metab.* 2007;92:963–968.