Type 1 Diabetes Mellitus in Children and Adolescents: Part 2, Management

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Although at present there is no cure for type 1 diabetes mellitus, good treatments are available that can enable affected children to lead healthy, active lives. Insulin regimens should be designed to optimize metabolic control while minimizing the risk of adverse events, such as hypoglycemic episodes, which can be more serious in children. Regimens of 3 injections per day work well for children who cannot receive an injection at lunchtime, while multiple daily injection (MDI) regimens provide more flexibility. Continuous subcutaneous insulin infusion (CSII) can provide better quality of life than MDI regimens, but CSII requires a high level of motivation and carries its own risks. In all children, insulin regimens must be adjusted to accommodate the physiological changes of growth and development. Long-term follow-up is important to monitor for complications of diabetes.

Case: A 10-year-old girl presents to her pediatrician with a 2-week history of polyuria and nocturia (she needs to go to the bathroom every couple of hours during the day and several times each night), polydipsia (she drinks 5 to 6 1-L bottles of water per day), blurred vision, fatigue, and 1 episode of vomiting. Her mother thinks she may have lost 5 kg (11 lb) in the past month. The child takes no regular medications and has no allergies or other medical conditions. Her mother and her maternal grandmother have Hashimoto thyroiditis. On examination, she is moderately dehydrated (stable vital signs, but dry lips), and her breath has a “fruity” smell. A glucometer test shows a capillary glucose level of 450 mg/dL, and a urine dipstick shows 3+ ketones with significant glucosuria. What should be included in the short-term and long-term management plans?

Type 1 diabetes mellitus (T1DM) is more common in children than type 2 diabetes mellitus (T2DM). At present, there are no definitive cures for T1DM. However, good management and monitoring are available.

Unlike T2DM, which can be managed with diet, exercise, and oral hypoglycemic agents, T1DM must be treated with insulin replacement. Family physicians and general pediatricians are often responsible for the treatment as well as the diagnosis of T1DM in children. In Part 1 of this article (on page 55 of this issue), we reviewed the epidemiology and diagnosis of pediatric T1DM. Here we focus on the management of T1DM in children and adolescents.

KEYS TO EFFECTIVE MANAGEMENT OF T1DM IN CHILDREN

Treatment of T1DM involves the subcutaneous replacement of insulin in a manner that attempts to mimic normal physiology. In acute situations, such as diabetic ketoacidosis (DKA) or settings in which oral intake cannot be maintained (eg, gastroenteritis, perioperative settings), intravenous insulin replacement may be required. Once a patient is stable, a subcutaneous insulin regimen is started. The goal of treatment is to optimize glycemic control while minimizing the risk of adverse events (eg, hypoglycemia, weight gain).

Challenges that are specific to the management of T1DM in children include the changes in insulin needs that result from growth, puberty, and variations in activity and food intake; poor adherence with injections and capillary blood glucose monitoring; and dependence on caregivers for management and supervision. Children and adolescents must have support from family, friends, dieticians, nurses, psychosocial teams, and physicians to help them cope with T1DM. Insulin regimens are chosen in conjunction with the family in order to accommodate unique schedules, needs for flexibility, financial situation, and abilities of the child and the caregiver.

INSULIN REGIMENS APPROPRIATE FOR CHILDREN

Insulin regimens are designed to provide basal insulin coverage for hepatic glycogenolysis, gluconeogenesis, and lipolysis, as well as bolus insulin to match carbohydrates ingested. Correction boluses are also used to treat hyperglycemia. Table 1 describes the various insulin types currently
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Three injections per day (TID) regimen. This is a common regimen used in children. Intermediate-acting insulin and a rapid-acting insulin analog (or short-acting insulin) are given before breakfast, a rapid-acting insulin analog (or short-acting insulin) is given before supper, and intermediate-acting insulin is given at bedtime. The combination of insulin types in the morning allows the child to forgo injection of rapid-acting insulin at lunchtime. This regimen works well when a responsible adult is unavailable to administer or supervise an injection at lunch; however, it requires that this meal include a fixed amount of carbohydrate and that it be eaten at a relatively consistent time. It also does not allow for correction of hyperglycemia in the middle of the day.

Multiple daily injection (MDI) regimen. Also called a basal-bolus regimen, this type of regimen is designed to be more physiologic. Intermediate-acting insulin or a long-acting insulin analog is administered once or twice a day as the basal insulin. When meals are consumed or corrections for hyperglycemia are required, a rapid-acting insulin analog (or short-acting insulin) is given. An MDI regimen allows more flexibility for the child but requires more frequent injections.

Continuous subcutaneous insulin infusion (CSII). Commonly known as the insulin pump, CSII involves inserting a catheter into the subcutaneous tissue of the abdomen, buttocks, or thighs and infusing rapid-acting insulin analogs in both continuous-basal and bolus amounts. Varying degrees of benefit have been reported from CSII. However, recent systematic reviews of the literature have reported slight improvements in glycated hemoglobin $A_1c$ ($HbA_1c$) level, decreased frequency of hypoglycemic events, and improved quality of life when CSII is used in children (as compared with MDI). Disadvantages of CSII include increased cost, risk of infection at infusion sites, and higher risk of DKA (resulting from situations such as pump malfunction or dislodgment of the catheter). Still, in highly motivated patients and families who have the support of a multidisciplinary team knowledgeable in pediatric CSII, this therapy is a good option.

Twice-daily (BID) regimen. In some cases, it is not possible to use intensive insulin therapy, and a compromise BID regimen must be used. Settings in which BID regimens might be most appropriate include families in which psychosocial concerns and nonadherence make it impossible to use more frequent insulin injections to achieve acceptable glycemic control. In these situations, premixed insulin (a mix of intermediate-acting insulin and short-acting insulin in fixed ratios) may be a useful tool (see Table 1). The same premixed insulin is administered at the time of both breakfast and supper.

Selecting the best regimen for a given patient. The 10-year-old girl in the case presented at the beginning of this part of the article would likely have difficulty in managing her own insulin injections during lunchtime at school. However, she should be able to manage to stick to fixed mealtimes with stable carbohydrate amounts. Thus, a TID regimen would probably be most appropriate for her. The starting total daily dose of insulin would be 0.7 U/kg/d. Of this total daily dose, two-thirds would be given in the morning and one-third in the evening. Of the morning insulin given with breakfast, two-thirds would be given as an intermediate-acting insulin and one-third would be given as rapid-acting insulin. In the evening, one-third would be given at supper time as rapid-acting insulin and two-thirds would be given at bedtime as intermediate-acting insulin.

A very different regimen, however, would be required to best meet the needs of the 15-month-old boy in Part 1 of this article, who has newly diagnosed T1DM and who eats sporadically and in varying amounts throughout the day. In a child such as this, an MDI regimen might be the most practical. A typical starting total daily dose of insulin in this setting would be 0.5 to 0.7 U/kg/d. Of this total daily dose, 50% would be given as a long-acting insulin analog in the evening, and the remaining 50%...
would be given as rapid-acting insulin at mealtimes during the course of the day. In both these patients, insulin needs would vary during the honeymoon phase and with growth, puberty, and seasonal changes in activity and routines. For trends such as the foregoing, the family in conjunction with either the physician or the diabetes team should make ongoing adjustments of insulin doses.

**TREATMENT GOALS**

The goal of treatment is to maintain euglycemia while minimizing occurrences of hypoglycemia. Because the risk of undetected or severe hypoglycemia is greater in younger children, recommendations for glycemic targets in children vary by age. Table 2 lists suggested preprandial blood glucose targets by age.

Monitoring of overall blood glucose control is accomplished by measuring HbA1c levels. The HbA1c level reflects the overall blood glucose control for the past 3 months. Depending on the assay used, a normal HbA1c level ranges from 4.3% to 6.1%. Target HbA1c levels for children with T1DM range from less than 7% to less than 8.5%; targets are dependent on the child’s age and abilities (see Table 2).

### COMPLICATIONS OF DIABETES

#### Acute complications. One of the challenges associated with striving for optimal glycemic control is the short-term risk of multiple hypoglycemic events. Hypoglycemia can range in severity from mild symptoms (hunger, shakiness, irritability, sweating) to seizures, loss of consciousness, coma, and death. Weight gain may become a problem in patients who eat greater amounts in an attempt to compensate for insulin excess and avoid hypoglycemia.

In the Diabetes Control and Complications Trial (DCCT), 441 patients with T1DM aged 13 to 39 years were randomly assigned to receive either conventional treatment (once-daily or twice-daily injections) or intensive treatment (CSII or injections 3 or more times daily) and were followed up prospectively for a mean of 6.5 years. The major adverse event reported in the patients aged 13 to 17 years who received intensive insulin treatment was an almost 3-fold increase in severe hypoglycemic events compared with the number of events in patients who received conventional treatment. One reason children are at greater risk for severe hypoglycemia is that they are dependent on caregivers for recognition and treatment of hypoglycemic symptoms. It is because of their increased risk of hypoglycemia that glycemic targets for younger children vary on the basis of age (see Table 2).

Another acute complication of T1DM is DKA. DKA is primarily the result of insufficient insulin, which causes fatty acid metabolism with resultant metabolic acidosis. In children and adolescents, DKA can occur at the time of initial diagnosis of T1DM, can be associated with an intercurrent illness, or may result from nonadherence to diabetes self-care measures (eg, insulin administration, monitoring, insulin adjustment for illness). DKA can be life-threatening and has an estimated mortality rate in children of 0.15% to 0.3%. Of deaths associated with DKA, cerebral edema is estimated to be the cause in 60% to 90% of cases. Appropriate resuscitation and correction of the metabolic acidosis may help prevent cerebral edema, and various published protocols are available for guiding therapy in children.

#### Chronic complications. Children and adolescents do not often manifest long-term complications of diabetes, such as macrovascular disease (cardiovascular disease) or microvascular complications (retinopathy, nephropathy, or neuropathy). However, it is clear that metabolic control of T1DM in childhood is an important factor that can affect the future development of these complications. The DCCT demonstrated that for each 10% decrease in HbA1c, there was a 39% decrease in the risk of retinopathy and a 25% decrease in the risk of microalbuminuria. Thus, maintaining optimal glycemic control in childhood and adolescence is critical for future prevention of chronic
Table 3 suggests screening measures and clinical assessments that can be used to monitor children with T1DM. Screening for long-term complications of diabetes does not need to begin until puberty.

**FUTURE DIRECTIONS FOR THE MANAGEMENT OF T1DM IN CHILDREN**

Research is currently under way to find cures for diabetes, ways to prevent diabetes, and improved treatments for diabetes. Islet cell and pancreas transplantation offer the possibility of cure but carry the risks of long-term immunosuppression. There has been some research into using hematopoietic stem cell therapy as a treatment for T1DM, but the results are still very preliminary. Anti-CD3 monoclonal antibodies have been used in attempts to preserve endogenous insulin secretion in patients with new-onset T1DM, but the duration of benefit is not clear and further research is ongoing. Environmental and dietary factors have also been examined as potential strategies for preventing diabetes. Such strategies include vitamin D supplementation, cow’s milk protein exposure, and exposure to oral insulin. Better treatment options currently being studied include improved methods of insulin delivery and blood glucose monitoring. Continuous blood glucose monitors have been developed that when used with CSII can improve HbA1c levels. Closed-loop systems are being developed that automatically adjust insulin administration on the basis of continuous glucose monitoring.

**References:**


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