Type 1 Diabetes in Children and Adolescents

Canadian Diabetes Association
Clinical Practice Guidelines Expert Committee

INTRODUCTION

Diabetes mellitus is the most common endocrine disease and one of the most common chronic conditions in children and adolescents. This section addresses those areas of diabetes management that are specific to children. Unless otherwise specified, the term 'child' is used for individuals 0 to 18 years of age, and the term 'adolescent' for those 13 to 18 years of age.

MANAGEMENT

Children and adolescents who present with diabetic ketoacidosis (DKA) require a short period of hospitalization to stabilize the associated metabolic derangements and to initiate insulin therapy. Outpatient education for new-onset diabetes in children and adolescents who are not experiencing DKA has been shown to be less expensive and associated with similar or slightly better outcomes in terms of metabolic control, and rates of rehospitalization, DKA and severe hypoglycemia compared to an inpatient education program (1-6).

Children and adolescents with new-onset type 1 diabetes and their families require intensive diabetes education by an interdisciplinary pediatric diabetes healthcare (DHC) team to provide them with the necessary skills and knowledge to manage this disease. The complex physical, developmental and emotional needs of children and their families require specialized care to ensure the best long-term outcomes (7). Education topics must include insulin action and administration, dosage adjustment, blood glucose (BG) testing, sick-day management and prevention of DKA, nutrition therapy, exercise, and prevention and treatment of hypoglycemia. As part of routine care, children and their families should also receive psychoeducational sessions and interventions, as required, on emotional adjustment at each age and stage, behavioural-developmental growth, childhood and adolescent depression, school issues, diabetes camp, substance abuse, driver's licence and career choices.

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RECOMMENDATIONS

1. All children and adolescents with diabetes should have access to an experienced DHC team and specialized care starting at the time of diagnosis *[Grade D, Level 4 (7)]*.
2. For children and adolescents with new-onset type 1 diabetes who are medically stable, initial education and management in an outpatient setting should be considered, providing appropriate personnel and daily telephone consultation service are available in the community *[Grade C, Level 3 (3)]*.

Glycemic targets

As improved metabolic control reduces both the onset and progression of diabetes-related complications in adults and adolescents with type 1 diabetes (8,9), aggressive attempts should be made to reach the recommended glycemic targets outlined in Table 1. However, clinical judgement is required to determine which children can reasonably and safely achieve these targets. Treatment goals and strategies must be tailored to the child, with consideration given to individual risk factors. Repeat episodes of severe hypoglycemia appear to increase the risk of cognitive impairment in preschool-aged children (10-17).

RECOMMENDATION

3. Adolescents should employ the same therapeutic strategies and aim for the same glycemic targets as adults *[Grade A, Level 1A (8)]*. Children 5 to 12 years of age should aim for a glycosylated hemoglobin (A1C) target of ≤8.0%, with glycemic and A1C targets graduated according to the child's age *[Grade D, Consensus]*. In children <5 years of age, an A1C of ≤9.0% is acceptable, and extreme caution should be exercised to avoid hypoglycemia because of the risk of cognitive impairment that may occur in this age group *[Grade D, Level 4 (11,15,17)]*.

Insulin therapy

Insulin therapy is the mainstay of medical management of type 1 diabetes. A variety of insulin regimens can be employed, but few have been studied specifically in children and adolescents with new-onset diabetes. The initial insulin regimen in children and adolescents with new-onset type 1 diabetes should include at least 2 daily injections of intermediate- and fast-acting insulin. The choice of insulin regimen will depend on other factors, including the child's age, family lifestyle, socioeconomic factors, and individual family, patient and physician preferences.

Regardless of the insulin regimen used, all children should be treated to meet glycemic targets. Most children will require intensification of their regimen over time. Two major methods of intensive diabetes management have been employed to achieve recommended glycemic targets: multiple daily injection routines and continuous subcutaneous insulin infusion (CSII, insulin pump therapy). CSII is a safe and effective way of delivering intensive diabetes management in children and adolescents with type 1 diabetes, and can be initiated at any age. Rapid-acting insulin analogues are the insulins of choice for pump users (18). When used as part of a multidimensional approach to therapy, improvements in metabolic control may be achieved without increased risk of severe hypoglycemia (19-21). Enhanced attention to meal planning, BG monitoring and insulin pump function are essential components of this therapy.

Insulin glargine (Lantus®), an extended long-acting insulin analogue approved, but not yet available, in Canada, has been approved and is in use in Europe and the United States. The only 2 published reports of its use in children and adolescents both confirmed improved fasting blood glucose levels and fewer episodes of nocturnal hypoglycemia (22,23).

RECOMMENDATION

4. Consideration should be given to increasing the frequency of injections or changing the type of intermediate-acting insulin and fast-acting insulin, or changing to CSII (insulin pump) therapy when the 2 or 3 daily insulin injection regimen fails to optimize metabolic control and/or for quality of life reasons *[Grade D, Consensus]*.

Smoking prevention and cessation

In view of the importance of smoking as a modifiable risk factor for both macrovascular and microvascular complications of diabetes, antismoking counselling should be part of diabetes management (24-27).

RECOMMENDATION

5. Formal smoking prevention and cessation counselling should be part of diabetes management for adolescents with diabetes *[Grade D, Consensus]*.

Contraception and sexual health counselling

As pregnancy in adolescent females with type 1 diabetes with poor metabolic control results in higher risks of maternal and fetal complications, unplanned pregnancies should be avoided (see "Pre-existing Diabetes and Pregnancy," p. S94).

RECOMMENDATION

6. Adolescent females with type 1 diabetes should receive counselling on contraception and sexual health in order to avoid unplanned pregnancy *[Grade D, Consensus]*.

Eating disorders

Adolescent females with type 1 diabetes have a 2-fold increased risk of developing an eating disorder compared to their peers without diabetes (28). Furthermore, in adolescents with type 1 diabetes, eating disorders are associated with poor metabolic control and earlier onset and more rapid progression of microvascular complications (29) and should be suspected in those adolescent and young adult females with type 1 diabetes who are unable to achieve and maintain metabolic targets. It is important to identify those patients with eating disorders because different management strategies are required to optimize metabolic control and prevent microvascular complications (30). Screening should be conducted by health professionals by asking appropriate nonjudgemental questions about weight and shape concerns, dieting, binge episodes and insulin omission for the purpose of weight control (28).

RECOMMENDATION

7. Adolescent females and young women with type 1 diabetes should be regularly screened for eating disorders using nonjudgemental questions about weight and shape concerns, dieting, binge eating and insulin omission for weight loss *[Grade B, Level 2 (28)]*.

Table 1. Glycemic targets for children and adolescents

Age (years)	*A1C (%)*	*Preprandial PG (mmol/L)*	*Considerations*
<5	≤9.0	6.0–12.0	Extreme caution is required to avoid severe hypoglycemia because of the risk of cognitive impairment in this age group
5–12	≤8.0	4.0–10.0	Targets should be graduated to the child's age
13–18	≤7.0	4.0–7.0	Appropriate for most patients
	≤6.0	4.0–6.0	Consider for patients in whom these targets can be achieved safely

A1C = glycosylated hemoglobin
PG = plasma glucose

DKA

DKA occurs in 15 to 67% of patients with new-onset diabetes, depending on geographic location (31-33), and with a frequency of 1 to 10 episodes per 100 patient years in those with established diabetes (31,32). In the patient with established diabetes, DKA results from failing to take insulin or poor sick-day management. Special caution should be exercised in children with DKA and new-onset diabetes or a greater degree of acidosis and dehydration because of the increased risk of cerebral edema (CE). While most cases of DKA are corrected without event, 0.7 to 3.0% of cases are complicated by CE (34-37), which is associated with significant morbidity (21 to 35%) and mortality (21 to 24%) (38). Although the cause of CE is still unknown, several factors are associated with increased risk, including age <5 years, new-onset diabetes, high initial serum urea nitrogen, low initial partial pressure of arterial carbon dioxide (pCO_2), rapid administration of hypotonic fluids, failure of serum sodium to rise during treatment, and use of bicarbonate (34-36,38-41).

Detailed clinical protocols for the management of DKA in children to reduce the risk of CE have been published (42), and others are available through some provincial ministries of health (43) and medical colleges (44).

COMPLICATIONS

There are important age-related considerations regarding the initiation of surveillance for diabetes complications and the interpretations of investigations (Table 2).

Nephropathy

A first morning urine albumin to creatinine ratio (ACR) has high sensitivity and specificity for the detection of microalbuminuria (45,46), the first clinical marker of diabetic nephropathy. Although screening with a random ACR is associated with greater compliance than with a first morning sample, its specificity may be compromised in adolescents due to their higher frequency of exercise-induced proteinuria and benign postural proteinuria. Due to the false-positive rate and low positive predictive value for the random ACR, especially in adolescents, confirmation of microalbuminuria is required (47) using a first morning ACR, or a timed overnight or 24-hour split urine collection for determination of the albumin excretion rate. At least 1 month should elapse between the abnormal screening test and the confirmatory test.

Microalbuminuria is rare in prepubertal children, regardless of the duration of diabetes or metabolic control (48), so prepubertal children need not be screened. Furthermore,

Table 2. Screening for complications in children and adolescents with type 1 diabetes

Complication	*Indications and intervals for screening*	*Screening test*
Nephropathy	• Yearly screening commencing at puberty in those with duration of type 1 diabetes ≥5 years • Postpubertal adolescents should be screened yearly after 5 years' duration of type 1 diabetes	• First morning ACR • If compliance prohibits a first morning urine sample, a random ACR should be obtained • Abnormal screening tests require confirmation with a first morning ACR or timed overnight or 24-hour split urine collection for determination of the albumin excretion rate. At least 1 month should elapse between sampling, and repeat sampling should be conducted every 3 to 4 months over a 12-month period to demonstrate persistence and/or progression
Retinopathy	• Yearly screening should commence 5 years after diagnosis of diabetes in individuals ≥15 years of age • Follow-up screening should occur annually or be tailored to severity of retinopathy, if present	• 7-standard field, stereoscopic-colour fundus photography with interpretation by a trained reader (gold standard), or • Direct ophthalmoscopy or indirect slit-lamp fundoscopy through dilated pupil, or • Digital fundus photography
Neuropathy	• Postpubertal adolescents should be screened yearly after 5 years' duration of type 1 diabetes	• None, other than routine clinical assessment
Dyslipidemia	• Screening necessary only in those with BMI >95th percentile, family history of hyperlipidemia or premature CAD, or poor metabolic control	• Fasting lipid profile
Hypertension	• Routine	• Use appropriate cuff size

ACR = albumin to creatinine ratio
BMI = body mass index
CAD = coronary artery disease

the likelihood of transient or intermittent microalbuminuria is higher during the early peripubertal years (49,50). It is not known if individuals with transient or intermittent microalbuminuria are at risk of progression to overt nephropathy. As it can take 12 to 18 months of observation to determine whether the microalbuminuria is going to resolve, persist or progress, annual screening should begin with onset of puberty in order to follow the natural history of the microalbuminuria. Abnormal screening results require confirmation and follow-up to demonstrate persistence and/or progression (i.e. to demonstrate that the patient has nephropathy).

Prior to initiating treatment, persistence and/or progression of microalbuminuria must be demonstrated by repeat sampling conducted every 3 to 4 months over a 12-month period. Treatment is indicated only for those adolescents with persistent and/or progressive microalbuminuria. There are no long-term intervention studies assessing the effectiveness of angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists in delaying progression to overt nephropathy in adolescents with microalbuminuria. Therefore, treatment of adolescents with persistent and/or progressive microalbuminuria is based on the effectiveness of various interventions in adults with type 1 diabetes (51-53). A short-term randomized, controlled trial in adolescents demonstrated that ACE inhibitors were effective in reducing microalbuminuria compared to placebo (54).

RECOMMENDATIONS

8. In children with duration of type 1 diabetes of ≥5 years, screening for microalbuminuria should commence at onset of puberty and be performed yearly thereafter. Postpubertal adolescents should be screened yearly after 5 years' duration of type 1 diabetes. Prepubertal children need not be screened *[Grade D, Consensus]*.
9. Screening for microalbuminuria in adolescents with type 1 diabetes should be conducted using a first morning urine test for determination of the ACR *[Grade B, Level 2 (45)]*. If compliance prohibits a first morning urine test, a random urine ACR should be obtained. Abnormal results require confirmation *[Grade B, Level 2 (47)]* with a first morning ACR, or a timed overnight or 24-hour split urine collection *[Grade D, Consensus]* for determination of the albumin excretion rate. At least 1 month should elapse between the abnormal screening test and the confirmatory test *[Grade D, Consensus]*.
10. Prior to initiating treatment, persistence and/or progression of microalbuminuria must be demonstrated by repeat sampling conducted every 3 to 4 months over a 12-month period *[Grade D, Consensus]*.

Retinopathy

In children with type 1 diabetes of at least 5 years' duration, screening for retinopathy should begin at age 15 years, and occur yearly thereafter (see "Retinopathy," p. S76).

Neuropathy

When present, neuropathy is mostly subclinical in children (55,56). While prospective nerve conduction studies and autonomic neuropathy assessment studies have demonstrated increased prevalence of abnormalities over time (55,57-59), persistence of abnormalities is an inconsistent finding (56). With the exception of intensifying diabetes management to achieve and maintain glycemic targets, no other treatment modality has been reported in children and adolescents. It is therefore not necessary to use formal investigations other than routine clinical assessment of neuropathy in postpubertal adolescents with type 1 diabetes of ≥5 years' duration.

Dyslipidemia

Children and adolescents with type 1 diabetes have a higher frequency of dyslipidemia compared to their peers and siblings without diabetes (60,61). Dyslipidemia in adolescents and adults with type 1 diabetes is associated with a higher frequency of progressive microalbuminuria, retinopathy and macrovascular disease. There are, however, no intervention trials for dyslipidemia in children or adolescents. In general, the dyslipidemia found in type 1 diabetes is associated with poor metabolic control and can be reversed with intensification of therapy and achievement of metabolic targets. In a small proportion of individuals, pharmacologic lipid-lowering therapy may be indicated, although experience with these medications in children and adolescents is limited.

RECOMMENDATION

11. Only those children and adolescents with type 1 diabetes and other risk factors, such as severe obesity (body mass index >95th percentile), and/or a family history of hyperlipidemia or premature coronary artery disease, or those with poor metabolic control should be screened for dyslipidemia *[Grade D, Level 4 (60,61)]*.

Hypertension

Children and adolescents with type 1 diabetes should have routine blood pressure (BP) measurement using an appropriate cuff size. Those with BP readings persistently above the 95th percentile for age should be referred for assessment and possible treatment.

TRANSITION TO ADULT CARE

Regular medical follow-up within a trusting and collaborative patient-doctor relationship or patient-DHC team relationship is very important to achieving metabolic targets. The change of physician or DHC team can have a major impact on disease management and metabolic control in the person with diabetes. Between 25 and 65% of young adults have no medical follow-up during the transition from pediatric to adult diabetes care services (62,63). Those with no follow-up are more likely to experience hospitalization for DKA during this period.

RECOMMENDATION

12. To ensure ongoing and adequate metabolic control, pediatric and adult diabetes care services should collaborate to prepare adolescents and young adults for the transition to adult diabetes care *[Grade D, Consensus]*.

COMORBID CONDITIONS IN CHILDREN WITH TYPE 1 DIABETES

Autoimmune thyroid disease, Addison's disease and celiac disease can occur with increased frequency in children with diabetes. For a brief discussion on the prevalence of these comorbid conditions and indications for screening in children with type 1 diabetes, see Appendix 13.

OTHER RELEVANT GUIDELINES

Organization and Delivery of Care, p. S14
Targets for Glycemic Control, p. S18
Monitoring Glycemic Control, p. S21
Insulin Therapy in Type 1 Diabetes, p. S32
Hypoglycemia, p. S43
Psychological Aspects of Diabetes, p. S50
Influenza and Pneumococcal Immunization, p. S53
Nephropathy, p. S66
Retinopathy, p. S76
Type 2 Diabetes in Children and Adolescents, p. S91
Pre-existing Diabetes and Pregnancy, p. S94

RELEVANT APPENDIX

Appendix 13: Comorbid Conditions in Children With Type 1 Diabetes, p. S139

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