

Initiating insulin therapy in children and adolescents with type 1 diabetes mellitus

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ABSTRACT

The primary clinical goals to be achieved with insulin initiation are elimination of ketosis and hyperglycemia with prevention of chronic complications. Insulin therapy is the mainstay in management of type 1 diabetes, which should be aimed at achieving good glycemic control, with achievement of hemoglobin A1c (HbA1c) <7.5%, pre-meal self-monitored blood glucose (SMBG) of 90–130 mg/dL, bed time SMBG of 100–140 mg/dL, mean blood glucose level of 120–160 mg/dL and no ketonuria. Two classes of insulin are available for use in T1DM viz. bolus/prandial insulins (rapid-acting insulins and short-acting insulins) and basal insulins (intermediate-acting insulin and long-acting insulin). Insulin glargine and glulisine can be used in children above 6 years, lispro in children above 3 years and detemir and aspart in children above 2 years. The caution for hypoglycemia should be exercised while prescribing them. Degludec is currently not approved for pediatric use. The initial insulin regimen should comprise of ≥ 2 daily bolus and ≥ 1 basal insulin injections. Insulin intensification would be required if the initial regimen fails, which can be achieved by increasing frequency of long and rapid acting insulin analogues. The American Diabetes Association guidelines recommend HbA1c targets of <8.0% for children <6 years of age, $\leq 7.5\%$ for children 6 to 12 years of age, and $\leq 7.0\%$ for adolescents, 12–18 years of age. However, the evidence is now in favor of a single target HbA1c of $\leq 7.5\%$ for all children and adolescents <19 years of age.

Key words: Adolescents, insulin initiation, type 1 diabetes mellitus

INTRODUCTION

Few decades back, India did not have pediatric endocrinologists and pediatric endocrine disorders were treated by adult endocrinologists. The present day endocrinologists, however, have focused on individualizing treatment for diabetic patients based on age, physical activity, meal timing, and daily schedule of the patient. The regimens and therapy by various physicians for diabetes management also differs.

Education plays a significant role in controlling this epidemic. Education should be imparted starting from

diagnosis to insulin therapy. It is a complex process, touching on a range of medical and social issues. It is best done by a multidisciplinary team trained in pediatric diabetes. Children with new-onset type 1 diabetes (T1D) and their families require intensive diabetes education and counseling by an interdisciplinary pediatric diabetes healthcare team. Education should be imparted on insulin action and administration, dosage adjustment, blood glucose (BG) and ketone testing, sick-day management, prevention of diabetic ketoacidosis, prevention, detection and treatment of hypoglycemia and nutrition and exercise.

Guidance and lifestyle counseling should be embedded as a part of routine care during critical developmental switches (e.g., school entry, beginning of high school). Regular discussion should be conducted by healthcare providers with children and their families about school, diabetes camps, psychological issues, driving, and career choices.

Insulin therapy is the only treatment for type 1 diabetes mellitus (T1DM). Before the initiation of insulin

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therapy, psychological aspects of the disorder should be adequately assessed and addressed. This includes child/adolescent versus parental concerns and routine screening for psychosocial problems such as depression and diabetes-related distress, anxiety, eating disorders, and cognitive impairment. Initiation, as well as follow-up dose regulation, should be done by specialists.^[1]

Initiation of insulin should be targeted to achieve defined clinical goals. The primary clinical goals to be achieved are elimination of ketosis, elimination of hyperglycemia and its symptoms and prevention of chronic complications. Additional goals of insulin therapy should include maintenance of a desirable weight, maintaining normal growth and sexual maturation, maintaining psychosocial well-being, achieving normal fertility and pregnancy and sustaining normal family and sexual life. The main aim of any anti-diabetic therapy is to achieve good glycemic control. This includes achievement of hemoglobin A1c (HbA1c) <7.5%, premeal self-monitored blood glucose (SMBG) of 90–130 mg/dL, bed time SMBG of 100–140 mg/dL, mean BG level of 120–160 mg/dL and no ketonuria.

Two classes of insulin are available for use in T1DM viz. bolus/prandial insulins (rapid-acting insulins and short-acting insulins) and basal insulins (intermediate-acting insulin and long-acting insulin). Some important insulins used in the treatment of T1D are: Degludec, glargine, detemir, lispro, aspart and glulisine; however, these are recommended to be administered with precaution in children. Degludec is currently not approved for pediatric use. Avoid the use of glargine and glulisine in children <6 years, lispro in children <3 years and detemir and aspart in children <2 years.

Other insulin types include U-500 insulins and these are to be used in doses similar to conventional insulins. These can be used in insulin resistant T1DM patients; however no well controlled studies had been conducted in children. The caution for hypoglycemia should be exercised while prescribing them. The physician can mix analog insulins with conventional basal insulins in the same injection syringe.

Insulin is the mainstay of medical management for T1DM and the choice of insulin regimen should depend on the child's age; family, patient, and physician preferences; and cumulative insulin doses in a day. The initial insulin regimen should comprise of ≥ 2 daily bolus injections and ≥ 1 basal insulin injection. If the initial regimen fails to meet glycemic targets, more intensive management may be required. Three methods of intensive diabetes management can be used at any age viz. similar regimen with more

frequent injections, basal bolus regimens using long and rapid acting insulin analogues, continuous subcutaneous insulin infusion (CSII, insulin pump therapy).^[2] Literature supports the fact that insulin pumps, when compared with multiple daily injections (MDI), are more effective at reducing HbA1c.^[3-10] CSII also has reduced the incidence of severe hypoglycemia episodes when compared with MDI.^[5,7,11] A meta-analysis, of 22 studies, was carried out for the mean difference in HbA1c between CSII and MDI. Severe hypoglycemia was reduced with CSII by a rate ratio of 2.89 for randomized controlled trials (RCTs) and 4.34 for other studies. The mean difference in HbA1c was 0.21% for RCTs and 0.72% for other studies ($P < 0.001$). Insulin pump therapy has been used in the past.^[12] Sensor augmented insulin pumps, and low glucose suspend (LGS) pumps are being used presently in diabetes management. Future therapies are looking forward to fully automated closed loop predictive LGS systems.

Common errors in insulin therapy include improper administration (technique, site and rotation), excessive self-titration, improper mixing, insulin syringe (insulin vial mismatch), and sliding scale. Achieving adult targets for metabolic control is not always indicated and may be unsafe for some children, and achieving targets may require much work on the part of family and care team to find the right insulin system. The American Diabetes Association (ADA) clinical practice guidelines recommend HbA1c targets of <8.0% for children <6 years of age, <7.5% for children 6–12 years of age, and <7.0% for adolescents, 12–18 years of age.^[13] However, the evidence is now in favor of a single target HbA1c of <7.5% for all children and adolescents <19 years of age.

A lead author of the ADA's position statement has been quoted as saying that "evidence shows that there is a greater risk of harm from prolonged hyperglycemia that would occur if children maintained an HbA1C of 8.5% over time. The 7.5% target is evidence-based; however, we want to emphasize that BG and A1C targets must be individualized to safely achieve the best outcomes."

Self-monitoring of BG is an essential part of the management of T1DM. Subcutaneous continuous glucose sensors allow detection of asymptomatic hypoglycemia and hyperglycemia and they may have a beneficial role in children and adolescents, but evidence of their use is not as strong as in adults.

Glucose (15–20 g) is the preferred treatment for symptomatic/asymptomatic hypoglycemia. Patients should be educated regarding the use of glucagon self-administration in all cases. Hypoglycemia unawareness or one or more episodes

of severe hypoglycemia should trigger a re-evaluation of the treatment regimen. Mild hypoglycemia may be inconvenient or frightening to patients/parents while severe hypoglycemia can cause harm to the patient or others around him/her, especially if it causes falls, motor vehicle accidents or other injuries.^[1] As children/teens transition into adulthood, care and close supervision of diabetes management is increasingly shifted from parents and other older adults. Education and awareness regarding transition should begin at least a year before the transition. Though scientific evidence continues to be limited, it is clear that early and ongoing attention be given to comprehensive, coordinated planning for a seamless transition of all youth from pediatric to adult health care.^[14,15]

SUMMARY

Type 1 diabetes mellitus requires insulin for management and it requires a multidisciplinary team work including a specialist who is well-versed with T1DM management, with education forming the cornerstone of management.

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