**Key elements of successful intensive therapy in patients with type 1 diabetes**

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**ABSTRACT**

An intensified diabetes management approach (including increased education, monitoring, and contact with diabetes team) should be used for adolescents and also for younger children if glycaemic control is not achieved by insulin therapy. Treatment options may include increased frequency of injections (e.g. the patients on 2 bolus may require 3 or 4 bolus injections), change in the type of basal and/or bolus insulin depending on multiple times monitoring for adolescents and for younger children, and change to continuous subcutaneous insulin infusion pump therapy. Results of epidemiology of diabetes interventions and complications (EDIC) Research Group, where the Diabetes Control and Complications Trial patients were further followed up almost for a period of 7 years or more showed that intensive therapy significantly reduced and maintained glycated hemoglobin with relative risk reduction of microvascular complications in the intensive therapy group. In addition, intensive treatment reduced the risk of any cardiovascular disease (CVD) event by 42% and the risk of nonfatal myocardial infarction, stroke, or death from CVD by 57%. The reduction of microvascular and macrovascular events in the intensively-treated group persisted due to the “legacy effect” or “metabolic memory” of early intensive glycemic control. The main advantage of intensive insulin therapy is that it reduces the rate of diabetes complications, in the long run. Furthermore, it offers flexibility as the doses can be adjusted according to the activity and food consumed. The main disadvantage of intensive insulin therapy is the risk of hypoglycemia especially in type 1 diabetes mellitus and weight gain.

**Key words:** Epidemiology of diabetes interventions and complications/Diabetes Control and Complications Trial, intensive insulin therapy, type 1 diabetes mellitus

**INTRODUCTION**

The International Association of Diabetes and Pregnancy Study Groups recommendation on glycemic control says that without accurate monitoring, the risk of acute crisis as well as long-term micro- and macro-vascular complications are greatly increased, which implies that the patient has to monitor blood glucose more frequently. Glycated hemoglobin (HbA1c) should be monitored 4–6 times/year in younger children and 3–4 times in older children. The target HbA1c in all age groups is recommended to be <7.5%. There is evidence that intensive treatment with a goal of lowering HbA1c, as shown in the Diabetes Control and Complications Trial (DCCT), results in lower risk of long term complications.

As per 2013 Canadian guidelines, the glycemic targets should graduate with age. In children <6 years of age, target HbA1C should be <8%; for children between 6 and 12 years of age, it should be ≤8%; and for adolescents it should be ≤7.0%. But, glycemic goals should be individualized, and this requires the clinical judgment for the particular patient. Research suggests that patients and parents understanding of glycemic targets, along with consistent target setting by the diabetes team is associated with improved metabolic control in that particular patient.10

Children with persistently poor glycemic control (e.g. HbA1C >10%) should be assessed by a specialized pediatric diabetes team for a comprehensive interdisciplinary assessment and referred for psychosocial support.
Furthermore, an intensive family as well as individualized psychological intervention aimed at improving glycemic control should be considered, to improve chronically poor metabolic control.

Insulin is the mainstay of medical management. The choice of insulin regimen depends on many factors, which include child age, duration of diabetes, family lifestyle, socio-economic factors and family, patient, and physician preferences.

It is reasonable to introduce a basic insulin regimen, ≥2 daily bolus injections and ≥1 basal insulin injection (a minimum of three injections/day), but a more intensive system is indicated if success is not achieved despite all efforts. The rationale for intensive insulin regimen is that 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: Similar regimen with more frequent injections, basal bolus regimens using long and rapid acting insulin analogues, and continuous subcutaneous insulin infusion (CSII) or “insulin pump” therapy for some patients who are not able to achieve control even with basal and bolus therapy.

Insulin therapy should be assessed at each clinical encounter to ensure that it still enables the child to meet HbA1C targets, minimizes the risk of hypoglycemia, allows flexibility in carbohydrate intake and it should also allow flexibility in daily schedule and activities of the patient.\(^1\)

If glycemic control is not achieved by insulin therapy, an intensified diabetes management approach (including increased education, monitoring, and contact with diabetes team) should be used for adolescents and also for younger children. Treatment options may include increased frequency of injections (e.g. the patients on 2 bolus may require 3 or 4 bolus injections), change in the type of basal and/or bolus insulin depending on multiple times monitoring (when sugar level is not coming under control and diet therapy is of not much help) for adolescents and for younger children, and change to CSII pump therapy.

There are two methods of achieving glycemic control: Multiple daily insulin injections comprising of basal and bolus injections and CSII. The main advantage of intensive insulin therapy is that it reduces the rate of diabetes complications, in the long run. Also, it offers flexibility as the doses can be adjusted according to the activity and food consumed. The main disadvantage of intensive insulin therapy is the risk of hypoglycemia (especially in type 1 diabetes mellitus [T1DM]) and weight gain.\(^2\)

In the DCCT study conducted in 1983, patients were divided into 2 groups: Intensive group (n = 711) and conventional group (n = 730). In the intensive group, the main aim of the insulin therapy was to achieve symptom-free survival with blood glucose targets of 70.2–120.6 mg/dL before meals, <180 mg/dL after meals, >72 mg/dL at 03.00 am and HbA1c <6.5%. The patients were initially hospitalized. 3 or more insulin injections/day or insulin pump were provided, and 4 or more daily blood glucose tests were performed. A comprehensive education program was conducted for the patients. Monthly clinic visits were scheduled to assess the physical condition of the patients. Twenty four hours phone contact was also available. In the conventional group, the main aim of insulin therapy was to avoid symptoms of hyper-and hypoglycemia. Patients were given 1 or 2 insulin injections/day. Daily self-monitoring was planned, and initial diet and exercise education were provided. Quarterly clinic visits were scheduled to assess the physical condition of the patients. Results of the DCCT trial showed that intensive insulin therapy in people with T1DM significantly reduced HbA1c relative to those receiving conventional treatment. The intensively-treated group achieved a mean HbA1c of 7.1% (54 mmol/L/mol) while the conventionally treated patients had an HbA1c of approximately 9.0% (75 mmoL/mol). Thus, the DCCT study summarized that intensive therapy, to improve glycemic control, significantly reduces the appearance or progression of microvascular complications in T1DM. There is a continuous relationship between glycemic control (HbA1c) and the risk of hypoglycemia. The incidence of severe hypoglycemia is increased 3-fold with intensive therapy. Nevertheless, intensive therapy did not negatively impact quality of life, cognitive function or cardiovascular health of the patients.\(^3\)

In the epidemiology of diabetes interventions and complications (EDIC) Research Group, the DCCT patients were further followed-up almost for a period of 7 years or more. The risk factors for long-term microvascular and macrovascular outcomes of T1DM were prior diabetes treatment, and level of glycemic control during DCCT. All patients were advised to have intensive insulin therapy. Results of this extension study showed that intensive therapy significantly reduced and maintained HbA1c. The conventional group was encouraged to switch to intensive treatment. An appropriate glycemic control (HbA1c 8%) was thus achieved in both groups throughout the trial. Also, there was relative risk reduction of microvascular complications in the intensive therapy group: At 4 years risk of retinopathy decreased by 76%; and at 8 years, microalbuminuria by 59%, clinical albuminuria by 84%,
and neuropathy by 43%. Additionally, intensive treatment reduced the risk of any cardiovascular disease (CVD) event by 42% and the risk of nonfatal myocardial infarction, stroke, or death from CVD by 57%. Thus, the EDIC follow-up study summarized that glycemic control in intensively-treated patients was equivalent to that of conventionally treated patients during the follow-up period. However, reduction in microvascular and macrovascular events in the intensively-treated group persisted due to the “legacy effect” or “metabolic memory” of early intensive glycemic control.\[3\]

The International Society for Pediatric and Adolescent Diabetes has published a consensus guideline in 2014 related to the insulin treatment in children and adolescents with T1DM.\[4\]

**Summary**

Intensification of insulin therapy helps a patient to achieve glycemic treatment goals. MDI and CSII pump are two modes of delivering intensive insulin therapy. Proper glycemic control (HbA1c: 7 7.5) is not possible without intensive insulin therapy. Intensive insulin therapy reduces risk of long-term microvascular and macrovascular complications. Hypoglycemia is a major barrier in intensification of insulin therapy that can be reduced only by extensive monitoring. Insulin analogues have a distinct advantage over conventional human insulin preparations in this regard and are sometimes useful to reduce hypoglycemia in such patients.

**References**

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