Clinical guidelines for the management of type 1 diabetes in children in Saudi Arabia endorsed by the Saudi Society of Endocrinology and Metabolism, (SSEM)

Bassam Saleh Bin-Abbas a,*, Mohammad Awad Al Qahtani b,1

Abstract Several guidelines have been set by the American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD); however, there are no specific guidelines for our region. The following are the clinical management guidelines that were developed and are endorsed by the Saudi Society of Endocrinology and Metabolism (SSEM) for assisting patients and providers in choosing appropriate health care plans. While these guidelines are useful aids that help providers to determine appropriate practices for children with diabetes, they are not meant to replace the clinical judgment of the individual provider or to establish a standard of care. This article covers several insulin therapy regimens in children with diabetes in Saudi Arabia, including the management of acute complications, sick day management and follow-ups.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases that is characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action or both [1–3]. DM is classified as type 1 DM when beta cell destruction that typically leads to absolute insulin deficiency is present, and type 2 DM is secondary to insulin resistance and involves relative insulin deficiency [4–7]. DM is diagnosed based on
the appearance of the classical symptoms of polyuria, polydipsia, polyphagia and weight loss plus one of the following biochemical findings: a fasting plasma glucose level of ≥126 mg/dl (7.0 mmol/L), a casual plasma glucose level of ≥200 mg/dl (11.1 mmol/L), or a plasma glucose level of ≥200 mg/dl (11.1 mmol/L) 2 h following an oral glucose tolerance test. Other presenting features can include nocturnal enuresis, blurred vision, ketoacidosis, vaginal candidiasis, recurrent skin infections, and irritability [2].

Type 1 DM in childhood and adolescence typically progresses through four phases: the pre-diabetes phase, the clinical presentation of diabetes, the partial remission (or honeymoon period), and permanent insulin dependency [3–5]. In this summary, we will review the clinical guidelines for the management of type 1 DM in children in Saudi Arabia.

2. Initial DM management

Newly diagnosed patients with type 1 DM should be admitted to the hospital to initially confirm the diagnosis, to rule out and manage DKA when present, and to provide patient/parent education and insulin dose adjustments.

2.1. Insulin therapy

The aim of insulin therapy is to provide near physiological insulin replacement, which is difficult with commonly used forms of insulin and delivery methods. The availability of new insulin analogs and alternative delivery methods (e.g., insulin pumps) offer more physiological insulin replacements. The choice of insulin type and regimen will be guided by many factors that include the age of the patient, the metabolic control target, patient and family education and support, family status (e.g., stability, age of the parents, size of the family, education of parents, and income), lifestyle factors, duration of diabetes, and associated complications including hypoglycemia. The choice of insulin regimen should aim to provide appropriate baseline insulin requirements over 24 h, to provide sufficient insulin levels for meals, to achieve short-term and long-term metabolic targets and to minimize blood glucose fluctuations.

The majority of children in Saudi Arabia are likely to be started on twice-daily injections of insulin in the forms of a short-acting insulin (regular insulin) and intermediate-acting insulin (NPH) (which is not the recommended insulin regimen). Insulin doses are given in quantities of 0.5–1.0 unit/kg/day. Two-thirds of the total dose is given in the morning, and one-third is given in the evening. Two-thirds of the dose is given as NPH, and one-third is given as regular insulin. Patients should be observed for 3–4 days in the hospital; simultaneously, the mother/caregiver should be taught how to give insulin and how to monitor blood glucose. If the patient’s condition is stable, and the mother/caregiver is well-trained (i.e., familiar with the signs and symptoms of hypoglycemia and how to manage it). The patient can be discharged on twice-daily insulin injections, frequent home blood glucose monitoring, and close follow-up [8].

Intensifying insulin therapy using the basal-bolus concept, i.e., either multiple daily injections (MDIs) or continuous subcutaneous insulin infusion (CSII), has been shown to produce the best results regarding this respect [9–13]. Insulin is only successful as part of a comprehensive diabetes management plan that includes diet therapy [14], physical activity [15], education [16], rules for sick day management [17], and psychosocial support [18, 19]. Tight control with the goal of low HbA1c levels might increase the risk of severe hypoglycemia. However, there is evidence that cognitive impairment is more strongly related to long-standing hyperglycemia than to the frequency of severe hypoglycemic attacks during intensive therapy [20].

Newer insulin analogs can be classified into rapid-acting insulin and long-acting (basal) insulin analogs, and these newer analogs are replacing older insulin formulations, such as regular insulin and NPH, in the majority of clinics in Saudi Arabia. Rapid-acting analogs, such as Novorapid® (aspart), Humalog® (lispro), and Apidra® (glulisine) can be given immediately before meals because there is evidence that the rapid actions of these analogs not only reduce postprandial hyperglycemia but might also reduce nocturnal hypoglycemia [21]. These insulin analogs can be given after meals, particularly to children with unpredictable eating habits (e.g., infants and toddlers who are reluctant to eat). The benefit of the use of rapid-acting insulin analogs in children is related to the reported reduction in hypoglycemia rather than their effects on HbA1c [22].

Basal analogs exhibit more predictable insulin effects with less day-to-day variation compared to NPH insulin, and detemir (Levemir®) exhibits the lowest within-subject variability [23]. While the effects of basal analogs on HbA1c improvement are controversial, there is evidence that basal analogs reduce the rate of hypoglycemia and result in greater treatment satisfaction [22]. The use of external pumps (i.e., continuous subcutaneous insulin infusion, CSII) is increasing. The use of such pumps is acceptable and successful even in young infants when adequate education and support are provided [10, 12, 13]. The combination of intensive insulin therapy with glucose sensors with real-time displays is associated with a significant improvement in HbA1c compared to conventional blood glucose self-monitoring when the glucose sensor is worn continuously [24]. Prevention of DKA during insulin treatment warrants special attention as DKA is associated with considerable mortality and morbidity [24–26]. The potential for an increased risk of DKA due to the use of CSII is still under debate because some studies have found unchanged rates [27, 28], while an increase has been observed in a population with a low incidence of DKA [29].

2.2. Insulin dose adjustment

The majority of diabetic children require 0.5–1.0 units of insulin/kg/day. The American Diabetes Association recommends checking blood glucose four times per day; i.e., before meals and at bed time [5]. If the patient is on conventional insulin therapy with regular insulin and NPH, insulin dose adjustment depends on blood glucose monitoring. If the majority of morning blood glucose readings are elevated, the evening NPH may be increased by 10%. If the majority of the evening blood glucose readings are elevated, the morning NPH may be increased by 10%. If the
The majority of pre-lunch blood glucose readings are elevated, the morning regular insulin may be increased by 10%, and if the majority of bed time blood glucose readings are elevated, the evening regular insulin may be increased by 10%. The same concept can be applied in case of hypoglycemia. Insulin adjustment cannot succeed without proper diet therapy that involves carbohydrates counting or at least the exchange program [8]. If the patient is on intensive insulin therapy with MDIs, 50% of the total insulin dose may be given as basal insulin (detemir or glargine), and rapid acting insulin dose should be calculated based on the blood glucose readings and the amount of carbohydrates that will be eaten. The majority of diabetic children require one unit of rapid acting insulin for every 10–15 g of carbohydrates as a meal bolus and one unit of rapid acting insulin for each 50–75 mg/dl of blood glucose above the target as a correction bolus. These ratios must be adjusted based on pre- and 2-hour post-prandial/correction blood glucose readings. The target range for blood glucose control must be adjusted according to age. Old children should have target ranges from 80 to 130 mg/dl pre-meal and 100–140–180 mg/dl post-meal. Pre-sleep readings are recommended to be ≥120–150 mg/dl to avoid late night or early morning hypoglycemia [8].

2.3. Out-patient follow-up of diabetic children

Patient, parent and care-giver education should be reinforced. Adjustments of insulin dosages (due to changes in eating and exercise patterns outside the hospital and/or the honeymoon period) are needed. At each visit, home blood glucose readings should be discussed. Insulin doses, the method of injection and attacks of hypoglycemia should be evaluated. A complete clinical examination that includes weight, height and vital signs should be recorded. Laboratory evaluations should include annual thyroid function tests and tests for celiac disease even in the absence of classical symptoms. Celiac disease can cause growth failure and erratic glycemic control in diabetic patients. The prevalence of celiac disease in children with diabetes ranges from 2.9% to 5% [6]. The most accurate tests for celiac disease are the tests with anti-endomysial antibodies and anti-tissue transglutaminase antibodies. If these antibodies are not available, antigliadin antibodies should be used. Screening tests must be repeated after 4–5 years if the initial test result is negative or if there is clinical reason to reconsider the diagnosis of celiac disease. The conversion rate to positivity for celiac disease declines with time [6]. Other autoimmune diseases should be considered if signs or symptoms specific to a disorder are noted (e.g., adrenal insufficiency, gastric parietal cells and gonadal signs). Tests for microalbuminuria should be used to screen for renal impairment, and eye fundal examination should be used to screen for retinopathy after the age of puberty or 5 years after diagnosis. Lipid profiles may be examined after the age of 2 years [6].

2.4. Diabetic ketoacidosis (DKA)

The classic definition of DKA is a state of hyperglycemia >300 mg/dl, ketonemia, ketonuria, acidosis (pH < 7.3 and bicarbonate < 15 mmol/L) and glucosuria [30]. The goals of therapy include the correction of dehydration, acidosis and hyperglycemia and the identification and treatment of the precipitating factors. The patient should be admitted to a unit that has nurses who are experienced in the monitoring and management of DKA. Laboratory tests should include the following: CBC, electrolytes, creatinine, blood sugar, Ca, PO4, and venous blood gases. The two main parts of management are fluid replacement and insulin therapy. We typically keep the patient NPO until the bicarbonate level is >17 mmol/L. Patients with DKA usually exhibit degrees of dehydration of 5–10%. Except under unusual circumstances, do not give fluids in excess of 3000 ml/m² (i.e., twice maintenance) during the first 24 h. We usually recommend 1.5–2 times maintenance normal saline. K salt should be initiated if the patient is voiding well. Change the IV fluid to D5% 1/2 NS when the RBS reaches 270 mg/dl. For insulin therapy, use regular insulin with no insulin boluses. Start insulin infusion at 0.1 units/kg/h. Insulin infusion can be performed by mixing 50 units of regular insulin with 500 cc of normal saline. When the serum bicarbonate is above 15, the infusion rate should be reduced to 0.05 U/kg/h and stopped when the serum bicarbonate exceeds 18 years [8].

3. Sick day management

Intercurrent illnesses can cause high or low blood sugar [1]. All effects on patients’ glycemic control should be anticipated. Hypoglycemia is more commonly seen in tightly controlled patients, and hyperglycemia is more commonly seen in poorly controlled patients. We recommend that insulin not be stopped (especially intermediate-acting insulin and peak-less insulin) even if the patient is unable to eat; however, dose may be adjusted. Short-acting insulin can be stopped if severe hypoglycemia is anticipated. The patient must be examined for the presence of symptoms related to the underlying cause, such as infection (i.e., vomiting, sore throat, cough, and urinary tract infection), surgical abdomen (i.e., appendicitis), trauma or others. Frequent blood glucose monitoring is essential [1].

If the blood sugar is high (i.e., 200 mg/dl/11 mmol/L or more), check for urine ketones, if negative or mildly elevated, give 0.05–0.1 units of regular insulin/K; however, if the urine ketones are strongly positive (>2 or more), and repeated blood glucose readings are increasing, the patient should be moved to the emergency room for assessment. If the RBS is less than 70 mg/dl, the patient should eat easily digestible food or sugar-containing fluids. If the patient refuses to eat or exhibits repeated vomiting, hospital evaluation is recommended. Please note that urine strips measure aceto-acetate (AcAc), while blood strips measure beta-hydroxy butarate (BOHB). There may be a dissociation between urine ketones (AcAc) and blood (BOHB) concentrations, which might be increased to levels consistent with DKA even when the urine ketone test remains negative or indicates only trace ketonuria. Blood (BOHB) concentration measurement enables earlier identification and treatment of ketosis compared to urine ketone testing. During resolution of ketosis, blood (BOHB) normalizes sooner than urine ketones [8].
4. Diabetes management during surgery

Approximately 50% of all patients with diabetes will undergo surgery at least once in their lifetime. The management of a child with diabetes undergoing surgery aims to provide sufficient calories and insulin to prevent a catabolic state and hypoglycemia. Thus, pre-operative blood glucose control should be optimized, and frequent blood glucose monitoring is recommended. Major surgery should be delayed if possible when HbA1c >9%, fasting glucose >180 mg/dl (10 mmol/L), or post-prandial glucose >230 mg/dl (13 mmol/L). If the duration of DM is >5 years, screening for complications that might affect surgical risks is important. Aim for blood glucose levels of 110–180 mg/dl (6.0–10 mmol/L). Operations are best scheduled early on the list, preferably in the morning. We recommend giving the evening dose of NPH as usual, giving half of that dose in the morning and omitting the morning regular insulin if the patient is on an NPH/regular regimen or giving half of the evening dose of NPH as usual, giving half of that dose in the morning. We recommend giving (6.0)

5. Hypoglycemia management

Hypoglycemia can develop suddenly, and, if appropriate action is not taken, hypoglycemia can progress within a short period of time to unconsciousness and seizure. Hypoglycemia can lead to cognitive defects or even directly cause death, particularly in very young patients. It is difficult to precisely define hypoglycemia in the pediatric age group, and this condition is affected by many factors. It is safe to define hypoglycemia for pediatric age group as random blood sugar levels below 70 mg/dl (4 mmol/L) with symptoms or signs of hypoglycemia. We can divide hypoglycemic attacks into mild and severe attacks. The treatment of mild hypoglycemia should be provided via the oral route. The provision of easily absorbed forms of simple carbohydrate followed by complex long-acting carbohydrates is urgent for severe hypoglycemia (coma, agitation and convulsions). People who are either unconscious or seizing are unable to swallow, so the airway should be secured. The person should be placed on his/her side. Glucagon should be given immediately IM (0.5 mg for patients less than 5 years old and 1 mg for patients older than 5 years.). When the patient is awake, he should eat, and the RBS should be monitored. The treating doctor should be informed to allow for adjustments of the dose of insulin if needed. If glucagon is not available, glucose gel, jam, honey or dates should be given inside the buccal mucosa while patient is on his left side, and the patient should be transferred to the nearest health care center. On the way, if he awakens, give juice with added sugar. In the emergency room, the management of diabetic patients with severe hypoglycemia is to give 2–5 ml/kg of D10% IV followed by D10 in 1/2 normal saline at the maintenance rate and monitor the RBS. The dose can be repeated an addition time of the blood sugar did not increase to more than 100 mg/dl. If the patient continues to convulse or is in a coma despite an RBS ≥100 mg/dl, look for other cause. If the patient awakens and can tolerate oral intake, give small amounts of rapidly absorbed carbohydrate frequently. If well-tolerated additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or mealtime is imminent, and the IVF should be discontinued [1–3,8].

5.1. Diet therapy

The aims of nutrition therapy in type 1 DM are to optimize the nutritional status to promote normal weight, growth and development; to control diabetes to prevent severe hypoglycemia and/or prolonged hyperglycemic episodes; and to optimize blood lipid control.

Dietary recommendations should be based on healthy eating recommendations that are suitable for all children and adults [15] with special attention given to avoiding sucrose and highly refined sugar. The total daily energy intake should be distributed as follows: carbohydrates 50–55% with moderate sucrose intake (up to 10% total energy); Fat 30–35% with <10% saturated fat; and protein 10–15%. Carbohydrate counting is of great help for patients using peak-less insulin with ultra-short-acting insulin [8].

The aims of diabetes management include achieving optimal metabolic glycemic control, attaining normal growth and development, eliciting the best psychosocial adjustment, and individualizing diabetes care plans. These aims are best achieved through a multi-disciplinary diabetes team approach.

Conflict of Interest

The authors have no conflicts of interest to report.

References


