Anesthetizing the diabetic child: techniques, pitfalls, pumps, and new insulins

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There have been many recent advances in the management of diabetes mellitus. We will discuss the new types of insulin, their use, as well as newer monitoring methods available to patients and the physicians. In addition, we will review new modes of insulin administration. We will discuss perioperative management of children with diabetes in light of these changes.

Epidemiology

The prevalence of type 1 (insulin-dependent) diabetes in the US has remained stable for the past 15 years at 1 in 400–600 school-aged children, whereas the incidence of type 2 diabetes is increasing, especially among American Indian, Black, and Hispanic children and adolescents).[1] This increase in type 2 diabetes parallels the growing epidemic of obesity in American children, many of whom develop metabolic syndrome, presaging the development of type 2 DM.[2] Diabetes mellitus is the result of an absolute or functional deficiency of insulin production by the pancreas. In type 1 diabetes, this deficiency is caused by an autoimmune pathophysiologic process. Insulin deficiency results in abnormalities of glucose transport and storage and of lipid and protein synthesis. Over time, these metabolic derangements result in the vascular pathology that leads to end-stage complications of renal, cardiac, and eye disease—diseases that typically do not occur before adulthood. The anesthetic implications of type 1 diabetes in children differ from those in adults with the same disease, for whom the primary concern is the type and severity of end-organ disease.

Insulin therapy: what's new?

Children with insulin-dependent diabetes may be treated with various types of insulin on a daily basis to maintain tight glucose control, in combination with frequent blood glucose monitoring. Since 1982, most newly approved insulin preparations have been produced using recombinant DNA technology with laboratory-cultivated bacteria or yeast. This process allows the bacteria or yeast cells to produce complete human insulin. Recombinant human insulin has mostly replaced animal-derived insulin (e.g., pork and beef insulin) in diabetes management. Insulin products called *insulin analogs* are produced so that the structure differs slightly from human insulin (by one or two amino acids) to change onset and peak of action. Examples of analogs are human *lispro* (Humalog™)or *aspart* (Novolog™); both ultra-short-acting insulin that are given only 15 minutes before a meal. Their peak and duration of action parallel the glucose rise that results from carbohydrate ingestion. Insulin lispro was the first true rapidly acting insulin produced by recombinant DNA technology. The older form of short-acting insulin, regular insulin, when injected subcutaneously, produces hexamers and dimers, slowing the absorption. This aggregation is diminished with lispro, so it is more rapidly absorbed and has a shorter duration of action. The effect peaks in 30 min to 1 h and lasts from 3 to 4 h. Thus, the critical time during which hypoglycemia may develop is 0.5 to 1.5 h after administration. Because of their ultra-rapid onset, lispro or aspart are the insulins most commonly used in continuous subcutaneous insulin pumps.

Another new insulin is *glargine*, which almost mimics an insulin pump, providing a 24-hour, continuous low background level of insulin. The kinetics of some of the insulin preparations most commonly used in children are listed below.

Common Insulin Preparations

	Route	Onset	Peak	Duration
Ultra short-acting				
Lispro/Aspart	SC	15 min	30-90 min	3-4 hr
Short-acting				
Regular	IV/SC	30-60 min	2-3 hr	3-6 hr
Intermediate-acting				
NPH/Lente	SC	2-4 hr	4-10 hr	12-20 hr
Glargine (Lantus)	SC	1 hr	**NONE**	24 hr

Some children may be managed with an external insulin pump, which provides a low, background, subcutaneous infusion of insulin and the ability to give small boluses before meals. Most diabetic children administer insulin at least three times each day and check blood sugar at least four times each day. There have been recent developments linking blood glucose monitors with insulin pump bolus delivery as well as continuous blood glucose monitoring using subcutaneous sensors, but these technologies have not yet been widely implemented.

Type 2 diabetes in children and adolescents may be controlled with diet and exercise, but these children also may be taking metformin (Glucophage). Metformin was recently shown to decrease gluconeogenesis by directly modulating a liver protein (CBP), much as insulin itself does, rather than by overcoming the liver's decreased sensitivity to insulin as was formerly believed.[3]

Due to the effects of surgical stress on glucose homeostasis, insulin-dependent diabetic children are at risk for significant perioperative difficulties, even when their preoperative glucose control is good. Brittle or noncompliant diabetic patients have additional problems, including an increased risk of perioperative hypoglycemia or hyperglycemia, osmotic diuresis with resultant hypovolemia, and altered mental status. The physician must document the child's current insulin regimen, degree of compliance, preoperative glucose control, and risk of hypoglycemia from preoperative fast. Much of this information can be obtained from the patient's endocrinologist or by examination of the child's blood glucose monitoring log. A recent growth history can indicate how well controlled the child's diabetes may be. Coordination and cooperation among the patient, parents, pediatrician, endocrinologist, and anesthesiologist are essential if the goal of optimal perioperative glucose homeostasis is to be achieved. The anesthesiologist must particularly heed the recommendations of the diabetic child's primary physician.

Insulin is an anabolic hormone that promotes glycogen and triglyceride storage and protein synthesis. Present in small amounts even in the fasting state, it decreases glycogenolysis, gluconeogenesis, and lipolysis, with resultant ketogenesis and protein breakdown. Its complete absence at the time of surgery puts the patient in a state of starvation in which caloric intake is greatly restricted and substrate demands (e.g., for healing) are at their highest. The risk of a catabolic state is increased by the release of stress hormones, including catecholamines, cortisol, and glucagon. Perioperative insulin administration is essential to control glucose and to promote an anabolic state, which is most conducive to speedy healing and metabolic homeostasis. Preoperative anesthesia evaluation for elective procedures, informed by contemporaneous endocrine assessment of adequacy of glucose control, should be completed 7–10 days prior to the scheduled date of surgery to allow adjustment of treatment regimen or delay of procedure if control is not optimal. Rhodes and colleagues published a comprehensive review of concerns and perioperative management of pediatric diabetic patients; it features an extremely useful clinical practice guideline which incorporates both preoperative assessment and choice of preoperative insulin regimen.[4]

Preoperative Evaluation

The preoperative evaluation should include measurements of the hematocrit, electrolyte levels, and glucose levels. Hemoglobin A_{1C} level (i.e., glycosylated hemoglobin assay), although a useful index of long-term glucose control is unlikely to affect the anesthetic plan and is not a necessary preoperative test. If glycohemoglobin results are available, one must realize that different laboratories have different ranges for hemoglobin A_{1C} in normal subjects. Even in the same laboratory, the normal range may change from time to time. It is therefore important to know the laboratory's normal range to interpret results in diabetic patients. The normal range of hemoglobin A_{1C} is 4.5%–6.1%, but the normal range also varies with age.[3]

Several systemic abnormalities may be present in the child with diabetes mellitus. Nineteen percent of diabetic children have a vital capacity two standard deviations below the predicted mean value, suggesting the presence of restrictive lung disease.[5] No apparent association exists between decreased vital capacity and duration of diabetes or presence of other diabetic complications. Abnormal lung elasticity and thickening of the alveolar basal laminae have been reported in children with diabetes. Routine preoperative pulmonary function tests are not indicated in the asymptomatic diabetic child.

Decreased atlanto-occipital joint mobility, resulting in difficult intubation, may be present in a subset of adolescents with a syndrome of diabetes mellitus, short stature, and tightness of small joints of the fingers, wrists, ankles, and elbows.[6]

Perioperative Management

The primary determinant of management of type 1 diabetic patients in the immediate preoperative period is assessment of the plasma glucose level. Based on blood glucose level determined on arrival to the preoperative facility and prior to implementation of the regimens discussed below, glucose and/or insulin should be administered according to the scheme outlined in Table 2.

Table 2. Preoperative glucose and insulin management for diabetic patients

Blood glucose level	Management
<80 mg/dL	2 mL/kg D10W followed by glucose infusion
80–250 mg/dL	D5/0.45 NS or D10/0.45 NS solution at maintenance if insulin is to be administered; 0.9 NS if short case; no insulin
>250 mg/dL	Administer rapid-acting (lispro) or short-acting (regular) insulin SC to reduce blood sugar; use correction factor from patient's endocrine provider or 0.2 Unit/kg SC
>350 mg/dL	Consider canceling or postponing surgery, especially if ketonuria

NS, normal saline; SC, subcutaneously.

Various regimens for managing insulin therapy perioperatively have been proposed, three of which are discussed below and outlined in Table 3: classic regimen, subcutaneous infusion insulin pump, and IV insulin infusion.

Table 3. Protocols for perioperative insulin therapy

Regimen	Morning of surgery procedure
Classic regimen	Start IV infusion of 5% dextrose in 0.45% saline or Ringer lactate solution at 1500 mLm^2/day. Administer half of usual morning insulin dose as regular insulin. Check blood glucose before induction, during and after anesthesia
Continuous insulin infusion	Start IV infusion of 5% dextrose in 0.45% saline or Ringer lactate solution at 1500 mL/m^2/day. Add 1–2 units of insulin per 100 mL of 5% dextrose Starting insulin dose = 0.02 units/kg/hr Check blood glucose before induction, and during and after anesthesia
Insulin- and glucose-free regimen (for operative procedures of short duration)	Withhold morning insulin dose If indicated for procedure, give glucose-free solution (e.g., Ringer lactate) at maintenance rate. Check blood glucose before induction, and during and after anesthesia.

Essential to optimal management, regardless of regimen, is the scheduling of elective surgery for the diabetic child as early as possible in the day (first case) to minimize time that the patient must fast. Fasting interval should be the same as that recommended for non-diabetic patients: no solid food or milk for 8 hours, and clear liquids permissible until 2 hours before the scheduled time of surgery.[7] Children with diabetes should be encouraged to continue taking clear liquids until 2 hours before. If this is not possible, an intravenous (IV) fluid infusion should be started (described below). As recommended in adult patients with type 2 diabetes, Glucophage should be stopped 48 hours before surgery, based on reports of lactic acidosis in patients who remain on the drug and are in a fasting state perioperatively. Other orally administered medications (e.g., thiazolidinediones or sulfonylureas) may be continued through the day prior to surgery.

Although some investigators have recommended the withholding of preoperative sedation from diabetic patients to better monitor for signs of hypoglycemia, premedication is recommended in children. The use of agents such as benzodiazepines, opioids, or barbiturates does not alter glucose metabolism, and the failure to use such agents may elevate the blood sugar level due to anxiety, which causes a stress response with catecholamine release.

Classic Regimen

On the morning of surgery, one half of the usual dose of long-acting insulin (e.g., NPH) is administered subcutaneously after establishing an IV infusion of 5% glucose-containing solution at a rate of 100 mg/kg/hr of glucose (see Table 2). Plasma glucose concentrations should be maintained between 100 and 180 mg/dL. This target range is chosen because mild-to-moderate hyperglycemia (without ketosis) usually does not present a serious problem to the child, whereas hypoglycemia has devastating consequences. Hyperglycemia >250 mg/dL should be avoided because of associated mental status changes, diuresis, and subsequent dehydration, which can occur due to the hyperosmolar state. Hyperglycemia has been associated with poorer outcomes in patients at risk for central nervous system (CNS) ischemia, including those undergoing cardiopulmonary bypass.[8] Hyperglycemia has also been shown to impair wound healing and has adverse effects on neutrophil function in vitro.[9,10] When the classic regimen is employed, supplemental subcutaneous doses of short-acting insulin can be given on a sliding scale postoperatively to maintain the desired plasma glucose level. This regimen should be restricted to patients who are scheduled for short surgical procedures, after which they are expected to resume eating promptly.

Subcutaneous Infusion Insulin Pump

Increasing numbers of pediatric patients with type I diabetes are being managed with an external insulin pump that is capable of subcutaneous administration of both continuous and bolus doses of insulin. Such pumps afford excellent control, with changes in administration coordinated with eating, exercise, and stress. At this time, the proliferation of pumps from multiple manufacturers precludes the easy acquisition of knowledge and familiarity with their use in the perioperative setting. Some clinicians/institutions allow continued use of insulin pumps for short, uncomplicated procedures (e.g., <2 hours) [3] while most recommend transition to a continuous insulin infusion, as described below.[11] Recently The Children's Hospital of Philadelphia has implemented a “personal medical device” policy that is allowing children and parents to continue use of personal insulin pumps during short outpatient surgeries and for admissions other than DKA. Such a policy requires clear delineation of responsibility for the device and communication between parents, patient, nursing and medical staff. Sample guidelines for such a policy are outlined in Appendix 1.

Intravenous Insulin Infusion

If a long procedure or a prolonged period of postoperative fasting is anticipated, the continuous IV infusion of glucose and insulin may provide the best control. On the morning of surgery, a glucose infusion is begun at a maintenance rate of 100 mg/kg/hr, with an insulin infusion of 0.02–0.05 U/kg/hr "piggy-backed" into the glucose infusion. The glucose infusion can be D_5 or D_{10} in half-normal saline with 10–20 mEq/L of potassium chloride. These infusions should be begun 2 hours before surgery to minimize the duration of fasting and decrease the risk of the development of a catabolic state. Insulin is absorbed by IV bags and tubing. When the insulin solution is prepared, the first portion of the solution should be run through the tubing and discarded to saturate the sites in the tubing that bind insulin.[12] Blood glucose levels should be checked hourly for the first few hours, and adjustments of 0.01 U/kg/hr in the insulin rate should be made to keep the blood sugar in the acceptable range of 100–180 mg/dL. This continuous-infusion regimen has been shown to yield better control of glucose concentrations than does the regimen in which intermittent subcutaneous insulin is administered.[11] The administration of intermittent large IV insulin doses has no role, as it can result in large swings in glucose concentration (high and low) and a greater chance of lipolysis and ketogenesis. Patients with insulin pumps should have them turned off in the perioperative period and replaced by the continuous-infusion regimen, as most anesthesiologists are not familiar with the details of operation of such pumps. Fifty percent dextrose solution should be available for administration in case of the development of hypoglycemia; 0.1 g/kg of dextrose raises the blood glucose level by ~30 mg/dL.

The glucose and insulin should be infused through a dedicated IV cannula to enable it to be well regulated apart from the non–glucose-containing crystalloid solutions that are administered to replace blood or fluid losses—especially important if the maintenance glucose solution contains potassium. Many institutions avoid potassium-containing solutions to prevent their inadvertent rapid administration in the setting of rapid administration of fluid for blood or fluid replacement. Most investigators believe that lactated Ringers solution should not be used for blood and fluid replacement, as lactate is a glycogenic precursor and may result in higher blood glucose levels.

Alternative Procedure (Insulin- and Glucose-free Regimen)

For extremely brief procedures after which prompt resumption of oral intake is expected, an alternative protocol involves the administration of no insulin or glucose before or during surgery. When oral intake is established postoperatively, 40%–60% of the usual daily insulin dose is given.[13] Myringotomy with tube placement is an example of a procedure for which this regimen would be appropriate. The surgical procedure should be performed as the first case on the morning schedule to avoid prolonged fasting and excessive delay in insulin administration.

The most serious perioperative complication that can occur in the diabetic child is hypoglycemia. Common signs of low blood glucose levels include tachycardia, tearing, diaphoresis, and hypertension. In the anesthetized patient, these signs may be misinterpreted as caused by inadequate anesthesia. Because the clinical signs of hypoglycemia are masked by sedation or anesthesia, frequent (every hour) measurement of the serum glucose level is critical for the prevention of hypoglycemia, independent of the glucose-insulin regimen chosen. Glucose test strips, with or without the use of a reflectance photometer, provide quick, convenient, and reliable bedside blood sugar measurements to guide therapy. Postoperative insulin administration is determined by the time of resumption of oral or enteral feeding and by the postoperative blood glucose concentration. The endocrinologist and surgeon should be active partners in the choice of an appropriate insulin regimen because they will be responsible for monitoring glucose homeostasis after the patient leaves the recovery room. For day-surgery patients, contingency planning for insulin management and mechanisms for follow-up and consultation should be clearly defined for members of the care team and family.

Anesthetic Management

Regional or general anesthesia is appropriate for the child with diabetes mellitus. If tolerated with minimal sedation, regional anesthesia might be argued to offer the advantage of allowing for observation of the level of consciousness as a monitor of hypoglycemia. Practically speaking, most children require general anesthesia, even when regional techniques are employed. The ease and availability of point-of-care glucose determination from venous or fingerstick specimens obviate the need for monitoring of cerebral function.

Perioperative Management of Diabetic Ketoacidosis

Occasionally, diabetics require surgery for trauma or infection while in a state of ketoacidosis. Diabetic ketoacidosis includes hyperglycemia (plasma glucose concentration >300 mg/dL) with glucosuria, ketonemia (ketones strongly positive at greater than >1:2 dilution of serum), ketonuria, and acidemia (pH <7.30, or serum bicarbonate <15 mEq/L, or both). It is common for intraabdominal catastrophes with infection (e.g., appendicitis) to precipitate ketoacidosis. Foster and McGarry have succinctly summarized the pathophysiology of diabetic ketoacidosis.[14] The initiating event is usually cessation of insulin therapy or onset of stress that renders the usual dose of insulin inadequate. Glucagon, catecholamines, cortisol, and growth hormone levels rise. A catabolic state is produced as substrates are mobilized, resulting in hepatic production of glucose and ketone bodies, which causes hyperglycemia and ketoacidosis. Subclinical brain swelling nearly always occurs during diabetic ketoacidosis therapy, although most patients remain asymptomatic.[15] Fatalities from cerebral edema do occur, and some studies suggest that high rates of fluid administration early in treatment (>50 mL/kg in the first 4 hours) greatly increase the risk of herniation.[16] Studies using 4 L/m^2 for the first 24 hours followed by 1–1.5 times maintenance resulted in clearance of ketoacidosis equal to that in patients who were given more fluid, but a low but persistent incidence (0.35%–0.5%) of symptomatic cerebral edema remained.[17] Although the mechanism of cerebral edema has long thought to be because of osmotic cellular swelling, recent diffusion- and perfusion-weighted MRI studies have suggested a vasogenic mechanism.[18,19] The best methods to prevent the development of this devastating complication are administration of isotonic fluid only and frequent monitoring of serum osmolality (by direct measurement or calculation) to ensure that elevated osmolality is reduced gradually. Insulin therapy should be tailored to decrease the blood glucose concentration at a rate not greater than 100 mg/dL/hr. To prevent a more rapid decrease in blood glucose concentration, 5% dextrose and, if necessary, 10% dextrose should be added to the rehydration solution to slow the rate of fall, rather than decreasing the rate of insulin infusion.

Fortunately, the anesthesiologist is rarely called upon to administer anesthesia during this severe metabolic derangement. If an anesthetic is required during diabetic ketoacidosis, preoperative attention should be directed toward the correction of hypovolemia and hypokalemia, along with beginning an insulin infusion. Invasive hemodynamic monitoring may be indicated preoperatively to optimize the patient's fluid and electrolyte balance and to monitor the patient's hemodynamic status accurately. Surgery should not be delayed inordinately because it may be impossible to correct the metabolic derangements before the underlying source of infection or organ dysfunction is corrected. For patients with signs of cerebral edema, monitoring of intracranial pressure may be necessary. Unfortunately there has been a recent report of memory dysfunction in children with Type 1 diabetes with a history of DKA even in the absence of symptomatic cerebral edema.[20]

Appendix 1: Inpatient Pump Protocol

Goal: Encourage coordination of pumps for inpatient stay as long as patient/parent can care for and operate pump

Types of Admissions:

1. Surgery, injury, illness **other** than DKA
   - patient may use pump while inpatient
   - automatic consult if patient on another service
   - Fellow should confirm rates and ratios with parent to make sure usual dose and record accurately in chart
   - Have standard order written :
     i. "please continue Novolog via patient's pump at following rates"
     ii. "please give bolus to cover oral carbohydrates at ratio of __ units for every __ grams.
     iii. "give bolus for high glucose at standard meal times according to following scale………"
     iv. daily, resident should write order "continue insulin via pump at basal rate, carb coverage, and high correction as detailed above".
     v. to reduce errors, resident **does not** have to rewrite the whole scale, doses, rates, etc. each day
     vi. Blood sugar and ketone monitoring
       1. Check blood sugar before B, L, D, QHS, and 3 am
       2. Record all glucose monitoring on bedside flowsheet
       3. Check urine for ketones if blood glucose is greater than 240mg./dl.
       4. Call Endocrine Fellow if blood sugar high for 2 consecutive blood sugar tests or ketones present..
          a. if ketones present: Do not use pump to bolus. Change pump access site and give subcutaneous insulin injection with syringe. Recheck blood glucose and urine in two hours.
          b. if NO ketones: give correction bolus and recheck blood glucose in 2 hours.

2. Floor Issues

Have a summary sheet at bedside for the nurses reviewing insulin pump, basal rate, carb coverage, high correction dose, alternating sites, etc.

a. Nurses NOT responsible for hands on button pushing. Assure nurses that parent/patient will handle boluses. Nurses only have to document all boluses given. Nurses must be aware that bolus will be given and verify dose in conjunction with parents.
b. Parents responsible for responding to pump alarms

Parents not to give insulin bolus unless primary nurse aware.

3. DKA admissions
   - stop pump, insulin infusion
   - resume pump only after C02 > 18 and ketones < small

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