Perioperative Management of Infants and Children With Diabetes

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KEY POINTS

- Diabetes mellitus is the most common endocrine disorder in children.
- The perioperative period can disrupt glucose control, resulting in hypo- and hyperglycaemia.
- Multidisciplinary management is important to optimise glucose control and minimise complications.
- Insulin pump therapy is increasing in children, and anaesthetists should be familiar with management.
- Insulin pumps contain only rapid-acting insulin, and therefore, disconnection can lead to hyperglycaemia and diabetic ketoacidosis.

INTRODUCTION

Diabetes mellitus (DM) is an multisystem endocrine disorder caused by autoimmune-mediated destruction of insulin-producing beta-cells (type 1) or a relative lack of endogenous insulin combined with insulin resistance (type 2).[1] It is the most common metabolic disorder in childhood, thought to occur in approximately 497 000 children worldwide.[2] The national paediatric diabetes audit in the United Kingdom identified 28 443 children and young people with the condition: 96% with type 1 DM (27, 115 total) and 2.2% with type 2 DM (621 total).[3] Cystic fibrosis–related DM represents 0.6% of the total cases. The prevalence of children with type I DM in the United Kingdom is 195.4 per 100 000 of the general population. This is the largest in Europe. The incidence of type I DM is 25.9 per 100 000 of the general population in the United Kingdom, and in 2015-2016, this has increased compared with previous years.[4] This increase is greatest in younger children; however, the peak age of diagnosis remains 10 to 14 years old.[2]

AETIOLOGY

Type 1 DM is an autoimmune condition that results in the destruction of the insulin-producing beta-cells in the Islets of Langerhans in the pancreas. It is likely caused by the interplay of both genetic and environmental factors. The presence of HLA DR3 and DR4 antigens as well as a positive family history (30% of children develop type 1 DM if both parents are affected) increase the risk of disease.[5] The environmental factors leading to the development of autoantibodies in type 1 DM remain elusive, but it is thought that viral infections and dietary factors may play a role.[5]

Type 2 DM is being diagnosed increasingly in childhood, most frequently in early adolescence, around the time of puberty. Risk factors include obesity, female gender, ethnic minority, and a positive history in a first- or second-degree relative.[6,7]

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Genetic Defects of Beta-Cell Function	Maturity Onset Diabetes of the Young (MODY) Mitochondrial Disorders
Conditions affecting exocrine and endocrine pancreas function	Cystic fibrosis (20% develop DM by adulthood) Trauma Neoplasia Pancreatitis Partial or total pancreatectomy, eg, after surgery for hyperinsulinism
Steroid induced	Exogenous steroids, Cushing syndrome
Genetic syndromes	Turner, Down, Klinefelter, Prader-Willi, Wolfram

Table 1. Less Common Causes of Diabetes in Children

There are other less common causes of diabetes in children. These are shown in Table 1.

DIAGNOSIS

Symptoms in children suggestive of DM include polydipsia, polyuria, weight loss, and tiredness.[8] The World Health Organisation diagnostic criteria are either a fasting plasma glucose $>$7.0 mmol/L or a postprandial or post 75-g oral glucose load of $>$11.1 mmol/L.[9]

MANAGEMENT

The goal of glycaemic control is to minimise acute and chronic complications. Type 1 DM requires treatment with insulin. Type 2 DM can be managed by lifestyle interventions and oral hypoglycaemics, and it potentially requires insulin therapy.[2]

Type I DM Management

There are various insulin regimes available to mimic the body's normal endogenous insulin. Insulin can be categorised into rapid-, intermediate-, and long-acting forms depending on its duration of action. Most treatments use a combination of once- or twice-daily long-acting insulin in the morning and evening along with rapid-acting insulin with meals, also called a basal-bolus regime. The dose of insulin required depends on a variety of factors, including age, stage of puberty, weight, gender, daily routine, exercise, phase of diabetes, HbA1c and glucose monitoring, intercurrent illness, and nutritional status.[2,10] The amount given as a bolus depends mainly on the blood glucose measurement and amount of carbohydrate in the next meal. Most patients will use insulin-to-carbohydrate ratios (ICRs) to work out their insulin dose (for example, an ICR 1:10 means 1 unit of insulin for every 10 g of carbohydrates in the meal). Using this protocol, if someone is about to eat a meal that contains 40 g of carbohydrates and their ICR is 1:10, they would need to give 4 units of rapid-acting insulin. The insulin sensitivity factor (ISF) refers to the how much the blood sugar will drop in response to 1 unit of insulin; for example, an ISF 1:5 means that 1 unit of insulin is expected to bring the glucose level down by 5 mmol/L. Using the same example, if the blood glucose level is 15 mmol/L, a correction dose of 2 units of rapid-acting insulin would be given to correct the blood glucose level to a target between 4 and 7 mmol/L. The ICR will be adjusted by the diabetes team over time based on pre- and postprandial blood glucose readings. The ISF will roughly be equivalent to 100/(total daily dose of insulin) and will be adjusted by the diabetes team based on the blood glucose response to correction doses of insulin. There are glucose meters available with built-in calculators, which help to calculate the insulin bolus for a meal. The multidisciplinary team play an important role in the long-term management of children with diabetes. The team consists of diabetes nurse specialists, dietitians, and psychologists for support at diagnosis and ongoing titration of insulin around challenging periods such as adolescence. Multiple-dose insulin injection (MDI) regimes are demonstrated in Table 2.

Insulin Pump Treatment

The insulin pump is a battery-operated programmable device that is worn continuously and is the size of a pager. The pumps are external and deliver the insulin through a subcutaneously placed catheter that should be changed every 2 to 3 days. In a tube pump, the catheter will connect to the pump via plastic tubing, whereas in a patch pump, the pump including the subcutaneous catheter is stuck to the skin. A patch pump will have a separate hand set to operate the pump. Common examples of tube pumps include the Medtronic 640G (available on its own or with continuous glucose monitoring) and Accu-Chek insight. The Omnipod is an example of a patch pump.

Insulin pumps contain a reservoir of only rapid-acting insulin. The pump will deliver the background insulin as a continuous infusion rate ('basal rate' or 'basal insulin'); this replaces the long-acting insulin in MDI regimes. Insulin boluses are delivered by the push of a button, at meal times and in other times of hyperglycaemia, to correct high blood glucose levels. The basal rate can also be adjusted by the patient to account for different diurnal activities as well as to account for issues such as the 'dawn

Basal Bolus (Most Common)	Premixed Insulin Regimes: Twice-Daily Mix	Premixed Insulin Regimes: Three-Times-Daily Injections
Long-acting insulin once or twice daily in the evening/morning and rapid-acting insulin before meals	Biphasic (premixed rapid- and intermediate-acting insulin) injected before breakfast and before the evening meal	Biphasic insulin at breakfast, rapid-acting with evening meal, and basal insulin in the evening

Table 2. Examples of Multiple-Dose Injection (MDI) Regimes

phenomenon' (the increase in morning blood glucose levels caused by increased counterregulatory hormones).[11,12] The basal rate normally accounts for approximately 30% to 50% of the daily requirement of insulin. Since the pump contains only rapid-acting insulin, the pump should never be disconnected as blood glucose levels may rise rapidly.

Similar to some of the blood glucose meters, insulin pumps will have built-in calculators with ICRs and ISF. The patient will enter their blood glucose level and amount of carbohydrates in grams into the pump.

National Institute for Health and Care Excellence, UK (NICE) guidelines recommend using insulin pumps for children >12 years old whose diabetes is not well controlled with MDI regimes (HbA1c >8.5% or 69 mmol/mol) or who have unpredictable and frequent episodes of hypoglycaemia affecting quality of life. Children <12 years old can be considered for pump therapy if MDI is not considered appropriate.[13]

Glucose Monitoring

Continuous glucose monitors (sensors) measure the interstitial glucose every 3 to 5 minutes. There is a lag time of about 5 minutes between changes in blood glucose and the glucose result in the interstitial fluid. A sensor can be used with either pump or MDI regimes. The sensor readings become less reliable at extremes of blood glucose, particularly at low glucose readings. In the perioperative period, it is recommended that capillary glucose be measured, using an electronic blood glucose meter, because of changes in fluid balance, perfusion, and glucose control.[14] Some insulin pumps have a (predictive) low-glucose suspend feature, in which the insulin pump will stop administering insulin if the sensor predicts the glucose will reach a certain low level in the next few minutes, and it will resume insulin delivery when the sensor detects a rise in the glucose levels. This feature is predictive in that it looks at the rate of change of glucose levels and extrapolates the curve. In the future, additional features may become available, such as the ability of the pump to increase insulin delivery in response to high sensor glucose readings.

Complications of Insulin Pump Therapy

The anaesthetist should be aware of the infrequent but specific complications of insulin pump therapy that can occur in the perioperative period. These can be related to the catheter, patient, and the pump. Catheter-related issues include displacement, blockage, or kinking. Patient problems include reactions and infections at the catheter site. The pump itself can also malfunction, and this is more likely if it is in the surgical field.[11] An alternative would be to use a sliding scale instead of the pump if there are concerns.

It is important for the anaesthetist to consider compatibility of the insulin pump with other medical equipment.[12] This is demonstrated in Table 3.

Medical Equipment	Recommendations
Magnetic resonance imaging/computed tomography	Remove pump and cannula (if metal) Discuss management with paediatric diabetes team
X ray	Cover pump with lead apron
Ultrasound	Safe
Diathermy	Place pump site far from diathermy Use bipolar where possible Risk of electromagnetic pump malfunction
Laser	Safe
Cardiac catheterisation	Remove pump and cannula (if metal) Discuss management with paediatric diabetes team

Table 3. Compatibility of Insulin Pumps With Different Types of Medical Equipment

Solid Food 6 hours	Breast Milk 4 hours	Clear fluids 1 hour

Figure 1. Common practice for starvation times for theatre in the United Kingdom.

Type 2 DM Management

Children with type 2 DM are managed in a similar way to adults. Initial management is through lifestyle factors of diet, weight loss, and increased exercise. HbA1c measurements are used to assess good control, with the aim for an HbA1c level of $<$7%. If this is not achieved, oral hypoglycaemics are added, with metformin first line. Most patients will eventually require insulin therapy in their lifetime.[15]

PERIOPERATIVE MANAGEMENT OF DM

The combination of fasting, emotional stress, and surgical stress can make glycaemic control difficult in the perioperative period. Therefore, NICE guidance recommends multidisciplinary perioperative management of children with diabetes involving the surgical team, anaesthetists, ward staff, and diabetes team. In addition, centres providing paediatric surgery for children with diabetes should have written protocols on perioperative management. Elective surgery should be considered only when HbA1c is $<$8.5% (69 mmol/mol). Children with diabetes should ideally be scheduled first on the list to reduce the starvation period.

Normal fasting guidelines apply to children with DM, with the key being to keep fasting to as short a time as possible. See Figure 1.

Perioperative management should consider the type of surgery, time of day of surgery, expected fasting duration, and the current diabetes treatment regimen.

Capillary blood glucose monitoring ideally should be performed every 30 to 60 minutes during the perioperative period until normal oral intake and insulin regimen is resumed. Less tight blood glucose control is particularly important in children in whom the risk of hypoglycaemia is greater because of lower glycogen stores. Hyperglycaemia can increase infection postoperatively and the length of hospital stay. Recommended perioperative blood glucose levels are 5 to 11 mmol/L. See Figure 2.

There are different ways to modify a child's treatment regime prior to surgery. One method is to classify the type of surgery as minor or major. This depends on the duration of the operation and the period of starvation. Minor is surgery expected to last $<$30 minutes and only 1 missed meal. Major surgery is expected to last $>$30 minutes with more than 1 missed meal in which normal oral intake will not resume with the next meal. Whilst a useful method, not all cases will fit neatly into these categories, for example, day-case surgery lasting longer than 30 minutes with only 1 meal missed, necessitating clinical judgment to be employed in individual cases.

Perioperative Management of Children With Type I DM Having Minor Elective Surgery[2,14]

The principles for managing children with type 1 DM having minor elective surgery is to continue the long-acting insulin regardless of whether the surgery is in the morning or afternoon. The short-acting component is altered depending on whether the surgery is morning (omitted or delayed until after surgery and the child has resumed normal oral intake) or afternoon (where the child is allowed breakfast, it can be given as usual).

For children on premixed insulin (rapid- and intermediate-acting insulin is mixed together), the morning dose is omitted or delayed for morning surgery. For afternoon surgery, half the dose of the rapid-acting component of the premixed insulin should be administered in the morning as rapid-acting insulin only.

An example is if a patient's usual morning dose is 10 units of Novomix 30 or Humulin M3, then the usual fast-acting component is $3/10 \times 10 = 3$ units of rapid-acting insulin (eg, insulin aspart [NovoRapid], Humalog lispro [Humalog], glulisine [Apidra]); half $=$ 1.5 units of rapid-acting insulin only. The intermediate insulin dose is omitted. See Figure 3

Perioperative Blood Glucose Target
5 – 11 mmol/L
Capillary blood glucose should ideally be measured every 30 minutes – 60 minutes
Following an episode of hypoglycaemia <5 mmol/L it should be re-checked after 15 minutes

Figure 2. Perioperative blood glucose target range.

Figure 3. Perioperative management of children with type 1 DM having minor elective surgery.

Perioperative Management of Children With Type 1 DM Having Elective Major Surgery[2,14]

The principle for children on basal bolus regimes having major elective surgery in the morning is either to admit the night before or on the day of surgery (depending on the institution), continue the long-acting insulin, omit the rapid-acting morning insulin, and start intravenous (IV) fluids and an IV insulin sliding scale.[14] Patients on insulin pump therapy should have the usual rapid-

Blood Glucose, mmol/L	Sliding Scale Rate, U/kg/h
<4	0.01 and 2 mL/kg 10% IV dextrose
4-6.9	0.02
7-9.9	0.03
10-12.9	0.04
>13	0.05

Table 4. Blood Glucose Measurements and Corresponding Insulin Sliding Scale Rates

acting basal rate continued until 3 to 6 hours before surgery, at which point they should be switched to IV fluids and an IV sliding scale, with the morning rapid-acting insulin bolus omitted. Premixed regimens should omit the morning dose of insulin. IV fluids and IV sliding scale should be started on admission to hospital.

Patients on a basal bolus regime scheduled for afternoon surgery should continue their long-acting insulin, have their usual dose of morning rapid-acting insulin (depending on carbohydrate content), and start IV fluids and an IV insulin sliding scale on admission to hospital. Patients on insulin pump therapy should continue the usual rapid-acting basal rate until 3 to 6 hours before surgery, at which point they should be switched to IV fluids and an IV sliding scale. The usual morning rapid-acting bolus should be given. Premixed regimens should give half the morning dose of rapid-acting insulin. The intermediate insulin dose is omitted, and IV fluids and IV sliding scale are started on admission to hospital. See Figure 4.

Insulin Sliding Scale[14]

Dilute 50 units of soluble insulin (Actrapid) in 50 mL 0.9% saline (1 U/mL).

Monitor blood glucose every 30 to 60 minutes perioperatively until the child is able to resume normal oral intake.

If blood glucose is <4 mmol/L, stop the IV sliding scale for 10 to 15 minutes. Give 2 mL/kg IV 10% dextrose and re check blood glucose in 15 minutes. Restart the IV sliding scale when blood glucose is >4 mmol/L.

The maintenance fluid of choice is 0.45% saline with 5% dextrose. If sodium is low, 0.9% saline can be used. When blood sugar is <4 mmol/L, use 10% IV dextrose. When blood sugar is high, 5% dextrose should still be included, but the rate of insulin should be increased, as per Table 4. Electrolytes should be monitored when the sliding scale is ongoing, and 20 mmol/L potassium chloride should be included in maintenance fluids. This can be increased if potassium levels decrease.

Table 4 shows how to adjust the sliding scale rate based on blood glucose measurements.

Perioperative Management of Children With Type 2 DM Having Elective Surgery[2,14]

The principle of management of children with type II DM having elective surgery is to stop oral hypoglycaemics on the day of surgery, apart from metformin, which should be discontinued 24 hours prior to the operation. See Figure 5.

Perioperative Management of Children Having Emergency Surgery[2,14]

Children with diabetes presenting for emergency surgery should have their blood ketones measured as well as a venous blood gas to check for diabetic ketoacidosis (DKA). DKA guidelines should be followed if diagnostic criteria are met. For children not in DKA, IV fluids and a sliding scale should be started.[16] See Figure 6.

Perioperative Management of Hypoglycaemia[2,14]

Most paediatric diabetes teams define a blood glucose level <4 mmol/L as hypoglycaemia. It is, however, safer to use a threshold of 5 mmol/L in the perioperative period. Blood glucose levels <5 mmol/L can be treated with oral or IV glucose. For children without IV access, intramuscular glucagon can be given. Blood glucose levels should be rechecked after 15 minutes. See Figure 7.

Perioperative Management of Hyperglycaemia[2,14]

Children with hyperglycaemia (blood glucose >14 mmol/L) should have blood ketones checked to rule out DKA. Most families and hospitals have point-of-care ketone meters. This should be managed as per DKA guidelines if diagnostic criteria are met. For children not in DKA, IV insulin and fluids should be started as per the sliding scale. See Figure 8.

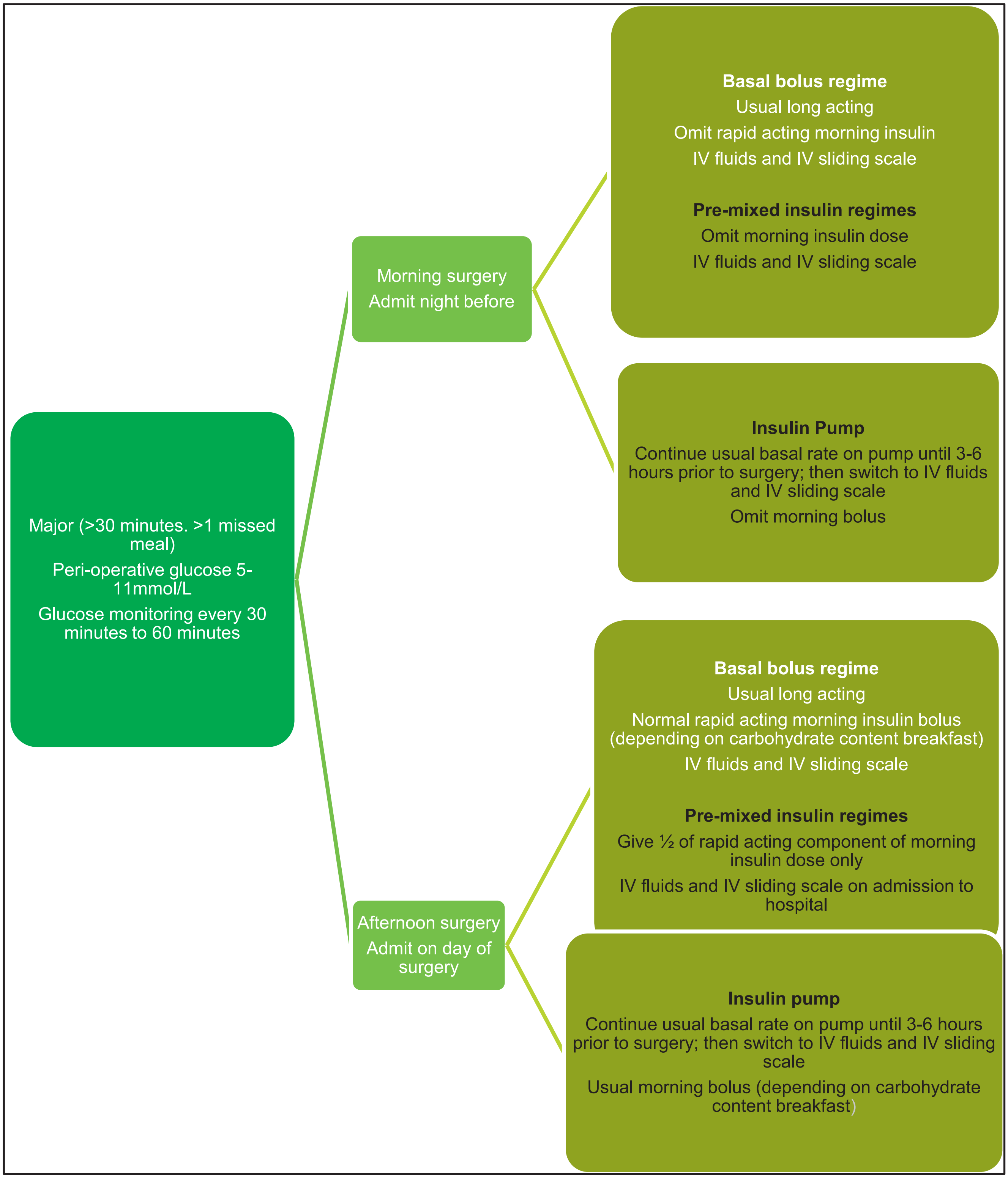

Figure 4. Perioperative management of children with type I DM having elective major surgery.

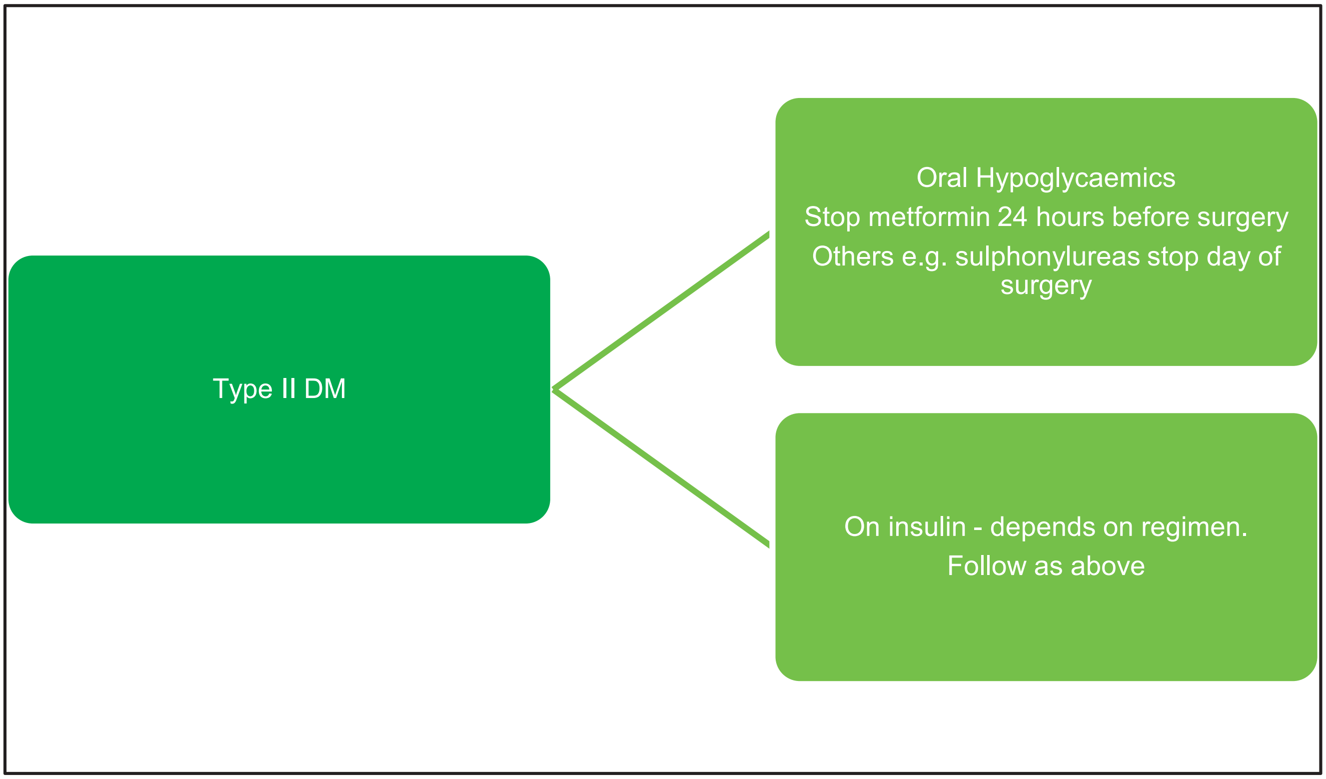

Figure 5. Perioperative management of children with type 2 DM having elective surgery.

The Concept of Open- and Closed-Loop Systems

An open-loop system is one in which the patient delivers the insulin to themselves at different times of the day. The 2 main open-loop systems are MDI and insulin pump therapy (as discussed above).

Future research to improve glucose control and insulin delivery is looking at closed-loop systems. A closed-loop system is one in which insulin delivery and blood glucose control occur with minimal patient involvement. Ideally, an external device

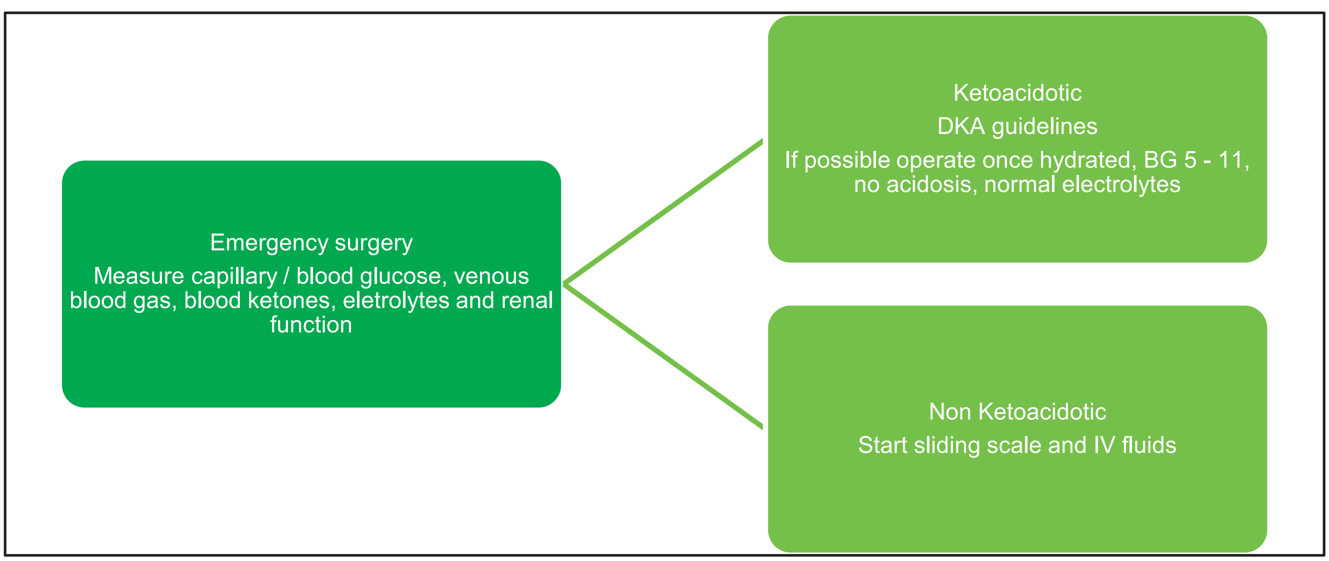

Figure 6. Perioperative management of children having emergency surgery.

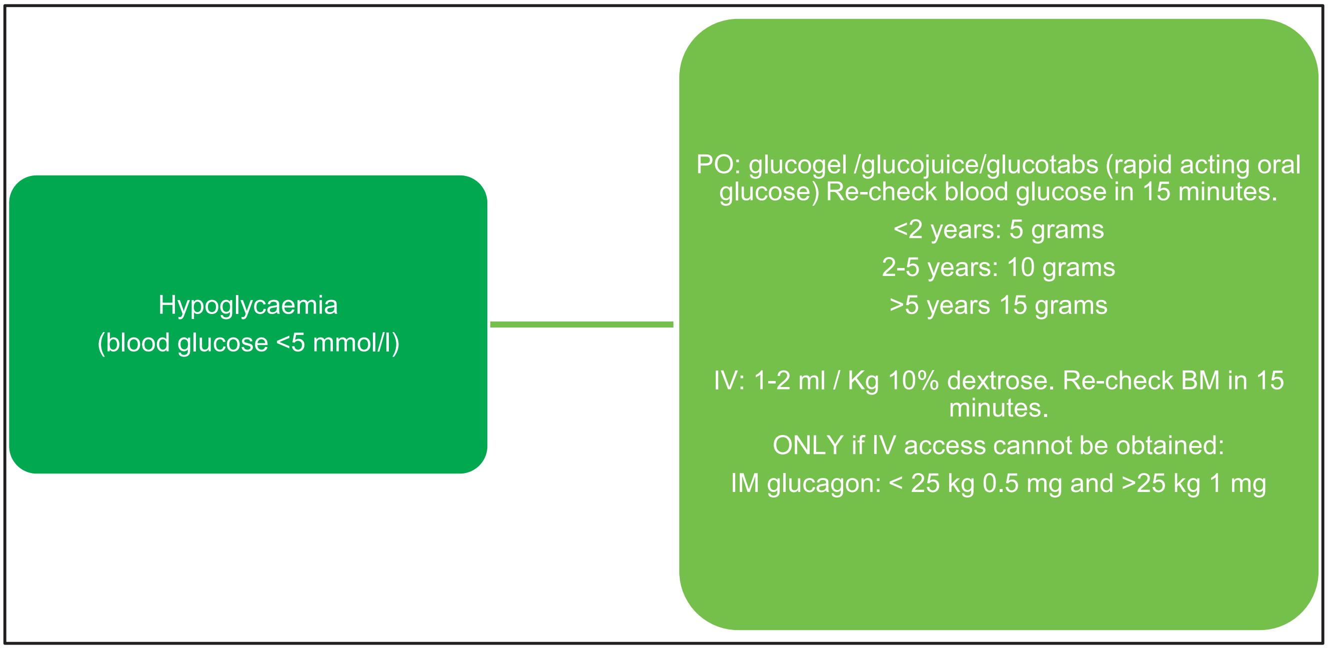

Figure 7. Perioperative management of hypoglycaemia.

would not be needed, and the requirement for injections would be reduced or eliminated completely. Examples of methods that could create a closed-loop system include pancreatic transplantation, restoration of insulin secretion in the original pancreas, transplant of encapsulated islet cells from a healthy donor pancreas, or creation of an 'artificial pancreas.' An artificial pancreas is based on algorithms and includes a glucose sensor under the skin and a wireless connection to the insulin pump.[17–19]

Research is currently ongoing in this area.

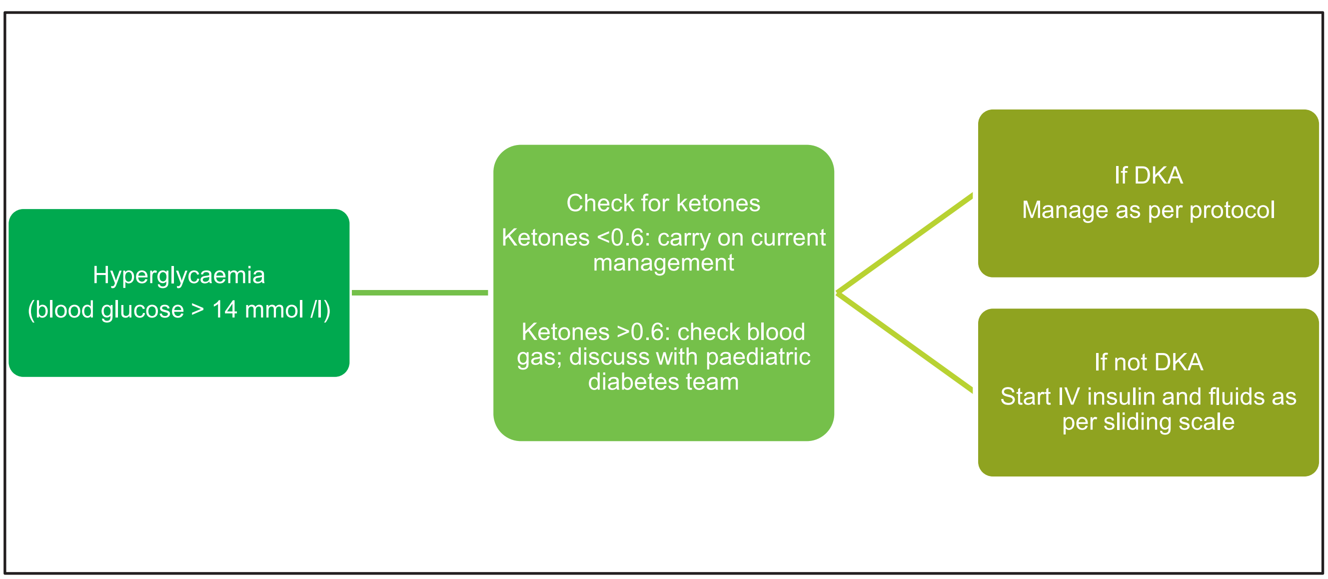

Figure 8. Perioperative management of hyperglycaemia.

SUMMARY

DM is the most common metabolic disorder in children, and its incidence is increasing. The perioperative period is a challenging time, with the potential for disruptions to glucose control. The anaesthetist is an important part of the multidisciplinary team involved in optimising diabetes management around the time of surgery, with an individualised plan depending on the type of surgery, diabetes treatment regime, and medical comorbidities. The aim is to allow normal oral intake and diabetes management to resume as soon as possible postoperatively. It should also be recognised that the above are ideal recommendations that may not always be possible in less-resourced settings, for example, considering difficulties with storing insulin in refrigerators and equipment availability required to facilitate the frequent monitoring of blood glucose.

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