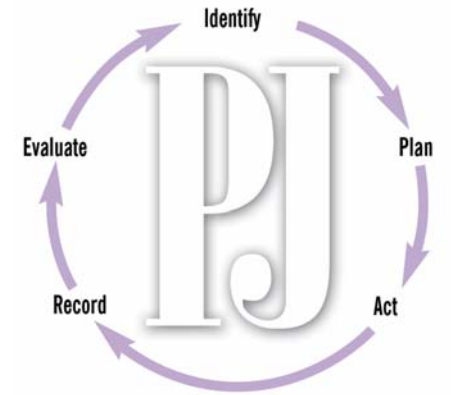
Peri-operative care and diabetes

In the second article in our series, **Mohamed H. Rahman** and **Jane Beattie** look at care of patients with diabetes mellitus who are to undergo surgery



Identify knowledge gaps

1. What special considerations are needed for patients with diabetes mellitus undergoing surgery?
2. Can you describe the differences between the surgical management of patients with type 1 diabetes and patients with type 2 diabetes?
3. What are the GLIK (Alberti) and sliding scale insulin regimens?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "clinical pharmacy" (see appendix 4 of "Plan and record").

Brian Yarvin/SPL

Maintaining optimal blood glucose levels helps avoid peri-operative complications

Patients with diabetes are considered to be at an increased risk of peri-operative complications and mortality. For example, they are prone to acute metabolic problems, complications due to renal and vascular manifestations of their diabetes (eg, impaired renal function and cardiovascular disease) and delayed wound healing. They are also at an increased risk of post-operative infections. Peri-operative care of patients with diabetes focuses on maintaining optimal blood glucose levels and avoiding these complications.

Hyperglycaemia

Surgery causes considerable stress in patients. In response, the neuro-endocrine system stimulates glycogenolysis (breakdown of glycogen to glucose) and gluconeogenesis (glucose synthesis from non-carbohydrate sources) via counter-regulatory hormones such as catecholamines, cortisol, growth hormone and glucagon. These hormones can antagonise the effects of insulin and cause insulin resistance. Hence, other important actions of insulin, such as suppression of lipolysis, proteolysis, fatty acid oxidation and ketone body formation, and stimulation of glycogenesis (conversion of glucose to glycogen) are also reversed. Fundamentally, the metabolic response to stress is characterised by decreased anabolism and increased catabolism.

People who do not have diabetes usually produce enough insulin to counteract the hyperglycaemic response to stress and can, therefore, maintain glucose homeostasis. This compensatory mechanism is absent in type 1 diabetes, and complications, such as diabetic ketoacidosis (DKA) can result. Although acute hyperglycaemic complications are less common in type 2 diabetes, if prolonged severe hyperglycaemia is left untreated, such patients may progress to a non-ketotic, hyperosmolar state (NKHS).

DKA occurs as a result of insulin deficiency and counter-regulatory hormone excess, and is characterised by hyperglycaemia, hyperosmolarity, severe dehydration, metabolic acidosis and raised ketone levels. Hyperglycaemia arises due to increased hepatic glucose output and inhibition of peripheral glucose utilisation. It leads to glycosuria, increased urinary loss and, eventually, dehydration. More importantly, insulin deficiency results in mobilisation of free fatty acids from adipose tissue and this provides the substrate for ketone production in the liver. Ketones are excreted by the kidneys and, initially, buffered in the blood. However, once the system fails (ketone bodies produced by beta-oxidation of free fatty acids exhaust extracellular and cellular acid buffers), metabolic acidosis develops. Severe cases can be fatal.

NKHS is less common than DKA but can be more sinister. It also occurs through a combination of insulin deficiency and counter-regulatory hormone excess. Any endogenous insulin that is available stops ketone production, but the quantity is insufficient to prevent worsening hyperglycaemia. The net result involves development of severe dehydration, hyperosmolarity and electrolyte derangement but no acidosis. The presence of insulin in NKHS, alone, does not explain the difference between DKA and NKHS and several theories have been postulated.

The detailed pathogenesis and treatment of DKA and NKHS are beyond the scope of this article.

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Hypoglycaemia

Conversely, hypoglycaemia can also occur in the peri-operative period due to the omission of food, residual effects of long-acting hypoglycaemic drugs or inappropriate administration of insulin. Symptoms are usually adrenergic (eg, sweating and tremor) and typically occur at blood glucose levels below 3mmol/L. If untreated, the condition can progress to coma or death.

Pre-operative preparation

Studies have shown the benefits of maintaining normoglycaemia in people with diabetes after stroke or myocardial infarction. Similarly, critically ill patients receiving insulin to achieve normoglycaemia have improved survival rates. Diabetes UK recommends that people with diabetes aim to keep their preprandial blood glucose levels between 4 and 7mmol/L and their postprandial levels no higher than 10mmol/L. However, many people with diabetes struggle to keep within the recommended limits. A measure of total glycosylated haemoglobin (HbA_1), or a specific fraction (HbA_{1c}), gives an indication of glycaemic control over the preceding two or three months.

People with well-controlled type 1 diabetes may be admitted to hospital a day before surgery, but patients with poor control will need to be admitted at least two or three days before their operation to ensure satisfactory control of fasting and postprandial blood glucose levels. Where emergency surgery is needed, a pre-operative blood glucose level below 10mmol/L should be aimed for, but this is not always achievable.

Management plan

The management of patients with diabetes who are to undergo surgery must take into account the type of diabetes, current treatment, metabolic status, pre-existing cardiac or renal problems and the proposed surgery and anaesthetic technique. Where possible, patients with diabetes should be operated on in the morning, to reduce the fasting period before surgery.

To minimise the risks of hypo- or hyperglycaemia while the patient is not eating normally, blood glucose levels should be monitored regularly and abnormalities acted upon quickly. Regular monitoring is also essential because symptoms of abnormal glucose levels are unrecognisable in an anaesthetised patient.

Panel 1: The GLIK regimen at RLUH

Glucose infusion bags used at the Royal Liverpool University Hospital (RLUH) include:

- 500ml of glucose 10 per cent without potassium, to which insulin is added
- 500ml of glucose 10 per cent with 10mmol potassium, to which insulin is added (unlicensed, special preparation)
- 500ml glucose 10 per cent with 20mmol potassium, to which insulin is added (unlicensed, special preparation)

Starting GLIK At RLUH, initially, for patients with a BMI of 20–30, 10 units of soluble insulin (eg, Humulin S) are added to a 500ml bag containing 10 per cent glucose and 10mmol potassium. The infusion is run at 100ml/h, aiming to give 2–3 litres of fluid a day. For patients with a BMI >30 or greater insulin requirements, a higher dose of insulin is considered (eg, 16 units). Similarly, patients with a BMI <20, or those who usually require less than 20 units of insulin per day, are considered for a lower dose (eg, 6–8 units).

Maintaining blood glucose between 5 and 12 mmol/L Blood glucose is monitored hourly. If it falls below 5mmol/L the infusion bag is changed, and the amount of insulin added to the new bag is reduced by 4 units. If it rises above 12mmol/L, the bag is changed and the insulin added is increased by 4 units. Patients requiring high doses of insulin pre-operatively may require greater increases in the insulin dose (eg, by 6–8 unit increments). This is common in patients who are obese, have liver disease or an infection, or are on long-term corticosteroid therapy. If blood glucose is maintained between 5 and 12 mmol/L, the bag is not changed.

In the event of a significant hypoglycaemic event (symptomatic or blood glucose level below 4mmol/L), the RLUH policy recommends that the insulin-containing infusion is not stopped but our guidelines for treating an acute hypoglycaemic event are initiated.

Plasma potassium A new infusion bag is also required each time plasma potassium levels fall outside the desired range. At our hospital, we usually use glucose 10 per cent with 10mmol potassium, unless contraindicated. This bag is continued as long as plasma potassium is maintained between 3.5 and 5mmol/L.

If plasma potassium falls below 3.5mmol/L, the infusion bag is changed to one containing glucose 10 per cent and 20mmol potassium. Similarly, if the plasma potassium exceeds 5mmol/L, a bag with no potassium is used. Plasma potassium varies according to the effect of insulin, fluid balance (dehydration can cause a shift of potassium from the intra- to extra-cellular space) and acid-base balance.

Rarely (eg, in fluid-restricted patients with persistently low plasma potassium), a higher, unlicensed strength (40mmol/ 500ml) is used. This unlicensed, special preparation is restricted to areas where electrocardiogram monitoring facilities are available, eg, high dependency units, intensive care units and post-operative critical care units. Central venous access is also recommended for administration of such high concentrations of potassium.

We recommend that plasma potassium is checked at four hours initially, then at eight hours and then, if the patient's condition is stable, every 24 hours.

Managing patients with type 2 diabetes Patients with diet-controlled type 2 diabetes do not usually need any specific intervention before surgery. Patients taking short-acting sulphonylureas (eg, gliclazide or tolbutamide), should omit their usual morning dose on the day of the operation. This helps to avoid the hypoglycaemia that can result from being "nil by mouth" (NBM). Longer-acting sulphonylureas (eg, glibenclamide) are stopped two to three days before surgery to prevent peri-operative hypoglycaemia and may be converted to either a short-acting sulphonylurea or insulin.

The manufacturers of metformin advise that the drug should be stopped 48 hours before elective surgery with general anaesthesia (for radiologic studies, discontinue metformin before or at the time of the test) and should not be resumed for at least 48 hours post-operatively. This is a precaution against lactic acidosis.

Patients who usually take oral hypoglycaemic agents may require insulin therapy in the peri-operative period if their diabetic control is poor. These patients may be converted to a short-term, subcutaneous (sc) insulin regimen or managed with intravenous (iv) insulin (see below). For major surgery, even those with previously good diabetic control may need to be managed with iv insulin therapy, especially if a prolonged NBM period is expected or if the stress of surgery has led to unacceptable blood glucose levels.

Managing patients with type 1 diabetes Patients with type 1 diabetes will have their usual sc insulin changed to an iv regimen because the latter has a more predictable absorption profile and allows easier dose adjustment. The key principles of management on the day of surgery include:

- Omitting breakfast
- Omitting the usual morning sc insulin
- Converting sc insulin to an appropriate iv regimen — eg, an infusion consisting of glucose, insulin and potassium (referred to as GLIK or sometimes as an Alberti regimen) or a sliding-scale insulin regimen

Glucose is given by infusion to avoid hypoglycaemia with potassium supplementation, if needed, because insulin therapy enhances movement of extracellular potassium into cells. Hypokalemia should be prevented because it can lead to arrhythmias, cardiac arrest and even death.

Some doctors recommend omitting the night-time dose of sc insulin on the night before surgery (especially intermediate and long-acting insulin), but this is usually unnecessary and can result in hyperglycaemia. It may be more appropriate to switch these patients to an iv insulin regimen earlier, particularly if there is poor control or the patient is receiving a long-acting insulin analogue such as insulin glargine. Patients who are not converted to iv insulin until the day of surgery and receive their long-acting insulin the night before must be monitored for hypoglycaemia.

The GLIK regimen The GLIK regimen is suitable for patients who are likely to remain NBM for less than 48 hours. The basic principle is to administer a single, combined infusion of soluble insulin and glucose. To avoid hypokalaemia, the infusion also contains potassium, adjusted to plasma levels. GLIK is not as flexible as the sliding scale regimen, but it is safe and easy to manage on a busy surgical ward. The glucose component can be either 5 or 10 per cent, which should prevent catabolism, starvation ketosis, and insulin-induced hypoglycaemia.

The initial amount of insulin added to the infusion bag must be decided for each individual and may be guided by body mass index (BMI) and usual pre-operative insulin requirements. However, in most hospitals a standard regimen is used, which is then adjusted according to subsequent blood glucose and potassium measurements. Regimens vary between hospitals, but the basic principles remain the same. The GLIK regimen used at our hospital is described in Panel 1 (p324). The main disadvantage of GLIK is that a new bag is needed every time blood glucose or plasma potassium falls outside the desired range.

Sliding scale insulin therapy The sliding scale insulin regimen is often used instead of GLIK and is a suitable alternative for patients likely to remain NBM for a prolonged period. It provides more titratable blood glucose control than the GLIK regimen, and has shown to provide a more stable blood glucose control in the peri-operative period. The sliding scale insulin regimen consists of a continuous iv insulin infusion, which is adjusted on the basis of blood glucose measurements, according to a prescribed (sliding) scale. Fluids (ie, glucose and potassium) are infused separately at a fixed concentration and rate. For example, glucose 5 per cent with 20mmol/L potassium running at 125ml/h.

The rate of insulin is fixed for a given range of blood glucose measurements, eg, 'The Oxford handbook of clinical medicine' states that for a blood glucose level of 5.0–10.0mmol/L, intravenous insulin should be given at a rate of 1 unit/h.[1] Different hospitals use different fixed ranges. Panel 2 decribes practice at RLUH. When setting up an insulin infusion it is important to flush the infusion apparatus with the glucose-potassium solution (run off 50 ml and discard) to prevent adsorption of insulin to the plastic tubing.

Patients with larger fluid requirements (eg, those with significant blood loss or burns), can be given additional fluids (eg, sodium chloride 0.9 per cent or colloid solutions) as appropriate. In patients who remain NBM for prolonged periods, a sodium chloride infusion may need to be run concurrently or alternately with the glucose infusions to avoid hyponatraemia. Fluids containing lactate (eg, Hartmann's solution) are usually avoided because they can exacerbate hyperglycaemia. The lactate present in this solution is used for gluconeogenesis especially in starved or catabolic patients.

The sliding scale system is more flexible than the GLIK regimen, because the rate of insulin infusion can be adjusted independently of the rate of glucose infusion. The main disadvantage is that there is a risk of hypo- or hyperglycaemia if one of the infusion lines fails. There is also potential confusion over infusion rates where two lines and two infusion devices are being used simultaneously. Whichever method is chosen, successful control of peri-operative blood glucose depends up on familiarity of ward staff with their hospital regimen, and the strict measurement of blood glucose levels at regular intervals.

Therapy after surgery After surgery, sulphonylureas are restarted at the patient's pre-operative dose, once he or she is able to eat and drink normally. Some doctors recommend that only half the usual dose should be taken on the first post-operative day, although this is not often seen in practice. The dose given should also be guided by the patient's blood glucose level during the peri-operative period.

Intravenous insulin is continued until the patient is able to tolerate his or her first post-operative meal. Therapy can then be converted to a regimen involving three daily injections (20–30 minutes before breakfast, lunch and supper time) of a short-acting soluble insulin, followed by a dose of an intermediate-acting insulin at night. This is commonly referred to as an "SSSI" (soluble, soluble, soluble, intermediate) regimen. The iv insulin should be continued for 30-60 minutes after the first sc insulin dose to allow for absorption of the sc insulin.

Examples of patients who may be converted to an SSSI regimen are those with previous poor control or post-operative complications. Upon full recovery (eg, resumption of a full diet), the SSSI regimen can be stopped and the patient's usual pre-operative regimen restarted, with careful blood glucose monitoring.

The SSSI regimen is not used by all hospitals, particularly where patients have had a minor surgical procedure. Close blood glucose monitoring is required until feeding returns to normal. It should be noted that there will be a reduction in insulin requirements as the release of counter-regulatory hormones due to surgical stress decreases.

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Panel 2: Sliding scale in practice at RLUH

At RLUH we use an amended version of the sliding scale principle. We do not use fixed insulin rates for a given blood glucose reading, because insulin sensitivity differs between patients. Also, a patient's insulin sensitivity can significantly change during the peri-operative period. The glucose infusion is infused at a standard rate. A separate syringe driver containing insulin (50 units of soluble insulin in 50ml sodium chloride 0.9 per cent — ie, 1 unit/ml) is also infused, but at a variable rate. The starting rate at RLUH is 2 units/h. A decrease in blood glucose is managed by decreasing the insulin infusion rate, while an increase in blood glucose will be dealt with by increasing the infusion rate. Our adjustment rates for insulin are as follows:

- If blood glucose is <5mmol/L and not rising, decrease rate by 1 unit/h to a minimum of 0.5units/h, but never stop insulin, (especially in patients with type 1 diabetes) because DKA can develop
- If blood glucose is within 5–12mmol/L, leave insulin running at present rate
- If blood glucose is >12mmol/L and not falling, increase rate by 0.5units/hour

The starting rates, incremental increases and reduction rates may need to be greater —as much as 5 units/h — in overweight patients with insulin resistance.

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Make sure your hospital has a policy for managing patients with diabetes mellitus and who are to undergo an operation.
2. Find out how DKA, NKHS and acute hypoglycaemia should be treated.
3. Consider how you might advise a patient with diabetes who is to undergo surgery.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

References and further reading

1. Wilkinson I, Torok E, editors. The Oxford handbook of clinical medicine, 5th edition. Oxford: Oxford University Press;2001.
- Drugs in the Perioperative period: corticosteroids and treatment for diabetes mellitus. Drug and Therapeutics Bulletin 1999;37(9):68–70.

Topics in this series

Further articles in this series on peri-operative drug therapy will look at:

- Peri-operative venous thromboembolism
- Peri-operative antibacterial prophylaxis
- Post-operative pain, nausea and vomiting