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The rationale and the strategies to achieve perioperative glycaemic control

Daniel J Stubbs BA BMBCh MRCP FRCA[1], Nicholas Levy MB BS BSc FRCA FFICM[2,*] and Ketan Dhatariya MBBS MSc MD MS FRCP[3]

[1]Academic Clinical Fellow in Anaesthesia, Addenbrookes Hospital, Hills Road, Cambridge CB2 0QQ, UK, [2]Consultant in Anaesthesia, Department of Anaesthesia, West Suffolk Hospital, Hardwick Lane, Bury St Edmunds IP33 2QZ, UK and [3]Consultant Diabetologist, Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospitals NHS Foundation Trust, Colney Lane, Norwich NR4 7UY, UK

*To whom correspondence should be addressed. Tel: +44 1284712819; Fax: +44 1284713100; E-mail: Nicholas.levy@wsh.nhs.uk

Key points

- Diabetes (DM) is the most common metabolic disorder. Diabetes leads to increased surgical morbidity, mortality and length of stay.
- Hyperglycaemia is associated with increased risk of infection, medical complications and death. Hypoglycaemia is associated with increased risk of death.
- Ideally, the elective patient should have a preoperative glycated haemoglobin <69mmol mol^{-1} (8.5%). The ideal perioperative capillary blood glucose (CBG) should be between 6.0–10.0 mmol litre^{-1} for all patients with diabetes.
- Perioperative glycaemic control has traditionally been maintained with the variable rate intravenous insulin infusion (VRIII). However, it is now recognised that the use of the variable rate intravenous insulin infusion (VRIII) is associated with complications, so strategies have been implemented to promote its safe use, as well as limiting its use.
- In the UK, it is recommended that perioperative glycaemic control is achieved by manipulation of the patients normal medication when possible. All elective and expedited patients should be seen in pre-assessment clinics to facilitate safe hospital admission.

Diabetes mellitus (DM) is the most common metabolic disorder and affects about 6–7% of the population and between 10 and 30% of the inpatient population.[1] There is now overwhelming evidence that both hypoglycaemia and hyperglycaemia (dysglycaemia) in the surgical patient with diabetes lead to increased risk of death, morbidity, and length of hospital stay.[2–5] Moreover, there is now evidence that surgical patients with previously undiagnosed diabetes who develop perioperative hyperglycaemia are at even greater risk of mortality and morbidity compared with the surgical patients with diabetes.[2,3] Therefore, it is necessary to ensure optimal glycaemic control during the perioperative period.

Cellular actions of glucose and insulin

Glucose is the main intracellular energy substrate, and its cellular absorption and metabolism are controlled by hormones, including insulin. Gluconeogenesis occurs in the absence of intracellular glucose, and lipolysis is an important component of this pathway. It involves the breakdown of lipids into glycerol and free fatty acids. Glycerol is metabolized into glyceraldehyde 3-phosphate, an intermediate compound for both gluconeogenesis and glycolysis. The free fatty acids produced by lipolysis are metabolized into β-hydroxybutyrate and other ketones. In an insulin-deficient state (i.e. a type 1 diabetic patient with no circulating insulin), the lack of insulin leads to unopposed lipolysis and high concentrations of circulating ketones with subsequent acidosis. Consequently, patients with type 1 diabetes mellitus (T1DM) must never be denied insulin.

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Chronic hyperglycaemia leads to a pro-inflammatory state and thus accelerated atherosclerosis. Acute hyperglycaemia/glucose toxicity can cause oxidative stress and a functional decline in the action of neutrophils, and thus is a risk factor for infection in the perioperative period. In addition, the β cells of the pancreas are impaired by the oxidative stress associated with glucose toxicity, and thus a vicious cycle is produced. Consequently, hyperglycaemia and insulin resistance must be treated.

It is important to note that because glucose is the obligate metabolic fuel of the brain, hypoglycaemia leads to neuroglycopaenia with subsequent cognitive impairment, seizures, coma, and ultimately death. Neuroglycopaenic effects begin to occur at approximately 2.8 mmol litre^{-1}.

Measuring glycaemic control

There are two main methods of assessing glycaemic control:

- Blood glucose.
- Glycated haemoglobin.

Blood glucose measurements

Blood glucose samples are used to measure immediate control. Capillary blood glucose (CBG) samples from point-of-care monitors are most frequently measured. In the UK, the units are millimoles per litre, whereas in the USA the units are milligrams per decilitre. Most guidelines suggest hourly measurement of the CBG whilst the patient is nil by mouth (NBM) and is on glucose-lowering medication (i.e. insulins and insulin secretagogues). The United States Food and Drug Administration (US FDA) allows a 15% margin error for glucose meters at concentrations below 5.6 mmol litre^{-1} (100 mg dl^{-1}). Thus a measured concentration of 4.0 mmol litre^{-1} will have an actual value between 3.4 and 4.6 mmol litre^{-1}. Many other factors commonly found in surgical patients can also affect their accuracy: poor peripheral perfusion, anaemia, increased bilirubin and uric acid, and drugs such as paracetamol, dopamine, and mannitol. Furthermore, it is vital that the practitioner double checks samples obtained from arterial lines to ensure erroneous results are not acted upon, which may occur because of the mistaken use of glucose in the flush line.[6]

Glycated haemoglobin

Long-term glycaemic control is assessed by measuring the amount of glycated haemoglobin (HbA1c). Glycated haemoglobin is an indicator of the exposure of haemoglobin to glucose over the preceding 3–4 months (the lifespan of a red blood cell). This used to be commonly expressed as a percentage, but now is more commonly expressed as millimoles per mole. Elevated HbA1c concentrations are associated with a worse outcome across a number of surgical specialities. Presently, there are no data demonstrating that actively reducing HBA1c concentrations before surgery improves outcome. However, it is recognized that a low preoperative HbA1c is a marker that better perioperative glycaemic control will be easier to achieve, and thus it can be used to predict those patients who will not necessarily require a variable-rate i.v. insulin infusion (VRIII) to achieve optimal glycaemic control. Furthermore, as the safe establishment, use, and discontinuation of the VRIII is a time-consuming process, VRIIIs are not frequently used in day surgery units. Consequently, an elevated HbA1c often precludes patients from ambulatory/day surgery.

Table 1 Diagnostic use of glycated haemoglobin (HbA1c)

	HbA1c (%)	HbA1c (mmol mol^{-1})
No diabetes	<5.6	<38
Pre-diabetes	5.7–6.4	37–47
Diabetes	>6.5	>48
Well-controlled diabetes	<6	<42
Controlled diabetes	<7	<53
Poorly controlled diabetes	>8.5	>69
Level at which studies show increased risk of complications	>6	>42
Level at which the AAGBI and JBDS guidelines suggest optimization before elective surgery	>8.5	69

Table 1 highlights the diagnostic interpretation of HbA1c results. Through affecting the red blood cell's lifespan, other co-morbidities may affect the usefulness of the test. These disorders include haemolytic anaemias, and kidney and liver diseases.

Perioperative glycaemic target

Over the past 40 yr, there has been much debate over the optimal perioperative glucose concentration. In 1979, Alberti suggested that it was 5–10 mmol litre^{-1}.[7] In subsequent years, there appeared to be a vogue of purely preventing unrecognized hypoglycaemia whilst the patient was anaesthetized, and thus the insulin infusion was often disconnected during surgery. More recently, it has become appreciated that perioperative hyperglycaemia is associated with a worse outcome,[2,3] and that disconnecting the insulin infusion in a patient with type 1 diabetes will predispose to a ketotic state.

The importance of perioperative glycaemic control is demonstrated by the fact that the National Health Service (NHS) World Health Organization surgical checklist includes a prompt for intraoperative glycaemic control. The exact perioperative optimal zone is still in debate, but the consensus appears to be reverting towards 6–10 mmol litre^{-1}.[8,9] This is remarkably close to the zone that Alberti suggested in 1979 and that he based on 'common sense'.

Hyperglycaemia

Hyperglycaemia is defined as a CBG greater than 6.0 mmol litre^{-1}. However, the level at which action is taken to reduce an elevated CBG is more clinically relevant, and this level has evolved over time. In 2003, after the Van den Burghe landmark paper,[10] there was a vogue that blood sugars above the physiological upper limit of 6 mmol litre^{-1} range should be aggressively treated; however, it has been subsequently demonstrated that widespread application of this tight glycaemic control leads to a poorer outcome.[11] The Joint British Diabetes Societies (JBDS)[8] and the Association of Anaesthetists of Great Britain and Ireland (AAGBI)[9] have now defined hyperglycaemia in the perioperative period as a CBG >10.0 mmol litre^{-1}, with a CBG of up 12.0 mmol litre^{-1} being acceptable.

In the surgical patient with diabetes, perioperative hyperglycaemia is associated with increased rates of infection (both surgical site infections and systemic infections, such as urinary tract infections and lower respiratory tract infections) and

medical complications, including acute kidney injury (AKI), acute coronary syndromes, and acute cerebrovascular events.[2,3] Therefore, the surgical patient with diabetes who suffers hyperglycaemia is at risk of increased rates of morbidity, mortality, and length of hospital stay. This association is seen across a number of surgical specialities (orthopaedic, colorectal, vascular, breast, transplant, and cardiac) and has recently been reviewed.[12]

In addition, the surgical patient without the diagnosis of diabetes who develops perioperative hyperglycaemia is at significantly increased risk of death even when compared with patients with known diabetes.[2,3] Whether this is undiagnosed diabetes or stress hyperglycaemia is currently unknown. It is estimated that approximately 35% of the UK population have 'pre-diabetes' and are at subsequent risk of developing diabetes; therefore; a significant proportion of surgical patients will have undiagnosed diabetes.[13] Risk factors for undiagnosed DM include age >40 yr, family history of type 2 diabetes (T2DM), on anti-hypertensive medication, on lipid-lowering drugs, BMI >23 kg m^{-2} in people of Asian or Afro-Caribbean heritage, or BMI >27 kg m^{-2} in people of European heritage. At present, the National Institute for Health and Care Excellence (NICE) does not recommend preoperative screening for undiagnosed diabetes, and only recommend preoperative assessment of HbA1c in all patients with known diabetes.[14]

Hypoglycaemia

Hypoglycaemia is defined as a CBG <4.0 mmol $litre^{-1}$ and in the patient with diabetes is caused by a relative excess of insulin or insulin secretagogues compared with carbohydrate intake. Hypoglycaemia is associated with increased mortality and in-patient length of stay.[4,5] Severe hypoglycaemia is defined as a blood glucose that is low enough for the individual to require third party assistance.

In the UK, the current teaching is 'four is the floor', and that a CBG only warrants treatment once the CBG is actually below 4 mmol $litre^{-1}$. However a CBG <4.0 mmol $litre^{-1}$ is not a benign condition as demonstrated by the recent critical care studies in which intensive insulin therapy (IIT) was used to aim for a CBG of 4.0–6.0 mmol $litre^{-1}$. *Post hoc* analysis of the Normoglycaemia in Intensive Care Evaluation–Survival Using Glucose Algorithm Regulation (NICE–SUGAR) study identified a CBG <4.0 mmol $litre^{-1}$ as being an independent risk factor for death.[11] In the USA, the recommendation is that a CBG <100 mg dl^{-1} (6 mmol $litre^{-1}$) warrants a re-evaluation of insulin and insulin secretagogue medication.[15,16] The most recent advice from the JBDS and the AAGBI is that the CBG should remain above 6 mmol $litre^{-1}$ in the surgical patient both before and during surgery and whilst on the VRIII.[8,9]

Strategies to achieve perioperative glycaemic control

Before 1979, perioperative glycaemic control was sporadic. In 1979, Alberti published his seminal paper and demonstrated that ketosis could be prevented and glycaemic control achieved by the simultaneous administration of glucose, insulin, and potassium.[7] The resulting 'Alberti GIK regimen' was rapidly and widely adopted. However, it was labour intensive, because whenever the CBG fell outside the range of 5.0–10.0 mmol $litre^{-1}$, the bag of 10% dextrose with the additional potassium and insulin had be taken down, and a new bag containing a different amount of insulin established. The GIK regimen is still in use in limited parts of the UK; however, in most centres the GIK regimen has been superseded by the simultaneous administration of glucose with premixed potassium at a fixed rate and an i.v. insulin infusion titrated according to the CBG. This has become known as the 'sliding scale'. In the US 'sliding scale' insulin refers to intermittent boluses of s.c. insulin to control the CBG. To remove the ambiguity, the 'sliding scale' in the UK is now called the variable-rate i.v. insulin infusion (VRIII). Before its introduction, the VRIII was never subjected to rigorous safety/efficacy studies, and only now is the level of harm associated with the VRIII being recognized. Complications associated with the use of the VRIII are summarized in Table 2. Safer management of the surgical patient with diabetes involves limiting the unnecessary use of the VRIII and introduction of safe working practices to make its use, when essential, non-harmful (Box 1).

Management of the patient with diet-controlled type 2 diabetes

As long as the patient has well-controlled DM, as defined by an HbA1c <8.5%/6.9 mmol mol^{-1}, no extra precautions need to be taken except to perform regular CBG measurements to ensure that the CBG remains below 10 mmol mol^{-1}.

Table 2 Complications associated with the use of the variable-rate i.v. insulin infusion. CBG, capillary blood glucose; DKA, diabetic ketoacidosis; T1DM, type 1 diabetes mellitus

Equipment-related dysglycaemia	Commencement and use	Errors in discontinuing	Metabolic
• Wrong programming • Wrong connection • Lack of use of one-way anti-siphon valves	• Delayed commencement leading to DKA • Insufficient/inadequate measurement of CBG resulting in poor titration • Titration scales that promote tight glycaemic control (e.g. CBG 4.0–6.0 mmol $litre^{-1}$) resulting in inappropriately high infusions of insulin • Acting on erroneous CBGs caused by use of glucose in arterial flush lines	• Delays because of medical and nursing staff lack of familiarity/safe practice • Premature discontinuation of the substrate but with continuation of the i.v. insulin infusion leading to hypoglycaemia. • Discontinuation in a patient with T1DM without prior administration of appropriate s.c. insulin leading to DKA	• Hyponatraemia because of inadequate sodium in the substrate fluid • Hypokalaemia because of inadequate potassium in the substrate fluid

Box 1 The salient points in the safe use of the variable-rate i.v. insulin infusion

As the use of the VRIII is associated with multiple incidents including:

- Hypoglycaemia.
- Hyperglycaemia.
- Ketosis because of either delayed establishment or delayed administration of s.c. insulin on discontinuation.
- Hyponatraemia.
- Hypokalaemia.

It is, therefore, imperative that the following is performed:

- In patients with type 1 DM, the establishment of the VRIII must never be delayed once the decision is made to manage the diabetes with i.v. insulin rather than s.c.
- The VRIII and the substrate solution must be administered through a dedicated cannula that includes appropriate anti-syphon one-way valves. No other drugs or fluids should be administered through this dedicated cannula.
- Hourly monitoring of CBG to maintain 'the range' of 6–10 mmol litre^{-1}.
- The substrate infusion is never inadvertently stopped, for example, during transfers.
- All hospitals must have guidelines for the safe use of the VRIII.
- It is now recognized that the use of the VRIII may often cause hypoglycaemia; furthermore, this may be because the many scales previously promoted a target zone of 4–8 mmol litre^{-1}, and there was no safety buffer zone between safe and dangerous use. Therefore, it is now advised that the scales be redesigned to promote all blood sugars to remain in the 6–10 mmol litre^{-1} zone. Table 6 is the titration scale that is recommended by the AAGBI and JBDS 2015 guidelines.
- As the half-life of soluble insulin is approximately 5 min, within 30 min of stopping a VRIII there will be no appreciable functioning insulin. If the patient has T1DM, DKA will ensue. Therefore, in T1DM patients the VRIII must never be taken down until alternative s.c. insulin has been administered.
- The hospital diabetic specialist nurse or diabetologist should be involved if there are concerns in transferring the patient off the VRIII.

Fluids to run alongside the VRIII

- The initial maintenance solution to be used alongside the VRIII is 5% dextrose in 0.45% saline with additional potassium chloride at a rate of about 1–1.25 ml kg^{-1} h^{-1} up to a maximum of 90 ml h^{-1}. The practice of alternating 5% glucose with 0.9% saline according to serum glucose is not recommended.
- To prevent hypoglycaemia, the substrate solution containing glucose must never be discontinued inadvertently, especially during transfers.
- Additional resuscitative fluids if required should be administered through a second cannula/central venous cannula and follow NICE CG 174 (i.v. fluid therapy in adults in hospital).
- Continuous administration of substrate fluid with glucose to permit continuous administration of insulin is mandatory in starved patients with T1DM; however, this may not be the case in patients with T2DM. Some cardiac centres are running their i.v. insulin infusions to patients with T2DM with no additional glucose in the fluids. Likewise, patients who are established on total parenteral nutrition (TPN) in critical care generally do not require additional substrate solution.

Treatment of CBG <4 mmol litre^{-1} whilst on VRIII

- Reduce insulin rate accordingly.
- Administer 100 ml of 20% glucose.
- Recheck glucose every 15 min until CBG >6 mmol litre^{-1}, and then revert to hourly.

Management of CBG 4.1–6 mmol litre^{-1}

- Reduce insulin rate accordingly.
- Administer 50 ml of 20% glucose i.v. to prevent the CBG falling to below 4.0 mmol litre^{-1}.
- Fastidiously recheck glucose every hour to ensure CBG does not fall below 4 mmol litre^{-1}.

Manipulation of diabetes drugs to facilitate perioperative glycaemic control

With the advent of modern surgical and anaesthetic techniques, including day surgery, the prolonged starvation periods that used to be associated with surgery are no longer typical, and early eating, drinking, and mobilization are now advocated. It is now recognized that if certain institutional and patient (Table 3) criteria are met, the patient can have their diabetes controlled perioperatively by simple manipulation of their normal medication. This strategy promotes less reliance on the VRIII and, by definition, less opportunity for the iatrogenic complications that are associated with its use. The pharmacology of diabetes drugs has been recently reviewed.[17] This article only discusses the perioperative manipulation of these drugs.

Manipulation of insulins

The advent of the longer-acting analogues and the increased use of the continuous sub-cutaneous insulin infusion (CSII) readily allows simple modification to cover the short period of starvation associated with modern surgical and anaesthetic techniques. Table 4 summarizes the manipulation of the

Table 3 Criteria for the surgical patient with diabetes to have their diabetes controlled by simple manipulation of normal medication

Patient/surgical factors	Institutional factors
• Normally adequate glycaemic control (as defined by HbA1c <69 mmol/mol or < 8.5%) • Stable and non-septic • Not requiring immediate or urgent surgery • Ability to understand instructions • No expected surgical reason for postoperative starvation/ileus	• Ability reliably to give the patient a time for surgery to ensure that the patient will only miss one meal • Ability to prioritize the patient on the operating list • Ability for a trained member of staff to discuss perioperative manipulation of drugs with the patient, ensuring that the patient is able to follow the instructions • Ability to perform safe discharge of the surgical patient with diabetes and ensure that the patient understands when to seek medical advice (i.e. follow 'sick day rules')

Table 4 Perioperative manipulation of insulin

Insulins	Day before admission	Day of surgery/whilst on a VRIII		
		Patient for a.m. surgery	Patient for p.m. surgery	If a VRIII is being used*
Once daily (evening) (e.g. Lantus® or Levemir® Tresiba® Insulatard® Humulin I®) Insuman Basal®)	Reduce dose by 20%	Check blood glucose on admission	Check blood glucose on admission	Continue at 80% of the usual dose
Once daily (morning) (Lantus® or Levemir® Tresiba® Insulatard® Humulin I®) Insuman Basal®)	No dose change	Reduce dose by 20%. Check blood glucose on admission	Reduce dose by 20%. Check blood glucose on admission	Continue at 80% of the usual dose
Twice daily (e.g. Novomix 30®, Humulin M3® Humalog Mix 25®, Humalog Mix 50®, Insuman® Comb 25, Insuman® Comb 50 twice daily Levemir® or Lantus®)	No dose change	Halve the usual morning dose. Check blood glucose on admission. Leave the evening meal dose unchanged	Halve the usual morning dose. Check blood glucose on admission. Leave the evening meal dose unchanged	Stop until eating and drinking normally
Twice daily—separate injections of short acting (e.g. animal neutral, NovoRapid® Humulin S®) Apidra® **and intermediate acting** (e.g. animal isophane Insulatard® Humulin I® Insuman®)	No dose change	Calculate the total dose of both morning insulins and give half as intermediate acting only in the morning. Check blood glucose on admission. Leave the evening meal dose unchanged	Calculate the total dose of both morning insulins and give half as intermediate acting only in the morning. Check blood glucose on admission. Leave the evening meal dose unchanged	Stop until eating and drinking normally
3, 4, or 5 injections daily (e.g. an injection of mixed insulin three times a day or three meal time injections of short-acting insulin and once or twice daily background)	No dose change	**Basal bolus regimens:** omit the morning and lunchtime short-acting insulins. If the dose of long-acting basal insulin is usually taken in the morning then the dose should be reduced by 20%* **Premixed a.m. insulin:** halve the morning dose and omit lunchtime dose. Check blood glucose on admission	Take usual morning insulin dose(s). Omit lunchtime dose. Check blood glucose on admission	Stop until eating and drinking normally

insulins that the JBDS and the AAGBI recommend to facilitate surgery.[8,9] It is vital to remember that in patients with T1DM, insulin must never be stopped because of the risk of diabetic ketoacidosis (DKA). Therefore, insulin must always be administered, either in the form of a reduced dose of their normal long-acting s.c. insulin, a reduced rate of their normal CSII pump, or via the VRIII.

Manipulation of the CSII pump therapy

CSIIs are becoming more common. Fundamentally, the CSII provides a constant basal infusion of a very rapid-acting insulin analogue, and at meal times, the patient carbohydrate counts and gives themselves an appropriate bolus via the pump depending on their CBG.

A review of the perioperative use of the CSII has recently been published.[18] Principally, if surgery is associated with only one missed meal, the patient is told to aim for a CBG of 6.0–10.0 mmol litre^{-1}. The patient does this by maintaining the basal infusion, or by reducing the basal infusion rate by up to 10–20%, depending on whether they are 'grazers' (constantly snack), and they also omit the bolus doses associated with meal times.

Prescribing and administering insulin

Insulin is frequently mal-prescribed and mal-administered, which is associated with patient harm including death; consequently, NHS England have issued alerts on correct prescribing.[19] When prescribing, it is essential to define the brand name, rather than the generic name, and additionally the word 'units' must be written in full, rather than abbreviated. The administrator must only use designated 'insulin syringes', and the use of prefilled insulin syringes for the VRIII is now recommended.

The perioperative manipulation of the non-insulin drugs to facilitate glycaemic control

There are currently eight different classes of non-insulin drugs that can be used to treat T2DM,[17] and when these fail to achieve an adequate HbA1c, insulin is added to the treatment.
The perioperative manipulation of these agents is based on:

- The risk of hypoglycaemia in the starved patient (the sulphonylureas and meglitinides will cause hypoglycaemia in the starved patient).
- The perceived risk of AKI or lactic acidosis (metformin has been associated with both lactic acidosis and AKI).
- The perceived risk of DKA (the new sodium–glucose cotransporter inhibitors have been associated with DKA).
- The length of starvation.

Table 5 summarizes the perioperative manipulation of these agents that the JBDS and the AAGBI recommend to facilitate surgery.[8,9]

Perioperative use of metformin

Metformin is a biguanide and by association has been linked with AKI and lactic acidosis. The summary of product characteristics for metformin suggests that that it should be stopped 48 h before

Table 5 Perioperative manipulation of non-insulin glucose-lowering agents

Tablets	Day before admission	Day of surgery/whilst on a VRIII		
		Patient for a.m. surgery	Patient for p.m. surgery	If a VRIII is being used*
Acarbose	Take as normal	Omit morning dose if NBM	Give morning dose if eating	Stop once VRIII commenced, do not recommence until eating and drinking normally
Meglitinide (repaglinide or nateglinide)	Take as normal	Omit morning dose if NBM	Give morning dose if eating	Stop once VRIII commenced, do not recommence until eating and drinking normally
Metformin (eGFR is greater than 60 ml/min/1.73 m^2 and procedure not requiring use of contrast media**)	Take as normal	If taken once or twice a day—take as normal. If taken three times per day, omit lunchtime dose	If taken once or twice a day—take as normal. If taken three times per day, omit lunchtime dose	Stop once VRIII commenced, do not recommence until eating and drinking normally
Sulphonylurea (e.g. glibenclamide, gliclazide, glipizide, glimeperide)	Take as normal	If taken once daily in the morning—omit the dose that day. If taken twice daily—omit the morning dose that day	If taken once daily in the morning—omit the dose that day. If take twice daily—omit both doses that day	Stop once VRIII commenced, do not recommence until eating and drinking normally
Pioglitazone	Take as normal	Take as normal	Take as normal	Stop once VRIII commenced, do not recommence until eating and drinking normally
DPP i.v. inhibitor (e.g. aitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin)	Take as normal	Take as normal	Take as normal	Stop once VRIII commenced, do not recommence until eating and drinking normally
GLP-1 analogue (e.g. exenatide, liraglutide, lixisenatide, dulaglutide)	Take as normal	Take as normal	Take as normal	Take as normal
SGLT-2 inhibitors (e.g. dapagliflozin, canagliflozin, empagliflozin)	Take as normal	Omit on day of surgery	Omit on day of surgery	Stop once VRIII commenced, do not recommence until eating and drinking

surgery because of the fear of these metabolic complications. It is now appreciated that this advice may deny many patients the benefits of glycaemic control that can be achieved with the use of metformin, as metformin is not as toxic as once thought.[20,21]

Recommendations by both the JBDS and the AAGBI[8,9] acknowledge that metformin is safe to continue during the perioperative period provided the patient is having a procedure associated with a short starvation period (one missed meal only) and has a low risk of AKI. In patients either at risk of AKI or having a prolonged starvation period, the metformin should be stopped when the preoperative fast begins and restarted after surgery once the patient is eating and drinking again and normal renal function has been assured.

Use of the VRIII

It is now recognized that the use of the VRIII, although it has the potential for achieving excellent and safe glycaemic control, in reality is associated with the incidents highlighted in Table 2. Therefore, each trust must have protocols/guidelines to try to prevent critical incidents. Box 1 highlights the main components of these accepted recommendations. In view of the fact that it is now recognized that driving the CBG to achieve normoglycaemia is harmful with IIT, most authorities now agree that in the preoperative, intraoperative, and the sedated patient, the ideal CBG is approximately 6.0–10.0 mmol litre^{-1}. Thus, the most recent JBDS and AAGBI guidelines now suggest the administration of i.v. glucose should the CBG fall below 6.0 mmol litre^{-1} when a VRIII is used (see Table 6).[8,9]

Safe use and discontinuation of the VRIII

Patients with T1DM will quickly develop DKA if no exogenous insulin is administered. Thus, once the decision is made to set up a VRIII, this must be done immediately. Difficult i.v. access is not an acceptable excuse for delayed establishment. Likewise, discontinuation without prior administration of s.c. insulin will lead to DKA. To overcome these pitfalls, the JBDS and the AAGBI[8,9] recommend continuation of the basal insulin at 80% of the usual dose whilst the patient is on a VRIII. Furthermore, the VRIII should only be taken down once the patient is eating and drinking, and at least 30 min post-administration of s.c. insulin.

Elective *vs* emergency surgery

In the vast majority of patients with diabetes, perioperative glycaemic control in the elective and emergency expedited setting can be achieved without resort to a VRIII by manipulating/omitting their standard medications provided the criteria in Table 3 are met (Plan A). In the emergency patient requiring either urgent or immediate surgery, the lack of preoperative preparation time, additional stressors, such as sepsis and pain as well as, and the potential for prolonged starvation or loss of the enteral route for feeding make the use of the VRIII often necessary.[22]

Maintaining glycaemic control during starvation

Treating imminent and actual hypoglycaemia

All surgical patients with diabetes who are on glucose-lowering medication (i.e. insulins and insulin secretagogues) need to have their CBG tested hourly whilst NBM. If the CBG decreases below 6.0 mmol litre^{-1} the patient will need treatment, and then the CBG should be taken every 15 min and further

Table 6 Recommended titration of variable rate i.v. insulin infusion to blood glucose

Glucose (mmol litre^{-1})	i.v. insulin infusion rates (ml h^{-1})						
	With soluble insulin of 1 unit ml^{-1}						
	Standard rate (Start on standard rate unless indicated)		Reduced rate (for use in insulin-sensitive patients, i.e. needing <24 units day^{-1})		Increased rate (for use in insulin-resistant patients, i.e. needing more than 100 units day^{-1})		Customized scale
	If no basal insulin	If basal insulin continued	If no basal insulin	If basal insulin continued	If no basal insulin	If basal continued	
<4	0.5 ml h^{-1} and administer 100 ml i.v. 20% glucose	0 ml h^{-1} and administer 100 ml i.v. 20% glucose	0.2 ml h^{-1} and administer 100 ml i.v. 20% glucose	0 ml h^{-1} and administer 100 ml i.v. 20% glucose	0.5 ml h^{-1} and administer 100 ml i.v. 20% glucose	0 ml h^{-1} and administer 100 ml i.v. 20% glucose	
4.1–6	0.5 ml h^{-1} and administer 50 ml i.v. 20% glucose	0 ml h^{-1} and administer 50 ml i.v. 20% glucose	0.2 ml h^{-1} and administer 50 ml i.v. 20% glucose	0 ml h^{-1} and administer 50 ml i.v. 20% glucose	0.5 ml h^{-1} and administer 50 ml i.v. 20% glucose	0 ml h^{-1} and administer 50 ml i.v. 20% glucose	
6.1–8	1	1	0.5	0.5	2	2	
8.1–12	2	2	1	1	4	4	
12.1–16	4	4	2	2	6	6	
16.1–20	5	5	3	3	7	7	
20.1–24	6	6	4	4	8	8	
>24.1	8	8	6	6	10	10	
>24.1	Ensure insulin is running, and not measuring an artefact						

treatment administered until the CBG is again >6.0 mmol litre^{-1}. The treatment options include:

- I.V. glucose (50–100 ml of 10–20% dextrose).
- 1 mg glucagon i.m. (may be less effective in patients prescribed sulphonylurea therapy).
- Buccal sugar, for example, one to two tubes of Glucogel®.
- Five to seven Dextrosol® tablets (or four to five Glucotabs®).
- 150–200 ml pure fruit juice, for example, orange.
- 90–120 ml of original Lucozade® (preferable in renal patients).
- Biscuit or fresh fruit.

In the preoperative hypoglycaemic patient, clinical judgement needs to prevail on appropriate treatment and whether to proceed with surgery.

Treating hyperglycaemia

Current advice by the JBDS and the AAGBI[8,9] is that a CBG >12.0 mmol litre^{-1} should be treated. Capillary ketones should also be checked to ensure that the patient has not developed DKA.

Treating hyperglycaemia in patients with type 1 diabetes

Give s.c. rapid-acting analogue insulin. Assume that 1 unit will decrease blood glucose by 3 mmol litre^{-1}, but wherever possible take advice from the patient about the amount of insulin normally required to correct a high blood glucose. Recheck the CBG 1 h later to ensure it is decreasing. Repeat the s.c. insulin dose after 2 h if the blood glucose is still above 12 mmol litre^{-1}. In this situation, the insulin dose selected should take into account the response to the initial dose—consider increasing the dose if the response is inadequate. Recheck the blood glucose after another 1 h. If it is not reducing, consider introducing VRIII.

Treating hyperglycaemia in patients with type 2 diabetes

Give 0.1 units kg^{-1} of s.c. rapid-acting analogue insulin, and recheck blood glucose 1 h later to ensure it is decreasing. Repeat the s.c. insulin after 2 h if the blood glucose is still above 12 mmol litre^{-1}. In this situation, the insulin dose selected should take into account the response to the initial dose—consider doubling the dose if the response is inadequate. Repeat the blood glucose after another hour. If it is not decreasing, consider introducing VRIII.

Conclusions

Perioperative dysglycaemia is associated with harm. Increasing numbers of surgical patients have diabetes and will need strategies to prevent perioperative dysglycaemia. Patients with T1DM need constant exposure to pharmacological insulin (either in the form of long-acting s.c. insulin, a CSII, or a VRIII) to prevent DKA and the harmful effects of hyperglycaemia. With modern surgical and anaesthetic techniques coupled with an understanding of diabetes drug pharmacology, patients with diabetes can often be managed with simple manipulation of their usual medication rather than the use of the VRIII. When the VRIII is required, there is a need for robust guidelines to ensure its safe use.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to *BJA Education*.

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