Perioperative management of diabetes mellitus

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Consultant Anaesthetist UHCW
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References

Peri-operative management of the surgical patient with diabetes 2015
Published by The Association of Anaesthetists of Great Britain & Ireland Sept 2015

JBDS-IP Joint British Diabetes Societies for Inpatient Care Management of adults with diabetes undergoing surgery and elective procedures: Improving standards Revised March 2016

Highs and Lows A review of the quality of care provided to patients over the age of 16 who had diabetes and underwent a surgical procedure


Perioperative management of the patient with diabetes requiring emergency surgery
Nicholas Levy, MBBS BSc FRCA FFICM1, Nigel William Penfold, MBBS FRCA1, and Ketan Dhatriya, MBBS MSc MD MS FRCP2
a) In a patient with diabetes mellitus, what clinical features may indicate autonomic involvement? (4 marks)

b) What are the other microvascular and macrovascular complications of diabetes mellitus? (6 marks)

c) What is the recommended upper limit of HbA1C for elective surgery (1 mark) and what is the Association of Anaesthetists of Great Britain & Ireland (AABGI) guidance for perioperative blood glucose monitoring in diabetic patients? (3 marks)

d) List 3 classes of oral hypoglycaemic agents that are available (3 marks) and describe the mechanism of action of each. (3 marks)
A 30 year-old 65kg Type 1 DM is awaiting appendicectomy on emergency list. CBG is 13 mmol/L preop. She does not appear dehydrated, no urine ketones, Na 137 mmol/L, K+ is 4.5 mmol/L. Which is the **ideal** fluid to prescribe with her VR III?

a. 5% glucose with 40 mmol/L KCL: 100 ml/hr
b. 5% glucose with 20 mmol/L KCL: 125 ml/hr
c. 0.45% NaCl/5% glucose with 40 mmol/L KCL: 125 ml/hr
d. 0.18% glucose/4% glucose with 20 mmol/L KCL: 125 ml/hr
e. 0.45% NaCl/5% glucose with 40 mmol/L KCL: 100 ml/hr
Scale of the problem

5 million people in England are at high risk of developing Type 2 diabetes.

Type 2 diabetes is a major cause of premature mortality, with around 22,000 people dying early every year in England.

There are currently 3.8 million people with Type 2 diabetes in England with around 200,000 new diagnoses every year.
The rising costs of Type 2 diabetes

Type 2 diabetes treatment accounts for just under 9% of the annual NHS budget. This is around £8.8 billion a year.

This is because of complications such as:
- Amputation
- Blindness
- Kidney failure
- Stroke

1 in 6 of all people in hospital have diabetes.
**Categories**

- **Type 1**
  - B-cell destruction and usually leads to absolute insulin deficiency

- **Type 2**
  - Progressive insulin secretory defect coupled with insulin resistance

- **GDM**
  - Diagnosed during pregnancy that may or may not resolve after delivery

- **Other**
  - Predisposed to hyperglycaemia, e.g. Diseases of the pancreas, glucocorticoid use and monogenic disorders causing maturity onset diabetes of the young (MODY)
Multisystemic disease

**Microvascular?**
- Neuronal damage and structural damage
  - Diabetic retinopathy
  - Diabetic nephropathy
  
- Retinal neurodegeneration
- Tubulointerstitial disease

**Other nonclassic targets**
- Microangiopathy and metabolic damage
  - Arterial wall
    - Atherosclerosis
  - Liver
    - Nonalcoholic fatty liver disease
  - Lung
    - Pulmonary microvascular disease

**Macrovascular?**
- Microangiopathy and metabolic damage
  - Lower limbs
    - Peripheral artery disease
      - Diabetic foot
    - Heart
      - Coronary artery disease
        - Diabetic cardiomyopathy
  - Brain
    - Stroke
      - Cerebral small vessel disease
    - Dementia and cognitive decline

**Other**
- Cancer
  - Increased incidence and mortality
Perioperative burden

• Pressure ulcers
• Autonomic dysfunction
• Arrhythmias, hypotension
• Hyperglycaemia and periop infection risk
• Metabolic stress
Normal HRV >15 bpm in deep breathing. Neuropathy likely if <10 bpm
Features of diabetic autonomic neuropathy

- Symptomatic involvement
  - Gustatory sweating
  - Respiratory arrests
  - Postural hypotension
  - Gastroparesis
  - Diabetic diarrhoea
  - Neuropathic bladder
  - Erectile failure
  - Neuropathic oedema
  - Charcot arthropathy

- Subclinical abnormalities
  - Abnormal pupillary reflexes
  - Oesophageal dysfunction
  - Abnormal cardiovascular reflexes
  - Blunted counter-regulatory responses to hypoglycaemia
  - Increased peripheral blood flow
Comprehensive care pathway for peri-operative management of diabetes

- Primary care referral
- Surgical outpatients
- Pre-operative assessment
- Hospital admission
- Theatre and recovery
- Post-operative care
- Discharge
1. All regular and single insulin (bolus) doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration.

2. The term ‘units’ is used in all contexts. Abbreviations, such as ‘U’ or ‘IU’, are never used.

3. All clinical areas and community staff treating patients with insulin have adequate supplies of insulin syringes and subcutaneous needles, which staff can obtain at all times.

4. An insulin syringe must always be used to measure and prepare insulin for an intravenous infusion. Insulin infusions are administered in 50ml intravenous syringes or larger infusion bags. Consideration should be given to the supply and use of ready to administer infusion products e.g. prefilled syringes of fast acting insulin 50 units in 50ml sodium chloride 0.9%.

5. A training programme should be put in place for all healthcare staff (including medical staff) expected to prescribe, prepare and administer insulin. An e-learning programme is available from NHS Diabetes: http://www.diabetes.nhs.uk/safe_use_of_insulin

6. Policies and procedures for the preparation and administration of insulin and insulin infusions in clinical areas are reviewed to ensure compliance with the above.

The deadline for completion of these action points is 16th December 2010.
Optimise elective patients

✓ Satisfactory HbA1c levels within 3 months of referral
✓ Control of co-morbidities
✓ A list of all current medications
✓ The patient’s body mass index (BMI)
✓ Estimated glomerular filtration rate (eGFR)
✓ Perioperative risk rating
Pathway interventions

- Aim for HbA1C < 69 mmol/mol
- Identify co-morbidities
- Patient information
- Optimize CVS risk, eGFR and weight
- Consider referral to diabetes specialist team

- Admit on day of surgery where possible
- Aim for only one missed meal
- Minimize starvation: 1st on list

- Periop control of glucose 6-10 (or 12) mmol/l
- Avoid hypoglycaemia (<4, or 3.5 mmol in awake patient): prescribe glucogel or glucagon
- Correct fluid management
- Avoid complications: feet! AKI! CVS!
- Choose techniques that allow early return to eating and normal regimes
## Perioperative dosing of insulin

<table>
<thead>
<tr>
<th>Insulins</th>
<th>Day prior to admission</th>
<th>Day of surgery / whilst on a VRII</th>
<th>If a VRII is being used*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Once daily (evening)</strong></td>
<td>Reduce dose by 20%</td>
<td>Check blood glucose on admission</td>
<td>Continue at 80% of the usual dose</td>
</tr>
<tr>
<td>(e.g. Lantus® or Levmir® Tresiba® Insulatard® Humulin I®/Insuman Basal®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Once daily (morning)</strong></td>
<td>Reduce dose by 20%</td>
<td>Reduce dose by 20% Check blood glucose on admission</td>
<td>Continue at 80% of the usual dose</td>
</tr>
<tr>
<td>(e.g. Lantus® or Levmir® Tresiba® Insulatard® Humulin I®/Insuman Basal®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Twice daily</strong></td>
<td>No dose change</td>
<td>Halve the usual morning dose. Check blood glucose on admission Leave the evening meal dose unchanged</td>
<td>Stop until eating and drinking normally</td>
</tr>
<tr>
<td>(e.g. Novomix 30®, Humulin M3®, Humalog Mix 25®, Humalog Mix 50%, Insuman® Comb 25, Insuman® Comb 50 twice daily Levmir® or Lantus®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Twice daily - separate injections of short acting</strong></td>
<td>No dose change</td>
<td>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 unchanged</td>
<td>Stop until eating and drinking normally</td>
</tr>
<tr>
<td>(e.g. animal neutral, NovoRapid® Humulin S® Apidra® and intermediate acting (e.g. animal isophane Insulatard® Humulin I® Insuman®)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulins</td>
<td>Day prior to admission</td>
<td>Day of surgery / whilst on a VRIII</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>------------------------</td>
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<td></td>
</tr>
<tr>
<td>3, 4 or 5 injections daily (e.g. an injection of mixed insulin 3 times a day or 3 meal time injections of short acting insulin and once or twice daily background)</td>
<td>No dose change</td>
<td><strong>Patient for a.m. surgery</strong></td>
<td></td>
</tr>
<tr>
<td>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%*</td>
<td></td>
<td><strong>Patient for p.m. surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Premixed a.m. insulin: halve the morning dose and omit lunchtime dose Check blood glucose on admission</td>
<td></td>
<td><strong>If a VRIII is being used</strong>*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stop until eating and drinking normally</td>
<td></td>
</tr>
</tbody>
</table>

*If a VRIII is being used*:
- **Patient for a.m. surgery**: Take usual morning insulin dose(s). Omit lunchtime dose. Check blood glucose on admission.
- **Patient for p.m. surgery**: Stop until eating and drinking normally.
## Perioperative dosing of OHA

<table>
<thead>
<tr>
<th>Agent</th>
<th>Day prior admission</th>
<th>Day of surgery/while on a VR III</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Patient for morning surgery</td>
</tr>
<tr>
<td>Drugs that require omission when fasting due to risk of hypoglycaemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meglitinide (repaglinide or nateglinide)</td>
<td>Take as normal</td>
<td>Omit morning dose if NBM</td>
</tr>
<tr>
<td>Sulphonylurea (For example glibenclamide, gliclazide, glipizide)</td>
<td>Take as normal</td>
<td>Once daily (morning) omit; twice daily omit morning dose</td>
</tr>
<tr>
<td>Drugs that require omission when fasting due to risk of ketoacidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGLT-2 inhibitors (For example dapagliflozin, canagliflozin, empagliflozin)</td>
<td>Take as normal</td>
<td>Do not take on day of surgery</td>
</tr>
<tr>
<td>Drugs that may be continued when fasting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acarbose</td>
<td>Take as normal</td>
<td>Omit morning dose if NBM</td>
</tr>
<tr>
<td>DPP IV inhibitor (For example sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin)</td>
<td>Take as normal</td>
<td>Take as normal</td>
</tr>
<tr>
<td>GLP-1 analogue (For example exenatide, liraglutide, lixisenatide)</td>
<td>Take as normal</td>
<td>Take as normal</td>
</tr>
<tr>
<td>Metformin (procedure not requiring use of contrast media*)</td>
<td>Take as normal</td>
<td>Take as normal</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>Take as normal</td>
<td>Take as normal</td>
</tr>
</tbody>
</table>
Drugs and mechanisms

- Increase release of endogenous insulin and cause a genuine reduction in the blood glucose (the sulphonylureas and meglitinides).
- Affecting gastrointestinal absorption and renal reabsorption of glucose (intestinal alpha-glucosidase inhibitors and the SGLT-2 inhibitors).
- Drugs that alter effector site sensitivity to endogenous insulin and reduce gluconeogenesis/glycogenolysis or endogenous metabolism (metformin and the thiazolidinediones).
- Drugs acting on the incretin pathway (GLP-1 analogues and the DPP4 inhibitors).

Dipeptidylpeptidase-4 inhibitors (~gliptins)
Sodium glucose co-transporter 2 inhibitors, (~flozins)
Controversies
Capillary blood glucose (CBG) levels should be monitored and recorded at least hourly during the procedure and in the immediate postoperative period.

Ensure blood glucose levels are appropriately maintained. The acceptable post-operative range in the awake patient not on a VRIII is 4-12mmol/L, however if a VRIII is used, then the acceptable range remains 6-10mmol/L.

Monitor electrolytes and fluid balance daily and prescribe appropriate fluids.

Treat post-operative nausea and vomiting to promote normal feeding.

Maintain meticulous infection control.

Inspect foot and pressure areas regularly.

The WHO surgical safety checklist bundle should be implemented. The target blood glucose in the pre-operative, anaesthetised or sedated patient should be 6-10mmol/L (up to 12mmol/L may be acceptable). The target of 6-10mmol/L is for those who are treated with glucose lowering agents – i.e. insulin, (either subcutaneously, or via an insulin infusion) or sulphonylurea therapy. In the awake patient on agents that do not produce hypoglycaemia, provided they have not been given insulin, lower blood glucose values down to 3.5mmol/L are safe and do not require IV glucose or other rescue treatment.
Never stop insulin in Type 1 DM

- If the starvation period is expected to require omission of more than one meal, use VRIII with concomitant glucose and electrolyte infusion
- Avoid hypoglycaemia: worsens catabolic effect of surgery
- Insulin requirements increased by:
  - Obesity
  - Prolonged or major surgery
  - Infection
  - Glucocorticoid treatment
VRIII - Indications

- Type I DM + miss >1 meal
- Type I DM missed background insulin
- Type II DM + missed >1 meal + CBG>12 mmol/L
- Patients with poorly controlled diabetes (HbA1c >69mmol/mol or 8.5%)
- Most patients with diabetes requiring emergency surgery
**VR III - Principles**

**Continue long-acting analogues**
- Glargine/Lantus®, Degludec/Tresiba®, Detemir/Levemir®
- Smooths out rebound hyperglycaemia when stopping VR III
- Reduce dose by 20%

**Fluid management**
- Provide glucose as substrate to prevent catabolism
- Keep glucose in range
- Keep electrolytes in range
- Replace losses

**Stopping VR III**
- Correct prescriptions
- Metformin if eGFR >60
- Oral agents if eating – consider dose adjustment if altered diet
- Basal bolus regime: start SC insulin with meal, stop IV VR III 30-60 min later
- Important that basal insulin is continued/given before taking down VR III
VRIII Equipment
If hyponatraemia, on VRIII:
0.9% saline with 5% glucose with 20 or 40 mmol/L KCl

Not on VRIII – which fluid intraop?
- Hartmann’s preferred over 0.9% NaCl
- Avoid Glucose unless hypoglycaemic

Ideal solution on VRIII:
0.45% saline with 5% glucose with 20 (0.15%) or 40 (0.30%) mmol/L KCl

Acceptable solution on VRIII:
- 5% glucose with 20 or 40 mmol/L KCl
- 0.18% NaCl with 4% glucose with 20 or 40 mmol/L KCl

125 ml/hr
- Lower rate if concerns about fluid overload
- If K+ 3.5-5.5: 20 or 40 mmol/L KCl in fluid
Patient knows best (probably)

Patient will adjust basal rate.

Avoid periop hypotension as absorption will be affected.

Mealtime boluses commenced when eating

If more than one meal missed: use VRIII

Seek advice from specialist team
What about metformin?

- Review the dose of metformin if the serum Cr > 130μmol/l or the eGFR is < 45 ml/min/1.73m²

- Stop the metformin if the serum Cr > 150μmol/l or the eGFR < 30 ml/min/1.73m²

- No need to avoid contrast if eGFR > 60 ml/min/1.73m²
  - Otherwise omit on day and for 48 hrs post procedure
Avoid using dexamethasone as anti-emetic

- Increased monitoring if benefits outweigh risks
- Increased dosage of hypoglycaemic agents may be required

Nocturnal and early morning hypoglycaemia if increased dosing

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**Dexamethasone/steroids**

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Potency (Equivalent doses)</th>
<th>Duration of action (Half-life in hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>20mg</td>
<td>8</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5mg</td>
<td>16-36</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4mg</td>
<td>18-40</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.75mg</td>
<td>36-54</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>0.75mg</td>
<td>26-54</td>
</tr>
</tbody>
</table>

*NB.* potency relates to anti-inflammatory action, which may not equate to hyperglycaemic effect
Rx of hypoglycaemia

- Hypo
  - 4 – 6 mmol/L + symptoms (or under GA): 50 ml 20% glucose IV over 15 min
  - < 4 mmol/L: 100 ml 20% glucose over 15 min
Rx of hyperglycaemia

CBG > 12 mmol/L and insulin omitted

Check capillary blood ketones or urine ketones

Capillary blood ketones > 3 mmol/L or significant ketonuria (> 2+ on urine dip)

Treat as DKA

Type I DM

SC rapid acting (e.g. Novarapid) up to 6 units

1 unit = 3 mmol/L decreased in CBG

Second dose considered after 2 hrs

Consider VRIII

Type 2 DM

SC 0.1 unit/kg rapid acting (e.g. Novarapid) up to 6 units

Second dose considered after 2 hrs

Consider VRIII
Sick day rules

What should I do if I am unwell?

- **NEVER** stop taking your insulin or tablets – illness usually increases your body’s need for insulin.
- **TEST** your blood glucose level every 2 hours, day and night.
- **TEST** your urine for ketones every time you go to the toilet or your blood ketones every 2 hours if you have the equipment to do this.
- **DRINK** at least 100ml water/sugar free fluid every hour – you must drink at least 2.5 litres per day during illness (approx. 5 pints!).
- **REST** and avoid strenuous exercise as this may increase your blood glucose level during illness.
- **EAT** as normally as you can. If you cannot eat or if you have a smaller appetite than normal, replace solid food during illness, with one of the following:
  - 400ml milk
  - 200ml carton fruit juice
  - 150-200ml non-diet fizzy drink
  - 1 scoop ice cream

**SUGAR**
- Check your blood glucose every 2 to 3 hours or as necessary!
- Always take your Insulin! Not taking it could lead to DKA!
- Drink lots of fluids!
- Check your urine or blood ketones every 4 hours

**INSULIN**
- Controlling very high blood sugar.
- Unaffected by illness insulin.
- Ketones 1.5mmol/l or more: normal.

**CARBS**
- Outside the local hospital
- Ketocytes are low drink carb-containing drinks.

**KETONES**
- Take rapid-acting insulin if ketones are present.
Obstetrics

- GDM > Type I/II DM
- Macrosomia
- Preterm delivery
- Stillbirth
- Congenital anomalies
- Increased CS delivery rate
- Sepsis and PET
- Worsening of pre-existing nephropathy/retinopathy
Gestational diabetes mellitus

Risk factors GDM

- BMI above 30 kg/m$^2$
- Previous macrosomic baby weighing 4.5 kg or above
- Previous gestational diabetes
- Family history of diabetes (first-degree relative with diabetes)
- Minority ethnic family origin with a high prevalence of diabetes

Fasting plasma glucose level $\geq 5.6$ mmol/litre

or

2-hour plasma glucose level $\geq 7.8$ mmol/litre
Steroids for fetal lung maturation: hyperglycaemia and may need VRIII
Intrapartum care

• Fetal wellbeing after 37 weeks
• Type 1 or type 2 diabetes + no other complications:
  • birth by induction / elective CS (if indicated), between 37+0 and 38+6
• Challenge of labour
• Avoid maternal hyperglycaemia to avoid neonatal hypoglycaemia
Intrapartum goals for CBG

- Hourly CBG: keep 4 - 7 mmol/L
- VRIII should be considered for women with type 1 DM from the onset of established labour
- GDM/Type II DM: consider VRIII if capillary plasma glucose is not maintained between 4 and 7 mmol/L
- Operative delivery: relaxed to 5 – 8 mmol/L, check half hourly if under GA
Intrapartum care: problems

- **Skill retention** of midwives administering VRIII
- **Set-up**: adequate venous access and clearly labelled pumps – multiple infusions
- **Maternal hyponatraemia** associated with VRIII, leading to cerebral oedema and seizures (exacerbated by oxytocin infusion). Can lead to neonatal seizures
- **Which fluid?**: Recommended 5% glucose in 0.9% saline with 20 or 40 mmol/L KCL – commence at 50ml/hr and adjust according to needs
- **If on SC pump** – continue with that as long as CBG < 7mmol/L
Postpartum care

- Perioperative Type I/poorly-controlled Type II or GDM: sudden decrease in insulin requirement after baby born
  - Monitor CBG every 30 min at least
  - Halve rate VRIII immediately after delivery
- Aim 6-10mmol/L
- Should have individualized care plan from diabetic team for postpartum, otherwise commence with 50% late-pregnancy dose of insulin
- Increased nutritional needs if breast feeding/expressing
History of the Event
The patient, a 73-year old female had an emergency admission to hospital for investigation of abdominal pain. She had insulin-treated type 2 diabetes and a very high ‘body mass index’ (BMI) with subsequently reduced mobility. As a result she used a high-dose insulin (500 units per mL) from an insulin pen device.

Common practice in the hospital concerned nurses were to use a patient’s medication if they brought it with them into hospital. The patient had brought her insulin pen, including an unused disposable insulin pen needle, and approximately six single-use insulin pen needles. The patient was moved to a different ward as her medication was transferred with her. However, the supply of pen needles had been used up on the previous ward. The second ward, like the first, did not have any disposable pen needles for administration of insulin from her pen.

The nurses improvised by using an insulin syringe to withdraw the insulin from the pen device and administered the insulin to the patient. However, they did not notice that the insulin was one of high concentration - five times the normal strength. The outcome was that the patient received a five times overdose. The patient experienced subsequent hypoglycaemic events (low blood glucose) and required treatment. The patient’s blood glucose levels recovered, and the next dosage was administered in the same way.

Later, the patient’s husband identified the error when enquiring about the recurrent hypoglycaemic episodes. The patient made a full recovery.
6. Overdose of insulin due to abbreviations or incorrect device when:

- a patient is given a 10-fold or greater overdose of insulin because the words ‘unit’ or ‘international units’ are abbreviated; such an overdose was given in a care setting with an electronic prescribing system
- a healthcare professional fails to use a specific insulin administration device – that is, an insulin syringe or pen is not used to measure the insulin
- a healthcare professional withdraws insulin from an insulin pen or pen refill and then administers this using a syringe and needle.
Summary

- Common comorbidity, often not managed well by patient/staff
- VRIII – indications, fluid, equipment, risks
- Monitoring targets preop, intraop and postop
- Managing perioperative dosing of insulin and OHAs
- Diabetes in pregnancy
- Never event