Managing diabetic emergencies

Diabetic emergencies can occur either in patients known to have diabetes or as an initial presentation of the disease. Ram Prakash Narayanan and Mark Peasley discuss their management.

The usual presentations of a diabetic emergency are hypoglycaemia, diabetic ketoacidosis (DKA) or a hyperglycaemic hyperosmolar state. Response to treatment is generally good but delays can lead to adverse outcomes (eg, brain injury and fatalities). In the absence of a strong evidence base, treatment is usually based on commonly accepted guidelines modified for local practice.

Acute hypoglycaemia

Hypoglycaemia is the most common complication of diabetes, accounting for around 90,000 ambulance call outs and 8,000 hospital admissions per year in the UK. Symptoms generally present at blood glucose levels of 2.5–3mmol/L but they also manifest outside this range and patients can report different symptoms. Patients should be told that any capillary blood glucose (CBG) less than 4mmol/L requires treatment — “four is the floor”.

Symptoms consist of anxiety, palpitations, tremor and sweating (adrenergic symptoms, sometimes called warning symptoms), irritability, incoordination, confusion, weakness, fatigue and seizures (neuroglycopaenic manifestations) and, later, loss of consciousness.

Hypoglycaemia can occur in both type 1 and type 2 diabetes. It is most commonly seen in patients treated with insulin or drugs that affect the activity of insulin (ie, insulinotropic drugs), such as sulphonylureas, or both. Long-acting sulphonylureas (glibenclamide and chloropropamide) are more likely to cause hypoglycaemia. These are renally excreted so should be avoided in those with impaired renal function — drug accumulation increases risk of hypoglycaemia — and in elderly patients (who are likely to have some renal impairment). Panel 1 describes diabetes treatments and their risk of hypoglycaemia. Hypoglycaemic events can also be a consequence of efforts to tighten glycaemic control and a balance is needed.

Non-antidiabetic agents that have been implicated in hypoglycaemia include quinine, quinolone antibiotics, pentamidine and co-trimoxazole — they may be insulinotropic. Alcohol can precipitate hypoglycaemia by inhibiting gluconeogenesis.

Conditions that can precipitate hypoglycaemia, either on their own or in combination with diabetes drugs, are end-stage liver disease, renal failure, starvation, infection and adrenal insufficiency. Insulinoma is an uncommon cancer that causes fasting hypoglycaemia. This is normally managed surgically but treatment with diazoxide can help to reduce hypoglycaemic episodes.

Hypoglycaemia is rated as mild, moderate or severe as follows:

- **Mild** The person is aware of the hypoglycaemia and can self treat orally.
- **Moderate** The person cannot respond to hypoglycaemia and requires assistance, but oral treatment is successful.
- **Severe** The person has impaired consciousness and requires assistance and parenteral therapy.

Autonomic neuropathy, drinking alcohol and beta-blocker therapy can all mask adrenergic symptoms so that a patient is unaware of hypoglycaemia. Those with recurrent episodes of hypoglycaemia may also lose adrenergic symptoms. In such patients a period of hypoglycaemia avoidance can, in most cases, help restore these warning symptoms.

In rare cases, hypoglycaemia can be triggered by accidental or intentional overdoses of insulin, sulphonylureas or meglitinides, and underlying reasons should be addressed. Management should consider drug half-lives. Where overdose is suspected, in order to distinguish between endogenous secretion and exogenous insulin administration, plasma glucose, insulin and c-peptide levels should be taken before treating hypoglycaemia (symptoms allowing). In endogenous insulin secretion...
there will be an equimolar rise in plasma c-peptide levels because islet secreted pro-insulin is cleaved into active insulin and residue c-peptide, whereas exogenous administration results in no c-peptide rise.

In suspected sulphonylurea overdose, sulphonylurea levels should be found.

**Mild to moderate hypoglycaemia**

The first-line treatment for mild to moderate hypoglycaemia is 10–20g of rapidly absorbed simple carbohydrates. This should raise blood glucose levels in about 15 minutes. Examples of 10g of simple oral carbohydrates include 55ml of high energy glucose drinks (eg, Lucozade), 100ml of Coca-Cola, two teaspoons of sugar, three glucose tablets or a tube of commercially available concentrated glucose (eg, Glucogel, which patients treated with short or biphasic insulins or sulphonylureas can be advised to carry).

The tendency to overcorrect hypoglycaemia (eg, by drinking a whole bottle of Lucozade) should be avoided. In the case of sulphonylurea overdose overcorrection of hypoglycaemia will stimulate further insulin release. Overcorrection can also lead to worsening glycaemic control. CBG should be measured after 10 to 15 minutes. If blood glucose is still less than 4mmol/L oral carbohydrates may be repeated and CBG rechecked up to three times. If still hypoglycaemic, intravenous 10 per cent dextrose at 100ml/h or 1mg intramuscular glucagon should be considered.

As soon as the patient is normoglycaemic, long-acting carbohydrates (eg, two biscuits, a slice of bread, oat-based cereal bars, a sandwich, cereals or fruits) or a meal (if due) should be given to maintain blood glucose levels.

**Severe hypoglycaemia**

In patients with impaired consciousness standard first aid measures (ie, airway, breathing and circulation) should be addressed. Where glucagon is not contraindicated 1mg can be administered intramuscularly in...
patients weighing above 25kg or older than eight years (0.5mg for those below 25kg or younger than eight years).

Glucagon promotes the conversion of glycogen stores in the liver into glucose. If the patient does not respond within 10 minutes, administration of intravenous dextrose becomes essential. Response to glucagon can be poor in patients with hypoglycaemia related to alcohol or liver disease and in cachectic patients (they have inadequate glycogen reserves). In hospital, rapid intravenous access and administration of 10 or 20 per cent dextrose is indicated until normoglycaemia is restored. The use of 50 per cent dextrose solutions is discouraged due to the high risk of thrombophlebitis. Again, complex carbohydrates should be given after intravenous glucose to maintain blood glucose levels.

Patients with sulphonylurea-induced hypoglycaemia can have prolonged periods of low blood glucose due to the longer half-lives of these drugs and have to be monitored more frequently. Glucagon is not indicated in sulphonylurea-related hypoglycaemia because it may be insufficient to correct the hypoglycaemia (because the sulphonylurea will cause further insulin release). Such patients need intravenous glucose and may require therapy with somatostatin analogues such as octreotide (unlicensed indication — hypoglycaemia is a side effect of somatostatin analogues because they inhibit the release of pancreatic hormones).

Contact with the hospital diabetes team is recommended to address the cause of hypoglycaemia, especially in patients without warning symptoms or in severe hypoglycaemia. Recurrent hypoglycaemia destabilises overall glycaemic control and education on avoiding future episodes and balancing diet and exercise, and multidisciplinary input are crucial.

Diabetic ketoacidosis

DKA involves hyperglycaemia, ketosis and acidosis. It is usually seen in type 1 diabetes but can also occur in patients with type 2 diabetes, especially in those of Afro-Caribbean or Hispanic backgrounds. Studies also show that nearly a fifth of children and young adults are admitted more than once with this complication and DKA is the most common cause of death in young people with diabetes. Overall mortality rates are below 5 per cent, but may be higher in the elderly.

Criteria for the diagnosis of DKA, as suggested by the Joint British Diabetes Societies (JBDS), include:

- Blood glucose >11mmol/L or known diabetes mellitus
- Blood ketones >3mmol/L or significant ketonuria (++ or more on urine dipsticks)
- Acidosis (arterial pH <7.3 or serum venous bicarbonate <15mmol/L)

DKA is usually precipitated by stresses that increase the release of glucagon, cortisol and catecholamines. Infections, myocardial infarction, surgery, missed insulin doses and drugs are some recognised precipitants. Generally, a relative lack of insulin, often in combination with a surge of catecholamines and endogenous steroids, is involved. Ketones are present in the blood and urine because catecholamine excess and the lack of insulin leads to the metabolism of free-fatty acids to acetoacetic acid. (This provides an alternative energy source because the lack of insulin leads to an impairment of glucose use.) Acetoacetic acid is then metabolised to acetone, giving rise to the fruity smelling breath classically associated with DKA.

The onset of DKA can be rapid — often within 24 hours. Patients can present with dehydration, polyuria, polydipsia, clinical features of an underlying infection, nausea, vomiting, abdominal pain and drowsiness. Hyperventilation (Kussmaul’s breathing) may be seen as a normal physiological response to the metabolic acidosis from ketone production, in an attempt to expel carbon dioxide and reduce the amount converted to carbonic acid.

The most important predictors of mortality in DKA appear to be an arterial pH <7.0 (indicating severe acidosis) and coexistence of severe illness.

Management

Although critical care admission is not necessary in all cases, it should be considered in pregnant women, as well as patients with hypoxia, altered consciousness, hypotension, tachycardia or severe acidosis (as indicated by blood ketones >6mmol/L, venous bicarbonate <5mmol/L or pH <7.1).

Panel 2: Recommendations for managing DKA

**Intravenous fluid infusion**

- Begin with 1L of 0.9 per cent sodium chloride over an hour. (If systolic blood pressure is <90mmHg give 500ml 0.9 per cent NaCl over 15 min.)
- Continue with 0.9 per cent NaCl, 2L over four hours, 2L over the following eight hours and then 1L over six hours. (Use a gentler regimen if the patient is old or has heart or renal failure). Further fluid therapy should be guided by fluid status.
- Once capillary blood glucose falls below 14mmol/L, start 10 per cent glucose at 125ml/h alongside 0.9 per cent NaCl.

**Insulin regimen**

- Dilute 50 units of soluble insulin in 50ml of 0.9 per cent NaCl solution in a syringe.
- Start a fixed rate insulin infusion at 0.1unit/kg/h. Continue any long-acting insulin the patient is on.
- Measure blood ketones (or venous bicarbonate) and CBG hourly. If CBG is out of the glucose meter’s range, measure plasma glucose — CBG, done at the bedside with test strips, is less accurate than plasma glucose, which requires laboratory analysis.
- Ketones should fall by 0.5mmol/L and blood glucose by 3mmol/h. Venous bicarbonate should rise by 3mmol/L. If the rate of change is insufficient the insulin infusion rate should be increased by 1 unit per hour each hour until sufficient.
- Insulin infusion should continue until blood ketones are <0.3mmol/L and venous pH is >7.3 (venous pH should be measured after one hour and then every two hours).
- Once acidosis and ketonuria is resolved and the patient is eating and drinking restart his or her short-acting insulin. (If the patient is not eating and drinking continue intravenous fluids and start a variable rate insulin infusion as per local guidelines.)

**Potassium replacement (guide)**

<table>
<thead>
<tr>
<th>Serum K+ (mmol/L)</th>
<th>KCl added per litre fluid</th>
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<tbody>
<tr>
<td>&gt;5.5</td>
<td>No replacement, recheck in two hours</td>
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<tr>
<td>3.5–5.4</td>
<td>40mmol/L</td>
</tr>
<tr>
<td>&lt;3.5</td>
<td>Urgent review by senior medical staff</td>
</tr>
</tbody>
</table>
Patients with DKA require fluids, insulin and potassium. (In those with impaired consciousness, airway and breathing should be secured first.)

Addressing dehydration is the initial priority and 0.9 per cent sodium chloride is the currently recommended fluid. Once plasma glucose falls below 14mmol/L, 10 per cent dextrose should be initiated alongside the NaCl. The 10 per cent dextrose allows the continuation of intravenous insulin which will correct the ketonaemia without hypoglycaemia.

Fluid replacement is initially rapid and then tailored to response. Care must be taken in the elderly and in patients with a history of congestive cardiac failure or renal impairment because they are at risk of fluid overload.

The JBDS recently recommended a fixed rate insulin infusion of 0.1 unit/kg/h adjusted to the rate of change in blood ketone concentration. Many hospitals use a variable rate insulin infusion adjusted to CBG but this may change in light of these new guidelines. Variable insulin infusions start low (usually 6 units per hour) and are adjusted to CBG. The low initial rate may lead to undertreatment in obese patients and those with insulin resistant states (eg, pregnancy or sepsis). Patients on long-acting insulin analogues (eg, glargine and detemir) should continue these at the same dose and time. Blood ketones is now the preferred method of monitoring response to treatment but because the availability of near patient blood ketone monitoring (ketone meters) is not widespread hospitals can use venous bicarbonate and pH to monitor response.

Electrolyte abnormalities are common in DKA, but potassium replacement, titrated to serum potassium levels, is the most important. Serum potassium levels can drop rapidly with insulin infusion and improvement in acidosis. Electrolytes and plasma glucose should be checked on admission and repeated every two hours. Blood bicarbonate is now the preferred method of monitoring response to treatment but because the availability of near patient blood ketone monitoring (ketone meters) is not widespread hospitals can use venous bicarbonate and pH to monitor response.

Panels 3: Sick day rules

The advice given to patients with type 1 diabetes on preventing loss of control of their diabetes during illness varies between hospitals. At University Hospital Aintree, the rules are:

- Never stop insulin, even if not eating (any stress will increase the body’s insulin requirements).
- If you are vomiting and unable to keep food down seek medical attention immediately.
- Check CBG and urine ketones every four hours. If your urine is positive for ketones contact the diabetes team or your GP.
- If your blood glucose levels are >13mmol/L, increase your insulin dose by 10–20 per cent but if you are unsure contact the diabetes team or your GP for advice.
- Drink plenty of sugar free drinks (especially water) because having high blood glucose can cause dehydration (osmotic diuresis). Aim for three to four litres per day.
- If you are unable to eat as normal, replace meals with carbohydrate-containing drinks (eg, milk). Small volumes of sugary drinks can be used if all else is not tolerated.
- If you think you have an infection contact your GP immediately.

Cerebral oedema Cerebral oedema is a dangerous complication of DKA. It is thought to be a consequence of treatment and requires specialist management. Although uncommon in adults, it occurs in 0.3–1 per cent of DKA episodes in children, with a 20–40 per cent fatality rate. Cerebral oedema can be difficult to differentiate from other causes of altered mental state. Contributory factors are suspected to be cerebral ischaemia, overhydration, rapid osmolar shifts (eg, over-rapid correction of hyperglycaemia) and bicarbonate infusions. Clinical features include headaches, bradycardia, hypertension, agitation, seizures and focal neurological deficits. Patients need urgent computerised tomography imaging of the head, and should be managed in a critical care environment with close neurological observation. The rate of fluid administration should be reduced and intravenous mannitol and other strategies to reduce intracranial pressure should be considered along with intubation and ventilation where necessary.

Further management Once acidosis is resolved intravenous insulin should be continued until the patient is eating and drinking adequately. Patients previously on short-acting insulin can restart it. It is important that insulin infusion is only stopped 30 minutes after short-acting or biphasic insulin is given. Patients in whom acidosis is resolved but who are unable to eat and drink can be converted to a variable rate insulin infusion until able to resume their full subcutaneous insulin regimen. Urine ketones can persist for
a few days and should not delay transfer to subcutaneous insulin in the context of an overall clinical recovery.

Those not previously on insulin can be started on a basal bolus regimen (short-acting mealtime insulin and longer-acting basal insulin) or a twice daily pre-mixed regimen, estimating the likely dose from intravenous insulin requirements since the resolution of acidosis. Patients using an insulin pump pre-admission may go back to their usual treatment once pump failure has been excluded as a precipitant of the DKA. Insulin doses in many cases will need readjusting in the first 48 to 72 hours.

The underlying precipitants for DKA should be identified and treated. The hospital diabetes team should be involved to ensure that patients get the relevant education to address triggers of DKA and minimise further events. Reinforcement of “sick day rules” (see Panel 3, p39) is particularly important because patients often mistakenly omit or reduce insulin doses when they are unwell.

**HHS**

Also known as hyperosmolar non-ketotic hyperglycaemia (HONK), hyperosmolar hyperglycaemic state (HHS) typically occurs in patients with type 2 diabetes and aged over 60 years but up to 40 per cent of cases are people previously unknown to have diabetes. Mortality is high — up to 15 per cent of presenting cases. HHS is generally of more gradual onset than DKA and can develop over many days, with signs of hypoglycaemia.

The triggers are similar to DKA (ie, sepsis, myocardial infarction or poor compliance with diabetes treatment). HHS involves:

- **Hyperglycaemia** (often >30 mmol/L)
- **pH >7.3**
- **Calculated serum osmolality >350mOsm/kg** (normal range is usually 280–300mOsm/kg)

Ketonuria is absent or minimal, and serum bicarbonate is ≥15mmol/L.

Measurement of laboratory serum osmolality is useful. A difference of greater than 20mOsm/kg between measured and calculated serum osmolality suggests the presence of an un-ionised compound such as alcohol, ethanol or glycol.

Patients can present as unwell, with dehydration and other underlying issues (eg, sepsis). Because the onset is gradual and patients are often elderly with comorbidities, treatment is less aggressive than in DKA. The basis remains fluid resuscitation and insulin infusions, but both are given at half the rate of DKA regimens. Patients should have hourly CBG monitoring, regular electrolyte checks, urinary catheterisation and close fluid balance charting. Again 0.9 per cent NaCl is the fluid of choice but it may be appropriate to use 0.45 per cent (“half-normal”) NaCl in some cases where serum sodium is above 155mmol/L. Serum electrolytes, full blood counts, a septic screen, chest radiographs and an ECG should be considered in all cases. Plasma glucose levels can fall rapidly with rehydration, reducing insulin requirements.

Thromboembolic disease is a significant risk in HHS and anticoagulation measures are recommended in all cases unless contraindicated. As in DKA, education and measures to address precipitant factors must be a part of the overall management. Because many cases of HHS occur in the elderly, community support arrangements and involvement of family members may be needed as part of an overall programme.

**References**

9. Ram Prakash Narayanan, MBBS, MRCP, is specialty registrar in diabetes and endocrinology, and Mark Peasley, PgDip, MRPharmS, is advanced clinical pharmacist, education and training diabetes and endocrinology, both at University Hospital Aintree, Liverpool.

**Act: 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 you patients starting sulphonylureas will recognise warning signs of hypoglycaemia.
2. Review your first aid training to ensure your staff know how to deal with hypoglycaemia.
3. Find out about your local management guidelines for hypoglycaemia.

**Evaluate**

For your work to be presented as CPD, you need to evaluate your reading and any other activities. 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?

**Record**

Consider making this activity one of your nine CPD entries this year.